

Original Research Article

Clinicopathological features and survival outcomes in bone-only metastatic breast cancer patients stratified by hormone receptor status: a tertiary care study

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ABSTRACT

Background: Bone metastatic disease is common across all breast cancer subtypes. Patients with hormone receptor (HR)-positive breast cancer tend to have the greatest predilection for developing bone metastases and have better survival outcomes; unlike organotypic metastasis to visceral organs in triple-negative breast cancer. In this retrospective study, we compared the features and survival of these bone metastatic breast cancer subgroups and demonstrated that different ER and PR statuses contribute to varied survival outcomes.

Methods: It was a single-institute retro prospective study. Out of the 200 HPR-proven cases of breast carcinoma, 100 patients were eligible for the study who presented/developed bone metastases. Patients with visceral mets were excluded from the study. Based on ER, PR and HER2 neu, status patients were divided into four groups.

Results: Out of 100 patients taken for this study 45 were ER+ PR+, 20 were Er-,PR-, 18 were ER-, PR +, and 17 were ER+,PR-.and the mean age in the study groups was 49.5±.5. Higher tumour grade and lymph node positivity was observed in ER- PR- and ER- PR+ as compared to hormone-positive groups. In our study group percentage of bone mets was higher in ER +, PR+(31.11%) and ER+ PR- (52.63%),While as it was similar in Er-,PR- and ER-, PR + patients. The overall survival of ER+ PR- was 94.1% followed by ER +, PR+(86.7%) while patients with ER-, PR- had 30.0% and ER-, PR + 27.8%.

Conclusions: Different ER and PR statuses in breast cancer exert a significant impact on bone metastasis incidence and survival condition of bone metastatic breast cancer. Hormone receptor-positive tumours show a predilection for bones as the first site of relapse and better overall survival as compared to hormone-receptor-negative tumours.

Keywords: Bone mets, Breast carcinoma, Hormone receptor

INTRODUCTION

Breast cancer (BC) is the commonest malignancy among women on a global scale. In 2020, it overtook lung cancer as the leading cause of cancer incidence, with approximately 2.3 million new cases-representing 11.7% of all cancer diagnoses.¹ In India, Breast cancer accounted

for 13.5% (178361) of all cancer cases and 10.6% (90408) of all deaths with a cumulative risk of 2.81as per the Globocan data 2020.²

Breast cancer can be classified using several criteria, such as its histologic type, tumor marker expression, and clinical characteristics.³ Notably, among the histologic

forms, ductal and lobular carcinomas are the most common, with ductal carcinoma representing the predominant subtype.^{3,4}

Key prognostic factors for breast cancer at the clinical level, include the age at diagnosis, tumor size, tumor grade, the presence of lymphovascular invasion, status of surgical margins, menopausal status, as well as lymph node involvement and distant metastasis.

At the molecular scale, breast cancer is divided into four distinct subtypes based on variations in estrogen (ER) and progesterone (PR) receptor expression which include Luminal A Characterized by positivity for ER or PR with a lack of human epidermal growth factor receptor 2 (HER2) overexpression., Luminal B defined by expression of ER or PR alongside HER2 positivity, HER2-enriched marked by the absence of both ER and PR, yet exhibiting elevated levels of HER2, Triple-negative: Lacking detectable levels of ER, PR, and HER2.⁵

Breast cancer progression often entails metastasis, a process in which cancerous cells migrate from the original tumor site to establish growth in distant organs.⁶ Bone only metastatic breast cancer represents a unique subset of advanced breast cancer characterized by absence of visceral organs involvement which poses distinct clinical challenges and treatment considerations.⁷

The median survival duration for patients with bone metastatic breast cancer generally falls between three and five years.⁸ On a mechanistic level, bone metabolism is a carefully regulated process sustained by the interplay between osteoblasts and osteoclasts, under the influence of steroid sex hormones and various cytokines.⁹ Any hormonal imbalance can disrupt this equilibrium, leading to alterations in bone structure and composition

Bone metastases are a frequent occurrence across all subtypes of breast cancer. However, patients with hormone receptor (HR)-positive breast cancer demonstrate a pronounced affinity for developing bone metastases and achieve superior survival outcomes compared to other subtypes such as triple-negative breast cancer (TNBC).¹⁰⁻¹²

In this retrospective study, we compared the features and survival of these bone metastatic breast cancer subgroups and demonstrated that different ER and PR statuses contribute to varied survival outcomes.

METHODS

It was a single-institute retro prospective study which was conducted in Government medical College, Srinagar. After obtaining information, 200 patients diagnosed with breast cancer between October 2020 and January 2023 were included in the study. Out of the 200 HPR-proven cases of breast carcinoma, 100 patients were eligible for the study who presented/developed bone metastases. Exclusion criteria were patients with visceral mets.

All of the patients' ages, habitats, tumour histology, tumour grade, lymph node status, TNM staging and ER/PR status were thoroughly recorded.

Based on ER, PR and HER2 neu, status patients were divided into four groups. In this study, all statistical analysis was performed with SPSS software 4.2.0. P values were two-sided, and $p < 0.0001$ was considered statistically significant.

The demographic and baseline clinicopathological characteristics of bone metastatic breast cancer patients with ER-positive/PR-positive, ER positive/PR-negative, ER-negative/PR positive, and ER-negative/PR-negative primary tumours were analyzed using the Chi-square test. Overall survival were determined by the Kaplan–Meier survival curve.

RESULTS

Out of 100 patients taken for this study 45 were ER+ PR+, 20 were Er-, PR-, 18 were ER-, PR+, and 17 were ER+, PR-.and the mean age in our study groups was 49.5 ± 5 as shown in table 1. The majority of patients in our study groups had intraductal carcinoma while 2 patients in er - .pr-group had mixed histology as shown in Table 1. Higher tumour grade and lymph node positivity were observed in ER- PR and ER- PR+ as compared to hormone-positive groups as shown in Table 1.

Table 1: Demographic and clinico pathological characteristics of breast cancer patients with bone metastasis stratified by hormone receptor status.

Parameters		All patients (100) (%)	Er +, pr+(45) (%)	Er -,pr-(20) (%)	Er-,pr +(18) (%)	Er +, pr-(17) (%)	Ch. Sq. value	P value
Age (in years)	<49	48 (48)	22 (48.8)	11 (55)	9 (56.25)	5 (26.31)	6.142	0.408
	50-69	41 (41)	20 (44.44)	7 (35)	5 (31.25)	10 (52.63)		
	>70	11 (11)	3 (6.66)	2 (10)	4 (22.5)	4 (21.05)		
Tumour grade	I	10 (10)	3. (6.8)	2. (10)	2. (11.1)	3 (17.6)	4.665	0.587
	II	47 (47)	24. (53.3)	8. (40)	6 (33.3)	9. (52.9)		
	III	43 (43)	18 (40)	10 (50)	10 (55.6)	5 (29.4).		

Continued.

Parameters		All patients (100) (%)	Er +, pr+(45) (%)	Er -,pr- (20) (%)	Er-,pr +(18) (%)	Er +, pr- (17) (%)	Ch. Sq. value	P value
	IV	0	0	0	0	0		
	Unknown	0	0	0	0	0		
T stage	T1	9 (9.0)	6 (13.3)	0 (0)	1 (5.6).	2 (11.8)	22.899	0.006
	T2	50 (50)	27 (60.0)	7 (35.0)	6 (33.3)	10 (58.8)		
	T3	37 (37)	8 (17.8)	13 (65.0)	11 (61.1)	5 (29.4)		
	T4	4 (4)	4 (4)	0	0	0		
N stage	No	9 (9)	9. (20)	0. (0)	0 (0)	0 (0)	18.453	0.030
	N1	20 (20),	10 (22.22)	4. (20)	4 (22.2)	2 (11.8)		
	N2	44 (44).	18 (40)	12 (60)	7 (38.9)	7 (41.2)		
	N3	27 (27)	8 (17.8)	.4 (20)	7 (38.9)	8 (47.1)		
	Unknown	0	0	0	0	0		
Histology	IDC	98 (98)	45 (100)	18 (90).	18 (100)	17 (100)	-	-
	ILC	0	0	0	0	0		
	Mixed (IDC and ILC)	2 (2)	0	2 (10)	0	0		
HER2 NEU status	Positive	33 (33)	17. (37.7)	4. (20)	0	12 (63.15)	21.723	<0.001
	Negative	67 (67)	28. (62.2)	16. (80)	18 (100)	5 (36.84)		
	Borderline	0	0	0	0	0		
Surgery	Yes	100	45 (100)	20 (100)	18 (100)	17 (100)	-	-
	No	0	0	0	0	0		
Chemotherapy	Yes	100	45 (100)	20 (100)	18 (100)	17 (100)	-	-
	NO	0	0	0	0	0		
Radiation	Yes	100	45 (100)	20 (100)	18 (100)	17 (100)	-	-
	No	0	0	0	0	0		
Vital status	Alive	72 (72)	35 (77.77)	15 (75)	10 (62.5)	12 (63.15)	5.698	0.458
	Dead of breast cancer	18 (18)	5 (11.11)	5 (25)	4 (25)	4 (21.05)		
	Dead of other cause	10 (10)	5 (11.11)	0 (0)	4 (25)	1 (5.88)		

Table 2: Incidence of bone metastasis in breast cancer patients stratified by hormone receptor status.

Bone mets		All patients n (100) (%)	Er +, pr+(45) (%)	Er -,pr- (20) (%)	Er-,pr +(18) (%)	Er +, pr- (17) (%)	Ch. Sq. value	P value
	Yes	25 (25)	14 (31.11)	4 (20)	3 (18.75)	10 (52.63)	6.411	0.093
	No	75 (75)	31 (68.88)	16 (80)	15 (83.25)	7 (41.36)		

Table 3: Distribution of survival rate of different receptors.

Factor	Total	No. of events	Censored	
			N	Percent
er+pr+	45	6	39	86.7
er-pr-	20	14	6	30.0
er-pr+	18	13	5	27.8
er+pr-	17	1	16	94.1
Overall	100	34	66	66.0

Her2 neu positivity was 37.7% in ER +, PR+, and 20% in ER- PR - patients and 63.15% in ER+, PR - and while

her2neu negativity was 100% in ER- PR+ followed by 80% in Er-, PR- and 62.2 % in ER+ PR+, and 36.84% in ER+, PR-.as shown in table 1. All the patients underwent surgery and received chemotherapy and radiotherapy as shown in Table 1. In our study group percentage of bone mets was higher in ER +, PR+(31.11%) and ER+ PR- (52.63%). While as it was similar in Er-, PR- and ER-, PR + patients as shown in Table 2

The overall survival of ER+ PR- is 94.1% followed by ER +, PR+(86.7%) while patients with ER-, PR- had 30.0% and ER-, PR + 27.8% as shown in Table 3 and figure 1. It is evident from above table 3 that the patients with ER+ PR- had maximum mean survival time followed by the

mean survival time of ER +, PR+ patients as compared to ER-, PR- and ER-, PR +, both have approximately the same mean survival time.

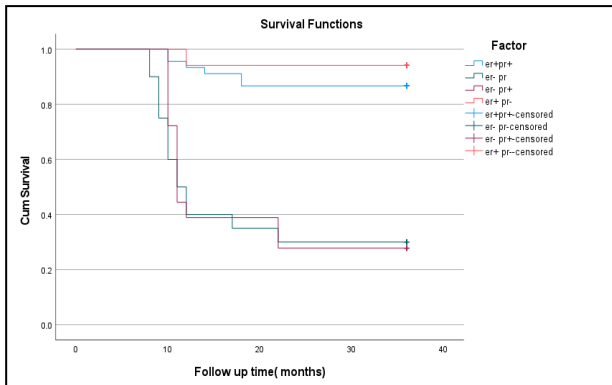


Figure 1: The survival times of different receptors.

DISCUSSION

Breast cancer exhibits significant heterogeneity in its patterns of metastasis, with bones being the most common site of recurrence. Over 50% of patients with metastatic breast cancer experience bone metastases as the initial site of disease progression.^{13,14} HR status plays a pivotal role in determining metastatic patterns and outcomes. Hormone receptor-positive tumors demonstrate a notable predilection for bone metastases and are associated with more favorable survival outcomes compared to HR-negative tumors.¹⁵

Our study aimed to investigate the four hormone receptor (HR) status subtypes of breast cancer, focusing on their prevalence of bone metastases, associated clinicopathological characteristics, and comparative survival outcomes.

In our study, patients with ER-positive/PR-negative tumors exhibiting bone metastases were generally older. Conversely, those with ER-positive/PR-positive and ER-negative/PR-negative tumors were more frequently diagnosed at the age of 49 years or younger. These findings are consistent with observations reported in the study by Jiang et al.¹⁶

Moreover, this study observed that ER-positive breast cancers were more likely to metastasize to bone, with histological characteristics such as intraductal carcinoma and lower tumor grade being predominant among HR-positive cases. In contrast, HR-negative tumors were associated with higher grades and advanced TNM stages. These findings are consistent with studies by Jiang et al and Pareekh et al, underscoring the unique clinicopathological profiles of HR subgroups.^{16,17}

In this study, patients with bone metastasis with ER-positive/PR-negative tumors exhibited the best overall survival (OS) rates, followed by those with ER-

positive/PR-positive tumors. Conversely, there was no significant difference in survival between ER-negative/PR-positive and ER-negative/PR-negative subgroups, highlighting a similarity in survival outcomes between these HR-negative categories. These findings align with prior research by Cazzaniga et al which demonstrated the prognostic significance of HR status in breast cancer with bone metastases.¹⁸

This study has some potential limitations due to the short period, limited sample size and the lack of more comprehensive molecular profiling.

CONCLUSION

In our study, we conclude that different ER and PR statuses in breast cancer exert a significant impact on bone metastasis incidence and survival condition of bone metastatic breast cancer. Moreover, the HR status in bone metastatic breast cancer is a significant prognostic factor which determines the survival probability. Hormone receptor-positive tumours show a predilection for bones as the first site of relapse and better overall survival as compared to hormone-receptor-negative tumours.

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