

Is estrogen receptor study useful in prognostication of breast cancer patients in India?

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Abstract

Background To assess the validity of estrogen receptor (ER) status of breast tumor as a prognostic marker in clinical practice in the Indian perspective.

Materials and methods Sixty-three patients of breast cancer attending breast clinic IPGMER, Kolkata were included in this study. All patients underwent surgery. Metastatic status and tumor were done. Immunohistochemistry was also used for further analysis.

Results Statistically we have proved that advancing course of the disease, there is a tendency of the tumors to become hormone insensitive.

Conclusions ER has a strong prognostic importance in early breast cancer and can play a major role in optimizing treatment modalities in node negative early breast cancer.

Keywords Breast cancer · Estrogen receptor status · Immunohistochemistry · Predictive and prognostic role · Nottingham prognostic index · Prognostic outcome in Indian patients

Introduction

Breast cancer is characterized by varied biological behavior. It becomes important thus, to know about the nature of the disease, so as to ensure optimum adjuvant therapy and predict the course of outcome. Estrogen receptor (ER) has an established role as a predictive marker in the treatment of breast cancer. Though ER status has been implicated by many as a valid marker for assessing the prognosis of the disease, its role is not universally accepted in Indian perspective.

Aims and objectives

To assess the validity of ER status of breast tumor as a prognostic marker in clinical practice in our perspective.

Methodology

This study included 63 patients of breast cancer attending breast clinic of the IPGMER, Kolkata. All patients underwent surgery. Subsequently specimens were studied macroscopically to note the size of the tumor. Axillae were analyzed to note the metastatic status (number of nodes showing metastasis out of total number of nodes isolated) and the tumor grade according to Scarf Bloom Richardson (SBR) method. Further analyses were done by immunohistochemistry from a single laboratory.

Because of high dropouts during follow up, it was difficult to note the overall survival and disease free survival. Hence, Nottingham Prognostic index (NPI), a multivariate index, involving tumor size, node and grade was calculated.

$NPI = \text{tumor size} \times 0.2 + \text{lymph node stage}$ (1 = no node, 2 = 1 to 3 nodes positive, 3 = 4 or more nodes positive) + grade (1, 2 or 3).

NPI was chosen as a parameter for comparing the survival chance in ER positive (ER+) and ER negative (ER-) tumors.

Results

Out of 53 patients, 5 had NPI score <3 (group 1), 4 had scores between 3.01 and 3.4 (group 2), 17 had scores between 3.4 and 4.4 (group 3), 19 between 4.41 and 5.3 (group 4) and the rest 18 had scores more than 5.4 (group 5) (Table 1). Out of these five sets of patients the ER positive patients were 5 in group 1, 3 in group 2, 10 in group 3, 12 in group 4 and 10 in group 5. Total number of patients showing ER positivity were 40 out of 63 (63.49%) irrespective of menstrual status. However the positivity rates in different groups were as follows – 100% in group 1, 75% in group 2, 59% in group 3, 61% in group 4 and 56% in group 5.

In order to assess the worst prognostic group, ER negativity was considered. The data were analyzed for statistically significant correlation using Student's *t* test. It was found that at low NPI scores, there was a strong association using with ER positivity. As the NPI scores increased, the proportion of ER negative patients in-creased. However it was noted that a plateau is achieved from a particular value onwards. The *P* value for the entire data was 0.03, which is statistically significant. The NPI value of 4.4 was taken as cutoff to divide the patients into two groups because those with low NPI values (<4.4) have excellent, good or moderate prognosis and those with high NPI values (>4.4) have poor prognosis. The *P* value for the group of patients with low NPI values was 0.001 and that for the group of patients with high NPI values was 0.75. This signifies that there is a strong association between

ER positivity and low NPI scores but the association between ER positivity and high NPI scores is very weak.

This shows that with advancing course of the disease, there is a tendency of the tumors to become hormone insensitive (hormone sensitivity escape phenomenon).

Discussion

Breast cancer is in many situations very unpredictable. Though various biomarkers have been studied, none of them have proved to be a consistent prognostic marker. Axillary nodal status as yet remains the gold standard prognostic marker. The dilemma regarding optimum adjuvant therapy lies in patients with N0 axillary status. Age, grade and tumor size are the three important factors which can prognosticate early breast cancer. ER has proved to be an important predictive factor in all stages of the disease. Its role as a prognostic factor has met with some controversies. Western data³ has shown the importance of ER status for risk assessment in N0 disease. But there is scanty Indian literature, which uses multivariate index for correlating ER status and prognosis. Mitra et al.⁴ has tried to correlate ER and PR status with other prognostic factors. But the technique used was immunoassay, whose specificity is less than immunohistochemistry. Other Indian studies have looked into the epidemiological pattern of ER, PR status but little literature is available regarding its prognostic role. Chopra⁵ compared ER status with nodal status and found positive correlation. This study is unique in its character as it included tumor size, grade and nodal status and compared it with ER status. The explanation of the above fact is complex. It may be that ER positive tumors behave differently from ER negative tumors and is genetically a favorable disease. Alternatively it may be hypothesized that tumors have a hormone escape phenomenon at some point of its natural history. This can only be concluded if a study correlating ER status and overall survival is undertaken. But Indian patients have a relatively poor follow up compliance compared to its counterparts in the West. Thus it was difficult to set overall survival and disease-free survival as the end-points of this study. NPI has a firm statistical validity and thus was our natural choice. Being an amalgamation of three cardinal variables, NPI is better than a single variate analysis. But it represents more of a cross-sectional analysis than a prospective cohort. However this study could firmly establish the fact that ER has a strong prognostic importance in early breast cancer and can play a major role in optimizing treatment modalities in node negative early breast cancer.

Table 1 Categories of patients based on NPI

NPI	N (number)	ER+	ER-	% of ER-
<3	5	5	–	0
3.01–3.4	4	3	1	25
3.4–4.4	17	10	7	41
4.41–5.3	19	12	7	39
>5.4	18	10	8	44

Overall *P* value = 0.03; *P* value for NPI < 4.4 = 0.001; *P* value for NPI > 4.4 = 0.75.

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