



## Original Research Article

# Nottingham Prognostic Index: Useful tool to assess outcome inpatients of breast carcinoma

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## ABSTRACT

**Introduction:** Breast cancer has been ranked number one cancer among the Indian females surpassing the incidence of cervical cancer. Multiple clinico-pathological-molecular prognostic factors are available in decision making about potentially suitable treatment options for breast cancer. Among all, Nottingham Prognostic Index (NPI) is the most powerful integrated index. Present study aimed to evaluate the significance of NPI in prognosis of operable breast cancer patients.

**Materials and Methods:** This longitudinal (Descriptive) study was carried on 60 female patients of operable breast carcinoma at tertiary care centre in central India.

**Results:** Two patients from good prognostic group ( $NPI \leq 3.4$ ) (30%) had metastasis to bone & CNS. From moderate prognostic group ( $NPI 3.4 - 5.4$ ) (50%), one patient had recurrence at previous surgical scar site and 3 patients had metastasis to liver, lung and supraclavicular lymph node each. However the worst outcome was found in patients from poor prognostic group ( $NPI > 5.4$ ) (10%). Five patients from poor prognostic group had metastasis in liver, bone, CNS and lung with two patients had simultaneous metastasis in liver & bone. Four patients from poor prognostic group had death within two and half years of primary diagnosis. Out of 60 patients, 34 patients had a follow up of more than 1000 days, so were included in statistical analysis of survival based on Cox Proportional Hazard Model. Among 7 variables, NPI was found to be statistically most significant with p value 0.001

**Conclusion:** Estimation of NPI is the powerful and reproducible index for assessing prognosis in patients with operable breast cancer in advanced resources deprived institute. Main strength of NPI lies in the fact that it is based on relatively simple data which can be provided in routine histopathology report of carcinoma breast.

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## 1. Introduction

Breast cancer is the most frequent malignancy in woman accounting for approximately 15% of female cancer death and leading cause of death in women aged between 44-50 years.<sup>1</sup> It has been ranked number one cancer among the Indian females surpassing the incidence of cervical cancer.<sup>2</sup>

Multiple clinico-pathological- molecular prognostic and predictive factors ranging from patient's age to recent most gene expression profiling are available in decision making about potentially suitable treatment options for breast cancer.<sup>3</sup> These prognostic factors influence design,

conduct and analysis of clinical trials in breast cancer. They can be also used to distinguish patients likely to have recurrence after treatment of primary tumor, from those with low risk of recurrence and those likely to benefit from adjuvant therapy.<sup>4</sup> Among all, three most powerful prognostic factors as tumor size, lymph node status & histopathological grade were incorporated into Nottingham Prognostic Index (NPI) first described in 1982.<sup>5</sup> This NPI further divides patients into three prognostic groups as; good ( $<3.4$ ), moderate (3.4- 5.4) and poor ( $>5.4$ ).<sup>6</sup> Despite of more advanced prognostication factors, NPI is internationally validated system for classifying early & locally advanced breast cancer into three prognostic groups.<sup>7-9</sup> NPI plays important role in decision making for

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adjuvant & neoadjuvant chemotherapy as a part of precision medicine.<sup>10</sup> Main strength of NPI lies in the fact that it is based on relatively simple data which can be provided in routine histopathology report of carcinoma breast.

In current study, NPI was constructed for patients with primary operable breast cancer and was further used to predict the outcome in the sufferings.

## 2. Methods and Materials

Present descriptive longitudinal (time series) study was carried at teaching institute & tertiary care center in central India. Ethical clearance was taken from ethical & research committee of the institute. 60 female patients of breast carcinoma in operable stage of the disease were included in study regardless of their age. After primary diagnosis of breast carcinoma which was done mostly by cytology, patient underwent surgical management with adjuvant and neoadjuvant chemotherapy.

Data was collected with predesigned questionnaire which contained information regarding tumor size (TNM staging system), histopathological grading (by Nottingham modification of Scarff-Bloom-Richardson-method) with subtypes and axillary lymph node status. Nottingham prognostic index (NPI) was calculated using three parameters i.e. size of tumor (S), tumor grade (G), number of lymph and nodes involved (L) and by incorporating these values in internationally accepted formula:  $NPI = (S \times 0.2) + G + L$

Further according to NPI, patients were divided into three prognostic groups.

Out of 60 patients, 34 had follow up of more than 1000 days were included in statistical analysis. Prognostic factors found to be significant in univariate analysis were entered into the multivariate analysis of survival based on the Cox Proportional Hazard Model.

## 3. Results

Total 60 patients in operable stage of breast cancer were subjected to surgery with adjuvant /neoadjuvant chemotherapy. Patients were followed up at regular interval at surgery department for local recurrence and distant metastasis.

### 3.1.

#### 3.1.1. Age

Youngest patient was of 25 years while oldest was 65 years. 40% patients were in the age group of 41-50 years.

#### 3.1.2. Side/Site

Left breast (58%) was more commonly affected with upper outer quadrant (58%) most commonly affected quadrant.

#### 3.1.3. Tumor size

Minimal recordable tumor size was 1.5 cm to maximum size of 13 cm with tumor size  $\leq 5$ cm (52%) slightly exceeded than tumor  $> 5$ cm.

#### 3.1.4. Histopathological grade

5 0% of breast carcinoma had morphologically grade I tumor, 40% had grade II and 10% had grade III tumor. Ductal carcinoma (NOS)-92% was most common morphological type while one case each of lobular carcinoma, invasive cribriform carcinoma, medullary carcinoma and adenoid cystic carcinoma.

#### 3.1.5. Axillary lymph node score

57% patients had lymph node score I, 33% had lymph node score II ( $< 4$  lymph nodes positive) while 10% had lymph node score III ( $> 4$  lymph nodes positive)

These three parameters, namely tumor size, histological grade and lymph node score were incorporated into the formula to get Nottingham Prognostic Index in all 60 patients.

Out of 60 patients, 34 had follow up of more than 1000 days were included in statistical analysis. Prognostic factors found to be significant in univariate analysis were entered into the multivariate analysis of survival based on the Cox Proportional Hazard Model. Out of 7 variables included into Cox univariate analysis, 5 variables namely tumor size, Axillary lymph node score, grade of tumor, stage of disease and NPI had statistically significant p values ( $< 0.05$ ). NPI had least and the most significant 'p' value of 0.0001 in univariate analysis.

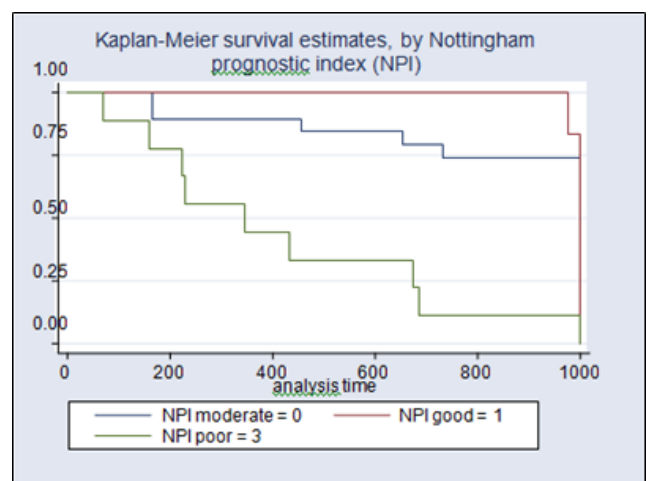


Fig. 1: Graph showing Kaplan – Meier survival estimates, by NPI

## 4. Discussion

Incidence of breast cancer cases are on rise in India is surpassing the incidence of cervical cancer.<sup>3</sup> In spite of

**Table 1:** Showing categorization and correlation of NPI with recurrence and metastasis.

NPI	No of pts. (%)	Recurrence	Liver Mets	Bone Mets	CNS Mets	Lung Mets	Other Mets	Death
≤ 3.4	20(30)	-	-	1	1	-	-	-
>3.4 - ≤ 5.4	30(50)	1	1	-	-	1	1	-
>5.4	10(20)	1	3*	2*	1	1	-	4

\* Patients with metastasis at two sites simultaneously.

**Table 2:** Summary of variables added to univariate analysis.

S. No.	Variable	Code	n (%)	P value (Log-rank test)
1	<b>Age</b>			0.4002
	≤0 yrs	1	11	
	> 40yrs	2	23	
2	<b>Menopausal Status</b>			0.2531
	Premenopausal	1	19	
	Postmenopausal	2	15	
3	<b>Tumor size</b>			<b>0.0029</b>
	≤ cm	1	17	
	> 5 cm	2	17	
4	<b>Axillary lymph node score</b>			<b>0.0131</b>
	Absent	1	16	
	Present	2	18	
5	<b>Grade of tumor</b>			<b>0.0018</b>
	I	1	13	
	II	2	17	
	III	3	4	
6	<b>Stage of disease</b>			<b>0.0006</b>
	II	2	17	
	III A	3	4	
	III B	4	13	
7	<b>NPI</b>			<b>0.0001</b>
	Good	1	6	(least p value)
	Moderate	2	19	
	Poor	3	9	

increasing trend breast cancer are diagnosed in advanced stage, attributed by the lack of awareness among the Indian women and absence of screening program.

#### 4.1.

##### 4.1.1. Age

Most common age group affected by breast cancer in our patient was 40-50 years correlating well with the data from other developing countries.<sup>4,11,12</sup> According to ‘Bombay Breast Group Study’ in 1997, 80% of Indian women are sufferer of breast cancer below the age of 65 years matching our findings with Indian study.<sup>13</sup>

##### 4.1.2. Side and site involved

Left breast (58%) was slightly more common side involved with upper outer quadrant more common site mirroring our findings mirroring with that of Pradhan et al.<sup>1</sup>

##### 4.1.3. Tumor size

Gross tumor size is directly proportional to chance of having positive lymph node metastasis and inversely proportional to the outcome in patients suffered by breast cancer as shown in various studies. The mean tumor size in our study was 5cm matching the findings of Hamza et al & Albergaria et al.<sup>4,14</sup>

##### 4.1.4. Microscopic grading

Microscopic grading is an important prognostic factor in the outcome of patients with breast cancer. However it was questioned previously for reproducibility and subjective variation. But widely adopted Nottingham modification of Scarff-Bloom-Richardson system of breast carcinoma offers clear criteria based on three component: tubular / glandular differentiation, nuclear pleomorphism and mitotic rate. In our study, 40% cases were of grade I, 50% of grade II and 10 % were of grade III correlating with Rakha et al & Ahmed et al.<sup>15,16</sup> The most common histological type of breast cancer

was infiltrating duct carcinoma (Not otherwise specified) findings similar to.<sup>4,11</sup>

#### 4.1.5. Axillary lymph node score

The positivity of Axillary lymph nodes for metastasis is one of the most important independent prognostic parameter in breast cancer with sharp difference in outcome between those with negative and positive nodes. In our study pN0 was 33%, pN1 was 57% and pN2 10% matching the findings of.<sup>4,11</sup>

#### 4.1.6. Nottingham prognostic index (NPI)

NPI is widely accepted and reliable prognostic index based on combination of three individually powerful and statistically significant prognostic variables namely, tumor size, lymph node score and microscopic grade by Nottingham grading system. The main strength of NPI is that it can be calculated from the routine histopathology report given by pathologist. In our study out of 60 cases, 20 cases (30%) were of good prognostic group, 30 cases (50%) from moderate prognostic group and 10 (20%) in poor prognostic group.

Out of 60 patients, 34 patients had a follow up of more than 1000 days so were included in statistical analysis. In our study 5 out of 7 variables namely tumor size, Axillary lymph node score, grade of tumor, stage of disease and NPI were found to be statistically significant with p value less than 0.05. NPI with p value 0.001 was found to be the most significant variable in univariate analysis mirroring the findings of.<sup>11,17,18</sup>

We found the positive correlation between NPI and outcome of patients having breast cancer. This outcome was assessed as recurrence at previously operated site, distant organ/lymph node metastasis and death. Two patients from good prognostic group ( $NPI \leq 3.4$ ) had metastasis to bone & CNS. Out of 30 patients from moderate prognostic group ( $NPI 3.4 - 5.4$ ), one patient had recurrence at previous surgical scar site and 3 patients had metastasis to liver, lung and supraclavicular lymph node each. However the worst outcome was found in patients from poor prognostic group ( $NPI > 5.4$ ). Five patients from poor prognostic group had metastasis in liver, bone, CNS and lung. Of these five patients, two patients had metastasis in both liver & bone. Four patients from poor prognostic group had death within two and half years of primary diagnosis of primary breast cancer. According to D'Fredita et al, Fong et al and Thangiam et al NPI is simple clinicopathological prognostic tool which not only gives accurate prediction of prognosis but also offer guidance for administration of adjuvant therapies.<sup>19–21</sup> Thus we found the validity of 'NPI as a prognostic tool in breast carcinoma' is very high.

## 5. Conclusion

Estimation of Nottingham Prognostic Index (NPI) is the only powerful and reproducible integrated index for

assessing prognosis in patients with operable breast cancer in advanced resources deprived institute. Main strength of NPI lies in the fact that it is based on relatively simple data which can be provided in routine histopathology report of carcinoma, hence recommend to incorporate it in routine histopathological report.

## 6. Source of funding

None.

## 7. Conflict of interest

None.

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