

# Various Prognostic Parameters in Carcinoma Breast Patients: A Prospective Study

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## Abstract

**Introduction:** Breast carcinoma is one of the foremost cancers in women in the world and by its frequent prevalence; the magnitude of the problem is a global one.

**Materials and Methods:** The present study has been conducted retrospectively and prospectively on all patients of histologically proved carcinoma of breast, who were admitted in the surgical wards of S V B P Hospital, Meerut, since January 1993 to October 2004. Retrospective study has been conducted from January 1993 to July 2003 and prospective study from June 2003 to October 2004.

**Results:** There are various prognostic factors involved in the management of breast cancer. Estrogen receptors and progesterone receptors factors being the most important prognostic factors. All of them help in early diagnosis and management of the patients.

**Conclusion:** Above study clearly indicate that prognostic factors help in the management of the case and in the days to come will help to modify the course of illness.

**Key words:** Breast, Carcinoma, Histologically, Retrospective

## INTRODUCTION

Breast carcinoma is one of the foremost cancers in women in the world and by its frequent prevalence; the magnitude of the problem is a global one. In the USA, one in every nine women developed some variant of breast carcinoma in her lifetime, and it accounts for 27% of their cancers.<sup>1-3</sup>

Carcinoma of the breast is not only common in Indian women but it also occurs in them a decade earlier than Western women (Mean age of occurrence is about 42 years in India as compared to 53 years in white women).

Lifetime risk of developing cancer is 12.2% or 1 in 8 women. A lifetime risk of death due to cancer of the breast is 3.6% or 1 in 282 women.

Incidence of breast carcinoma is increasing in most countries at a mean rate of 1-2% annually. And soon nearly one million of women will develop this disease every year throughout the world.<sup>4,7</sup>

Mortality rate for breast carcinoma in the Western world is of the order of 15-25 per 1 lakh women. This mortality rate is also increasing in Indian women, but at a much slower pace (Peckham, 1995). Breast cancer is responsible for 19% of all cancer-related death of women in the world.

Breast cancer is the second most common malignancy in Indian women, second only to carcinoma cervix (Park, 1995; Paymaster, 1964; Jussawala 1976; NCRP88-89). Breast cancer incidence in female by the site in India is 20%. The cumulative incidence up to the age of 64 years is 1-2%; thus one out of every 43-58 Indian women would develop breast cancer during her life (NCRP, 88-89).

In the last two decades, the treatment of breast cancer has undergone dramatic changes, and a much wider range of both local and systemic therapeutic options are now available. Early diagnosis, especially by the advent of mammographic breast screening, is detecting tumors which

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are likely to have a favorable outcome and it has become extremely important to assess prognosis for each patient before a therapeutic plan is agreed.<sup>7-15</sup>

Modified radical mastectomy has been considered the optimal treatment for locoregional breast cancer. Despite this, the reported incidence of locoregional failure after mastectomy varies from <5% to > 30%. Once a local recurrence is detected, treatment recommendations vary widely and frequently include different combinations of surgical resection, external radiation therapy, hormone therapy, and/or chemotherapy.

The factors concerned with the prognosis of breast carcinoma are complex. The prognosis of carcinoma of breast correlates with age at occurrence, menopausal status, tumor size, presence and number of involved axillary lymph nodes, family history, histological type of tumor, presence of tumor necrosis, lymphovascular embolization, extranodal extension, grade of tumor, treatment modality, skin involvement, etc.<sup>16-20</sup>

### Aims and Objectives

1. To analyze the efficacy of various prognostic factors in carcinoma breast.
2. To identify the most important prognostic factor in carcinoma breast.

## MATERIALS AND METHODS

The present study has been conducted retrospectively and prospectively on all patients of histologically proved carcinoma of the breast, who were admitted in the surgical wards of S V B P Hospital, Meerut, since January 1993 to October 2004.

Retrospective study has been conducted from January 1993 to July 2003 and prospective study from June 2003 to October 2004.

All the patients included in the prospective study have been thoroughly interrogated and clinically examined.

The patients included in the retrospective study have been studied from old records of central record section of S.V.B.P hospital; Meerut and these cases have been followed up by contacts and letters.

### Inclusion Criteria

All female patients with histologically proven breast carcinoma.

### Exclusion Criteria

Patients with significant comorbidities and Stage IV breast carcinoma.

## RESULTS

This study comprises 525 patients of carcinoma breast who were admitted in surgical wards of S.V.B.P Hospital Meerut, since January 1993 to October 2004. Patients with Stage I, II, and III disease at the time of presentation were included in the study but patients with Stage IV disease at the time of presentation were excluded due to lack of records.

These patients were investigated as per protocol. Follow-up was done by records and contacts and it was recorded on a pro forma.

Out of 738 patients, 82 presented with Stage IV disease so, were excluded from the study. The present study includes remaining 656 patients followed up for 5 years and within 5 years; follow-up could be evaluated in 525 patients (Tables 1-11).

## DISCUSSION

Out of these 525 patients, youngest patient was of 22 years of age and oldest was 80 years of age. Our most of the patients were in the age group of 41-50 years (28.19%), i.e., around menopause. It was found that the prognosis was best in the age group 41 to 50 years (5-year disease free survival [DFS] 60.81%). Furthermore, the survival was found to be 43.47% in age group 21-30 years and 46.42%

**Table 1: DFS according to age**

Age	No. of patients	N (%)				
		1 year DFS	2 year DFS	3 year DFS	4 year DFS	5 year DFS
21-30	23	19 (82.60)	15 (65.21)	14 (60.86)	13 (56.62)	10 (43.47)
31-40	127	110 (86.61)	88 (69.29)	80 (62.99)	74 (58.26)	64 (50.39)
41-50	148	133 (89.86)	114 (77.02)	108 (72.97)	100 (67.56)	90 (60.81)
51-60	107	91 (85.04)	74 (69.15)	69 (64.48)	63 (58.87)	54 (50.46)
61-70	92	79 (85.86)	62 (67.39)	57 (61.95)	53 (57.60)	44 (47.82)
71-80	28	23 (82.14)	18 (64.28)	18 (64.28)	16 (57.14)	13 (46.42)
Total	525	455 (86.66)	371 (70.66)	346 (65.90)	319 (60.76)	275 (52.38)

DFS: Disease free survival

**Table 2: Disease free survival according to clinical stage**

Clinical stage	No. of patients	N (%)				
		1 year DFS	2 year DFS	3 year DFS	4 year DFS	5 year DFS
I	109	98 (89.90)	88 (80.73)	83 (76.14)	79 (72.47)	73 (66.97)
II	173	155 (89.57)	131 (75.72)	121 (69.94)	111 (64.16)	100 (57.80)
IIIA	135	115 (85.18)	91 (67.40)	80 (59.25)	72 (53.33)	64 (47.40)
IIIB	108	90 (83.33)	65 (60.18)	55 (50.92)	49 (45.37)	38 (35.18)
Total	525	458 (87.23)	375 (71.42)	339 (64.15)	311 (59.23)	275 (52.38)

DFS: Disease free survival

**Table 3: DFS according to family history**

Family history	No. of patients	N (%)				
		1 year DFS	2 year DFS	3 year DFS	4 year DFS	5 year DFS
Negative	483	436 (90.26)	379 (78.46)	348 (72.04)	333 (68.94)	304 (62.93)
Positive	42	37 (88.09)	33 (78.57)	28 (66.66)	24 (57.14)	20 (47.61)
total	525	473 (90.09)	412 (78.47)	376 (71.61)	357 (68.00)	324 (61.71)

DFS: Disease free survival

**Table 4: Disease free survival according to menopausal status**

Age	No. of patients	N (%)				
		1 year DFS	2 year DFS	3 year DFS	4 year DFS	5 year DFS
Premenopausal	232	193 (83.18)	155 (66.81)	151 (65.08)	133 (57.32)	113 (48.70)
Postmenopausal	279	248 (88.88)	212 (75.98)	198 (70.96)	188 (67.38)	170 (60.93)
Total	511	441 (86.30)	367 (71.18)	349 (68.29)	321 (62.81)	283 (55.38)

DFS: Disease free survival

**Table 5: DFS according to tumor size**

Tumor size	No. of patients	N (%)				
		1 year DFS	2 year DFS	3 year DFS	4 year DFS	5 year DFS
T1	95	88 (92.63)	80 (84.21)	76 (80.00)	74 (77.89)	69 (72.63)
T2	164	150 (91.46)	134 (81.70)	130 (79.26)	123 (75.00)	114 (69.51)
T3	72	60 (83.33)	47 (65.27)	43 (59.72)	39 (54.16)	32 (44.44)
T4	194	159 (81.95)	123 (63.40)	107 (55.15)	97 (50.00)	78 (40.20)
Total	525	457 (87.04)	384 (73.14)	356 (67.80)	333 (63.42)	293 (55.80)

DFS: Disease free survival

**Table 6: DFS according to axillary lymph node status**

Node status	No. of patients	N (%)				
		1 year DFS	2 year DFS	3 year DFS	4 year DFS	5 year DFS
Negative	301	281 (93.35)	259 (86.04)	245 (81.39)	235 (78.07)	222 (73.75)
1-3 nodes	108	91 (84.25)	74 (68.51)	72 (66.66)	64 (59.25)	55 (50.92)
4-6 nodes	44	35 (79.54)	26 (59.09)	24 (54.54)	20 (45.45)	14 (31.81)
6-10 nodes	38	30 (78.94)	21 (55.26)	18 (47.36)	14 (36.84)	9 (23.68)
>10 nodes	34	24 (70.58)	16 (47.05)	14 (41.17)	9 (26.47)	3 (8.82)
Total	525	461 (87.80)	396 (75.42)	373 (71.04)	342 (65.14)	303 (57.71)

DFS: Disease free survival

in patients of 71-80 years of age. Similar observation was made by Host and Lund in (1986), in this study, the maximum number of patients were in Stage III and they showed least 5-year DFS (47.40% for Stage III A and 35.18% for Stage III B) as compared with patients in Stage I and II disease having 5-year DFS of 66.97% and 57.80%,

respectively. Fisher *et al.* in (1984) and William *et al.* in (1992) reported a similar observation.<sup>21-23</sup>

In this study, it was found that patients with positive family history had a 5-year DFS of 47.16% as compared to patients with negative family history (5 year DFS

**Table 7: DFS according to ER/PR status**

ER/PR status	No. of patients	N (%)				
		1 year DFS	2 year DFS	3 year DFS	4 year DFS	5 year DFS
ER/PR+ve	29	27 (93.10)	25 (86.20)	23 (79.31)	21 (72.41)	17 (58.62)
ER/PR-ve	101	86 (85.14)	67 (66.33)	57 (56.43)	49 (48.51)	40 (39.60)
ER/PR unknown	395	335 (84.81)	271 (68.60)	244 (61.77)	219 (55.44)	198 (50.12)
Total	525	448 (85.33)	363 (69.14)	324 (61.71)	289 (55.04)	255 (48.57)

DFS: Disease free survival

**Table 8: DFS according to histological grade**

Histological grade	No. of patients	N (%)				
		1 year DFS	2 year DFS	3 year DFS	4 year DFS	5 year DFS
I	93	83 (89.24)	73 (78.49)	69 (74.19)	64 (68.81)	59 (63.44)
II	249	219 (87.95)	182 (74.29)	166 (66.66)	156 (62.65)	136 (54.61)
III	108	88 (81.48)	63 (58.33)	56 (51.85)	46 (42.59)	36 (33.33)
Total	450	390 (86.66)	318 (70.66)	291 (64.66)	266 (59.11)	231 (51.33)

DFS: Disease free survival

**Table 9: DFS according to lymphovascular embolization**

Lymphovascular embolization	No. of patients	N (%)				
		1 year DFS	2 year DFS	3 year DFS	4 year DFS	5 year DFS
+nt	115	93 (80.86)	67 (58.26)	52 (45.21)	42 (36.52)	33 (28.69)
-nt	239	213 (89.12)	180 (75.31)	166 (69.45)	156 (65.27)	141 (58.99)
Total	354	306 (86.44)	247 (69.77)	218 (61.58)	198 (55.93)	174 (49.15)

DFS: Disease free survival

**Table 10: Disease free survival according to tumor necrosis**

Tumor necrosis	No. of patients	N (%)				
		1 year DFS	2 year DFS	3 year DFS	4 year DFS	5 year DFS
+nt	117	96 (82.05)	72 (61.53)	58 (49.57)	48 (41.02)	36 (30.76)
-nt	301	269 (89.36)	228 (75.74)	210 (69.76)	200 (66.44)	180 (59.80)
Total	418	365 (87.32)	300 (71.77)	268 (64.11)	248 (59.33)	216 (51.67)

DFS: Disease free survival

**Table 11: Disease free survival according to perinodal extension**

Perinodal extension	No. of patients	N (%)				
		1 year DFS	2 year DFS	3 year DFS	4 year DFS	5 year DFS
+nt	117	95 (81.19)	70 (59.82)	53 (45.29)	43 (36.75)	33 (28.20)
-nt	230	210 (91.30)	177 (76.95)	163 (70.86)	158 (68.69)	140 (60.86)
Total	347	305 (87.89)	247 (71.18)	216 (62.24)	201 (57.92)	173 (49.85)

DFS: Disease free survival

62.93). In our study, 232 patients were premenopausal and 279 patients were postmenopausal and the analysis revealed that prognosis was better in postmenopausal patients (5-year DFS was found to be 48.70% in premenopausal patients and 60.93% in postmenopausal patients).

Tumor size is an important prognostic parameter. In our study it was found that patients with T1 disease had 5-year DFS 72.63% and patients with T4 disease, 5-year DFS of 40.20%, this indicates better prognosis in patients with small

tumor size, this has already been emphasized by Carter *et al.* (1989), Valagussa *et al.* (1978), and William *et al.* (1992).

Hormone receptors status played an important role in the prognosis of carcinoma breast. It is an important determinant of response to endocrine therapy. The present study of 129 patients who had records about their hormone receptor status, clearly showed that patients with ER/PR positive tumors have better survival than patients without them.

In the present study, it was found that patients with positive and negative ER/PR status had a 5-year DFS rate of 58.62% and 39.60%, respectively. While patients with ER/PR status unknown had a 5-year DFS of only 39.60%. Similar observations have been made by Crowe *et al.* (1986), Anderson *et al.* (1990)<sup>1</sup> Battifora *et al.* (1993) Aaltoma *et al.* (1993), and Allred *et al.* (1990). While Fisher *et al.* (1990) found that the difference in 5-year DFS between 1426 patients with ER and 372 without it was negligible. Similarly, Donegan (1992) stated that estrogen and progesterone receptors provide prognostic information that is independent of axillary stage, but the influence is weak.

Axillary lymph node status is an important predictor of prognosis in carcinoma of breast patients. The number of involved nodes is directly related to the period of disease free interval. In the present series the 5-year DFS rate in lymph node negative patients was 73.75% and in those with 1-3 positive nodes was 50.92% while in the patients with more than 10 involved nodes, the 5-year DFS was found to be only 08.82%. This has already been proved by Voogd (2001), Wilner (1993), Williams (1992), and Crowe (1991).

Histological grade is an important determinant of prognosis. In our study of 450 patients, the 5-year DFS in Grades I, II and III tumors was found to be 63.44%, 54.61%, and 33.33%, respectively. The negative impact of poor histological grade on survival was also reported by Le Doussal *et al.* (1989).

Lymphovascular embolization is an important prognostic parameter. In the present of series at 354 patients, it was found that patients, in whom lymphovascular embolization was present, showed a 5-year DFS of 28.69% and in those patients not having lymphovascular embolization, 58.80. The poor prognosis in tumors with lymphovascular embolization has been shown by Davis *et al.* (1986), MacMillan *et al.* (1996). Pinder *et al.* (1994), and Clemente *et al.* (1992).

Tumor necrosis carries a worse prognosis. In our study of 418 patients, it was found that patients, in whom tumor necrosis was present, showed a 5-year DFS of 30.76% and patients without tumor necrosis showed a 5-year DFS of 59.80%. Similar observations have been made by Gilchrist *et al.* (1988).

Perinodal extension is an important prognostic parameter. In our study of 347 patients, it was found that patients having perinodal extension were found to have 5-year disease free survival of 20.20% as compared to patients without it with 5-year DFS of 60.86%. This has also been shown by Mambo *et al.* (1977). Dongan *et al.* (1993)

and Fisher *et al.* (1976) while Hartevit *et al.* (1984) found that extra nodal extension had no intrinsic prognostic significance and concluded that the presence of tumor cells in efferent vessels was the only indicator of poorer prognosis in patients with involved nodes.

Radiotherapy as a treatment modality improves the chances of survival. In our study 187 patients, treated by surgery and chemotherapy, showed 5-year DFS rate of 69.51%. Survival was improved to 72.85% when in 70 patients of the other group, radiotherapy was added surgery alone without any adjuvant therapy offered least chances of DFS (26.66%). The 5-year DFS improved to 69.51% with the introduction of chemotherapy and it further improved by adding radiotherapy (72.85%). Davis *et al.*, (1986) in their study also found better survival with the addition of adjuvant chemo or endocrine therapy in patients of breast cancer.

Neoadjuvant chemotherapy was given in locally advanced breast cancers to allow conservative surgery. However, it offered no survival benefit. In our study, it was found that 5-year DFS rate was 49.64% in patients who were given neoadjuvant chemotherapy as compared to 69.51% in whom chemotherapy was given after surgery.<sup>24-27</sup>

### Summary

The present study comprise 525 patients who were admitted in the indoor, Department of Surgery S.V.B.P Hospital Meerut, during January 1993 to October 2004.

Most of the patients were in the age group of 41-50 years (28.19%), i.e., around menopause.

Prognosis was best in the age group 41-50 years (5-year DFS 60.81%).

There was no significant difference in survival was between age group 2-30 years and 71-80 years of age. 5-year DFS was found to be 43.47% and 46.42% in the, respective, age groups.

Higher tumor grade was associated with poor prognosis. The 5-year DFS was found to be 47.40% for Stage III A and 35.18% for Stage III B as compared with 66.97% and 57.80% in patients with Stage I and II disease, respectively.

Positive family history was found to be associated with poor prognosis. 5-year DFS in patients with positive family history was found to be 47.16% as compared to patients with negative family history with 5-year DFS of 62.93.

Prognosis was found better in postmenopausal patients. 5-year DFS was found to be 48.70% in premenopausal patients and 60.93% in postmenopausal patients.

Tumor size is an important prognostic parameter and better prognosis was found in patients with small tumor size. Patients with T1 disease had 5-year DFS 72.63% and patients with T4 disease 5-year DFS of 40.20%.

Hormone receptors status is a powerful prognostic parameter. In the present study of 129 patients who had records about their hormone receptor status, patients with positive ER/PR status had better survival than patients with negative ER/PR status, with a 5-year DFS rate of 58.62% and 39.60%, respectively.

Axillary lymph node status is an important predictor of prognosis. The 5-year DFS rates were found to be reduced with the increase in the number of involved lymph nodes. The 5-year DFS rate in lymph node negative patients was 73.75% and in those with 1-3 positive nodes was 50.92% while in the patients with more than 10 involved nodes, showed a 5-year DFS rate of only 08.82%.

Histological grade is an important determinant of prognosis. The poor histological grade was associated with reduced survival. The 5-year DFS in Grade I, II, and III tumors was found to be 63.44%, 54.61%, and 33.33%, respectively.

Lymphovascular embolization carried a poor prognosis. The patients with lymphovascular embolization showed a 5-year DFS of 28.69% compared with 58.80% 5-year DFS rate in patients not having lymphovascular embolization.

Tumor necrosis was associated with poor prognosis. Patients in whom tumor necrosis was present showed a 5-year DFS of 30.76% compared with patients without tumor necrosis with a 5-year DFS of 59.80%.

Perinodal extension is an important prognostic parameter. Patients having perinodal extension were found to have 5-year DFS of 20.20% as compared to patients without it with 5-year DFS of 60.86%.

Radiotherapy improves the chances of survival. Patients treated by surgery and chemotherapy showed 5-year DFS rate of 69.51%. Survival was improved to 72.85% when radiotherapy was added.

Surgery alone without any adjuvant therapy carried a poor prognosis with 5-year DFS (26.66%). The 5-year DFS improved to 69.51% with the introduction of chemotherapy and it further improved by adding radiotherapy (72.85%).

Neoadjuvant chemotherapy offered no survival benefit. In our study, it was found that 5-year DFS rate was 49.64% in patients who were given neoadjuvant chemotherapy as

compared to 69.51% in whom chemotherapy was given after surgery.

## CONCLUSIONS

The conclusion derived from the present study is as follows:

1. Prognosis was best in age group 41-50.
2. There was no significant difference in survival was between age group 21-30 years and 71-80 years of age.
3. Higher tumor grade was associated with poor prognosis.
4. Positive family history was found to be associated with poor prognosis.
5. Prognosis was found better in postmenopausal patients.
6. Tumor size is an important prognostic parameter, and better prognosis was found in patients with small tumor size.
7. Hormone receptors status is a powerful prognostic parameter. Patients with positive ER/PR status had better survival than patients negative ER/PR status.
8. Axillary lymph node status is an important predictor of prognosis. The 5-year DFS rates were found to be reduced with the increase in the number of involved lymph nodes.
9. Histological grade is an important determinant of prognosis. The poor histological grade was associated with reduced survival.
10. Lymphovascular embolization carried a poor prognosis. The patients with lymphovascular embolization showed a worse 5-year DFS compared with patients not having lymphovascular embolization.
11. Tumor necrosis was associated with poor prognosis.
12. Perinodal extension is an important prognostic parameter patients having perinodal extension were found to have worse 5-year DFS as compared to patients without it.
13. 5-year DFS was improved when radiotherapy was added to the surgery. Thus, radiotherapy improves the chances of survival.
14. Surgery alone without any adjuvant therapy carried a poor prognosis. The 5-year DFS improved with the introduction of chemotherapy and it further improved by adding radiotherapy to the surgery.
15. Neoadjuvant chemotherapy offered no survival benefit.

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