

Evaluation of Quick score of Estrogen Progesterone receptor status of breast carcinoma and its correlation with other clinico-pathological prognostic parameters

Rai T, Rai GS, Sawke GK, Sawke N

ABSTRACT

Background: Breast cancer is one of the most frequently encountered cancers in women and is a leading cause of cancer death worldwide. Estrogen and progesterone appear to be major hormones involved in regulation of breast tumor growth. Hormone receptors role as a prognostic and therapeutic tool in breast cancer is widely accepted.

Aim: To evaluate the frequency of estrogen and progesterone receptor expression in the breast carcinoma cases and assessment of the value of quick score with reference to histological grade of tumour and its correlation with other prognostic clinico-pathological parameters.

Methods: Eighty four patients who underwent mastectomy for infiltrating duct carcinoma along with axillary lymph node dissection were studied. Demographical information like tumor size, histopathological diagnosis with Bloom Richardson grade of the tumor and lymph node metastases at the time of diagnosis was noted from the record. Immunohistochemistry was performed using commercially available antibodies from LABVISION for estrogen and progesterone receptor.

Results: Statistically significant inverse correlation between Bloom – Richardson grade and expression of estrogen and progesterone receptor was established between the grade of the tumor and the expression of the receptors. Tumor size had a significant inverse correlation with expression of estrogen and progesterone receptors ($P < 0.0001$). No statistically significant correlation could be established between the age of the patient and expression of estrogen and progesterone receptors.

Conclusion: Present study showed that with the increasing size of the tumor, lymph node metastasis and increasing Nottingham modification of Bloom-Richardson Grade of the tumor, expression of estrogen and progesterone receptors decreases.

Key words: breast cancer, estrogen receptor, progesterone receptor

INTRODUCTION

Breast cancer is the second most common type of non-skin cancer (after lung cancer) and fifth most common cause of cancer death (World Cancer report).¹ It comprises 10.4% of all cancer incidences among women. Estrogen and progesterone are major hormones involved in regulation of breast tumor growth. The role of hormone receptors as a prognostic and therapeutic tool in breast cancer is widely accepted.

The determination of estrogen receptor(ER) and progesterone receptor (PR) activity in breast cancer is a standard medical practice nowadays as it provide an important predictor of response to hormonal therapy and overall prognosis of the patient.²

The tumor that are estrogen receptor (ER)-positive and/or progesterone receptor (PR)positive have lower risks of mortality after their diagnosis compared to women with ER and/or PR-negative disease. Various clinical trials have also shown that the survival advantage for women with hormone receptor-positive tumor is increased by treatment with adjuvant hormonal and/or chemotherapeutic regimens.³

The prognosis or prediction of breast cancer survival is currently based on classical prognostic factors like histological type, grade, tumor size, lymph node metastasis and immunohistochemically detected estrogen (ER), progesterone (PR) and Her-2/neu receptors. Quick Score based on the intensity of staining and percentage of nuclei taking the

immunohistochemical stains also play an important role.

This study was taken up to determine the correlation of expression of these receptors with various clinico-pathological parameters at the time of presentation of disease and finally with the quick score system.

MATERIALS AND METHODS

Demographical information of eighty four cases that underwent mastectomy for infiltrating duct carcinoma along with axillary lymph node dissection was noted from the record and studied. The information considered were: tumor size, histopathological diagnosis with Bloom Richardson grade of the tumor and lymph node metastases at the time of diagnosis. Paraffin blocks of the above selected cases were taken for haematoxylin and eosin staining and reviewed.⁴ After confirming and noting the diagnosis and microscopy details, sections were taken for immunohistochemistry.

Immunohistochemistry was performed using commercially available antibodies from LABVISION for estrogen and progesterone receptor. The site of antibody binding is identified either by tagging the antibody, directly or indirectly with a visible label. The visual marker used was monoclonal antibodies and an indirect, polymeric detection method for antigen localization.^{5,6}

Strict precautions were taken to avoid drying of tissue section at any point of time during the entire procedure of immunohistostaining. All incubations were done inside the humid chamber. During staining of each batch, appropriate positive and negative controls were used. Negative controls were obtained by

omitting the primary antibody; positive controls were included in each batch. Finally a QUICK SCORING was done and the expression of estrogen and progesterone receptors were correlated with the age of the patient at the time of diagnosis of the disease, tumor size, lymph node status and finally with the Bloom – Richardson grade of the tumor. Carcinomas of male breast were excluded from the study.

RESULTS

Cases predominate in the age group of 30-50 years. Sixty eight cases had tumor size more than 2 cm. 44 cases presented with tumor metastasis. Most of the cases were in the Grade II of Bloom-Richardson's grading. 40 cases were ER+, 38 cases PR+, 44 cases ER- and 46 PR- respectively. Table.1.

Table 1. Distribution of cases according to various parameters

S.No.	Parameters		No. of cases (n=84)
1.	Age in years	30-50	49
		51-70	34
		>70	01
2.	Tumor size	<2cm	16
		>2cm	68
3.	Lymph node status	With metastasis	44
		Without metastasis	40
4.	Grade of the tumor	I	10
		II	50
		III	24
5.	Estrogen status	ER+	40
		ER-	44
6.	Progesterone status	PR+	38
		PR-	46

Tumor size, lymph node metastasis and Grade of the tumor had a significant correlation with ER,PR ($p < 0.005$).

It was observed that in maximum number of cases, as the tumor size increases expression of ER and PR decreases. In 60% cases with tumor size >2cm were ER- and 69% cases with tumor size >2cm were PR-. In most of the cases (62%)

with lymph node metastasis expression of ER decreases, similar findings were noted with the expression of PR i.e in 69%cases with lymph node metastasis expression of PR decreases. 63% cases had an inverse correlation of the grade of the tumor and expression of ER and PR. Table.2

Table 2. Correlation of various parameters with ER and PR expression.

Sl.no.	Parameter	No.of cases n=84	ER +ve	PR+ve	ER-ve	PR-ve
1.	Age <50yrs	49	22(45%)	21(43%)	27(55%)	28 (57%)
2.	Age >50yrs	35	18 (51%)	17(49%)	17(49%)	18(51%)
3.	Tumor size <2cm	16	13(81%)	14 (87%)	3 (19%)	2 (13%)
4.	Tumor size >2cm	68	27 (40%)	24 (35%)	41 (60%)	44 (69%)
5.	lymph node with metastasis	44	16 (40%)	12 (31%)	28 (60%)	32 (69%)
6.	lymph node without metastasis	40	24 (60%)	26 (68%)	16 (40%)	14 (32%)
7.	Grade I	10	09 (90%)	09 (90%)	01(10%)	01(10%)
8.	Grade II	50	28 (56%)	26(52%)	22 (44%)	24 (48%)
9.	Grade III	24	02 (08%)	02 (08%)	22(92%)	22 (92%)

No significant correlation could be established between the age group and expression of ER and PR. However it was observed that in 54% of cases expression of ER and PR increases as the age increases.

Nottingham Modification of Bloom – Richardson grade of the tumor was assessed microscopically and compared with the expression of the receptors. Out of 84 cases maximum number of cases (50) were of grade II, 24 cases were of grade III and 10 cases were of grade I. Quick score was done for estrogen and progesterone receptor and it was correlated with the Bloom – Richardson grade of the tumor. 90 % cases of Grade I were ER positive as well as PR positive and 91.67 % cases of Grade III were ER negative as well as PR negative. 63.09% cases had an inverse corelationship of Nottingham Modification of Bloom – Richardson grade and expression of estrogen receptor and progesterone receptor. Table. 3

Table 3. Correlation of Nottingham Modification of Bloom – Richardson grade and Quick Score for Progesterone receptor

Bloom – Richardson grade of the tumor	No. Of cases	Quick score 0	Quick Score 2-3	Quick score between 4-6	Quick score between 7-8
Grade I	10	0	0	1	9
Grade II	50	22	9	11	8
Grade III	24	22	0	1	1

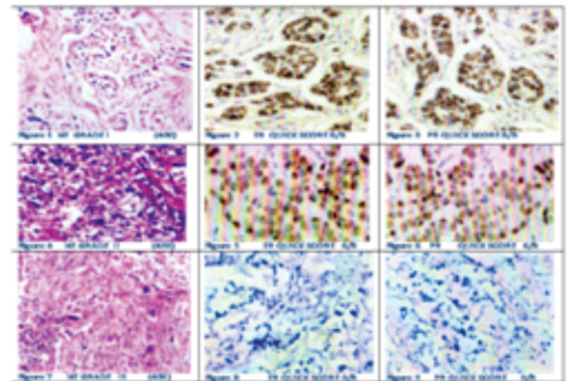


Fig. 1,2,3. showing infiltrating duct carcinoma Grade I, haematoxyline & eosin stain, ER Quick score and PR Quick score respectively.

Fig.4,5,6. showing infiltrating duct carcinoma Grade II, haematoxyline & eosin stain, ER Quick score and PR Quick score respectively.

Fig. 7,8,9 showing infiltrating duct carcinoma Grade III, haematoxyline & eosin stain, ER Quick score and PR Quick score respectively.

DISCUSSION

This study was designed to explore the utility of immunohistochemistry for the assessment of estrogen and progesterone receptors in the cancerous breast tissue and the correlation of these receptors with the age of the patient, tumor size, lymph node status and the Bloom – Richardson grade of the tumor at the time of diagnosis.

Mean age of the subjects was 49.9 years. It was found that the expression of estrogen and progesterone receptor increases as the age of the patient increases. This finding was comparable with other similar studies.^{7,8,9}

The tumor size among the subjects of this study varied from 0.5 cm to 13 cm in the greatest diameter; in considerable percentage, it was

between 2-5 cm. It was observed that as the tumor size increases expression of estrogen and progesterone receptor decreases respectively which was found in concordance with the findings of other similar studies.¹⁰⁻¹³ Donegan w et al., showed in his studies that large sized tumors with tumor size more than 2 cm were more likely to be receptors negative.¹⁰ Cianfrocca et al., in his studies found that smaller sized tumors express receptors more frequently as compared to large sized tumors (more than 2 cm).¹¹ Nidal et al., In his study on 91 confirmed breast carcinoma cases found that ER and PR positive cases were on average 1.6 smaller than carcinomas lacking ER expression (p=0.009).¹²

It was noted that in 61.9% cases with lymph node metastasis, expression of estrogen receptors decreases; similar findings were noted with the expression of progesterone receptors i.e. in 69.04% cases with the lymph node metastasis expression of the progesterone receptors decreases. Killinc et al., in their study found that higher grade tumors with lymph node metastases are less likely to express estrogen and progesterone receptors.¹⁴ Nidal et al., in his study found that the fraction of ER+ve cases among those with up to 3 lymph node status were 39 % slightly lower than 48 % seen among those with more than 3 lymph node metastases ,however it was neither

significant statistically nor any correlation between lymph node metastases and PR expression was detected.^{15,16}

In present study Nottingham Modification of Bloom – Richardson grade of the tumor was assessed microscopically and compared with the expression of the receptors. Quick score was done for estrogen and progesterone receptor and it was correlated with the Bloom – Richardson grade of the tumor. With the higher Nottingham Modification of Bloom-Richardson grading the tumor expression of estrogen and progesterone receptor decreases. Many other studies had similar conclusion.¹⁷⁻²¹

CONCLUSION

In view of the significant correlation of the estrogen and progesterone receptor expression with various other parameters of the breast carcinoma cases immunohistochemistry would give the best management guidelines for better survival and consequently optimal quality of life to the patient.

AUTHOR NOTE

Tina Rai, Assistant Professor of Pathology
Garjesh Singh Rai, Associate Professor of Radiology
G K Sawke, Professor of Pathology
(Corresponding Author);
Email: sawke_gopalkrishna@yahoo.com,
Contact: +919981690733
Nilima Sawke, Professor of Pathology
People's College of Medical Sciences & Research
Centre, Bhopal, India

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