ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 6, Issue – 1, February - 2023, Page No. : 124 - 131

A comparative study of molecular subtypes with clinicopathological factors in carcinoma breast

[1]Dr. Buthukuri Sunayana, Final year PG, Department of General Surgery, Alluri Sitarama Raju Academy of Medical Sciences Eluru, West Godavari district, Andhra Pradesh, India, 534005

[2]Dr. M Sri Akshay, Assistant Professor, Department of General Surgery, Alluri Sitarama Raju Academy of Medical Sciences Eluru, West Godavari district, Andhra Pradesh, India,534005

[3]Dr. Kondreddy Suhas**,** Professor & HOD, Department of General Surgery, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari district, Andhra Pradesh, India, 534005

Corresponding Author: Dr. Buthukuri Sunayana, Final year PG, Department of General Surgery, Alluri Sitarama Raju Academy of Medical Sciences Eluru, West Godavari district, Andhra Pradesh, India, 534005

How to citation this article: Dr. Buthukuri Sunayana, Dr. M Sri Akshay, Dr. Kondreddy Suhas, "A comparative study of molecular subtypes with clinicopathological factors in carcinoma breast", IJMACR- February - 2023, Volume – 6, Issue - 1, P. No. 124 – 131.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Aim and objectives: To study the correlation between molecular subtypes and other clinical and pathological prognostic factors in carcinoma breast.

Materials and methods: This is a prospective study done from June 2021 to August 2022. In this study 50 patients who were admitted in our institution, diagnosed with breast cancer above the age of 18 years of age were included. The Clinico-Pathological factors such as Menopausal Status, T & N Stage of the tumor, Pathological type, Histological Grade Mitotic index, Lymph vascular Invasion, Ki 67 were correlated individually with the Molecular subtype of tumor

Results

Molecular subtype vs menopausal status: Most of the women in study belonged to post-menopausal age group, in which Luminal B and Triple negative were the most common subtype.

a. In our study most of the pre-menopausal women were found to have triple negative/basal like molecular subtype.

Molecular subtype vs t stage

b. Most of the patients in our group were T2 stage and triple negative was the most common subtype in T2 tumors.

Molecular subtype vs n stage

c. Most of the patients in the study were found to be node negative 64%

Molecular subtype vs pathological type

d. Most of the patients in the study belonged to the pathological type- ductal carcinoma (NOS) type

Molecular subtype vs histological grade

Most of the patients in our study were Grade II (57.4%) in which Luminal B was the most common molecular subtype.

Molecular subtype vs mitotic index

Most of the patients were found to have Grade II mitotic index in which Luminal B was the most common subtype

Molecular subtype vs lymph vascular invasion

Most of the Luminal A and Triple negative subtypes were found to have no lympho-vascular invasion and the correlation was found to be statistically significant.

Molecular subtype vs ki-67

Most of the Triple negative tumors were found to be associated with high Ki 67 index.

Conclusion

The correlation is found to be statistically significant with a p value< 0.0000, On comparing of molecular subtypes with Histological grade and mitotic index - Triple negative was associated with higher histological grade and mitotic index.Lympho-Vascular invasion - Most of the Triple negative subtype patients were found to have no lympho-vascular invasion. Ki-67 index - Triple negative patients were found to have High Ki- 67 index Whereas Luminal A and Luminal B were found to have Low Ki-67 index.

Keywords: Carcinoma breast, Molecular Subtype, clinicopathological factors, correlation

Introduction

Breast cancer has been ranked as one of the top most cancers among women all over the world with an estimated 1.67 million new cancer cases diagnosed every year(1). Contrary to West where it is more common in the elderly, it is more common at a younger age in the Indian women, who present themselves in advanced stage with poor features and have worst outcome when compared to their counterparts in western countries(2).

The purpose of classification and grading of the breast cancer at the histopathological level is a key to identifying the prognosis and management of breast cancers. It is essential to identify the invasion of the tumors in to vasculature thereby Staging the tumor based on the nodal and multi organ infiltration and also presence of expression of various bio markers and receptors. (3)

Analyzing the presence or absence of these tumor markers and receptor expression helps in predicting the invasiveness of the cancers. This will have a direct bearing on the choice of treatment including surgical,chemotherapeutic or radiotherapy.

Therefore, analysing the correlation between molecular typing and histopathological and clinical features of breast cancers is outmost requirement in order to obtain an in -depth view of the pattern of presentation of breast cancers at the clinical level and also for predicting survival outcomes and effective therapeutic management of breast cancers (4).

Aims and objectives

To study the correlation between molecular subtypes and other clinical and pathological prognostic factors in carcinoma breast.

Materials and methods

- Site of the study: Alluri Sita Rama Raju Academy of Medical Sciences, Eluru
- Type of the study: Prospective study -Observational
- Period of the study : June 2021 to August 2022
- Sample size: 50

In this study 50 patients who were admitted in our institution, diagnosed with breast cancer above the age of 18 years of age were included.

A detailed clinical history and physical examination was recorded and all patients underwent modified radical mastectomy.

Postoperatively the specimen was sent for histopathology and the tumor size, nodal status, histological grading, pathological type of the tumor, mitotic rate, lymphovascular invasion,Estrogen, Progesterone, Her-2 Neu receptors status,Epidermal Growth Factor Receptor status, Androgen Receptor status, Ki-67 and Molecular subtyping was done and recorded. The data was statistically analyzed and correlated using SPSS 15 software.

Inclusion criteria

- This study includes patients of age above 18 years diagnosed with carcinoma breast and undergoing modified radical mastectomy

Exclusion criteria

- Patients below age of 18 years
- Post Neo-adjuvant chemotherapy
- Recurrent lesions
- T stage- not known

Study parameters and variables

1. Age
2. Menopausal Status
3. Histological grading
4. Pathological type
5. Mitotic rate/index
6. Tumour size (pT)
7. Nodal status (pN)
8. Lymph vascular invasion
9.KI-67 proliferation index

Results

Total Number of patients in our study - 50

Table 1: Age distribution

AGE	No. Of Patients	% Of Patients
18-39	4	8%
40-49	11	22%
50-59	20	40%
60-70	15	30%

Table 2: Distribution of molecular subtypes

Molecular subtype	No. Of Patients	% of Patients
Luminal A	7	14%
Luminal B	17	34%
Her 2 Neu Type	7	14%
Triple Negative	19	38%

Table 3: menopausal status

Menopausal status	No of Patients	% Of Patients
PRE	13	26%
POST	37	74%

Table 4: molecular subtype’s vs menopausal status

Menopausal status	Luminal A	Luminal B	Her 2 Neu Enriched	Triple Negative	Total
PRE	2 (15.38%)	4(30.76%)	1(7.69%)	6(46.15%)	13
POST	5(13.51%)	13(35.13%)	5(13.51%)	13(35.13%)	37
TOTAL	7	17	7	19	50

- There was no statistical significance between molecular subtypes and menopausal status (p-0.831).

Table 5: molecular subtype vs t stage

T Stage	Luminal A	Luminal B	Her 2 Neu Enriched	Triple negative	Total
T1	1(14.28%)	3(42.85%)	2(28.57%)	1(14.28%)	7
T2	6(17.14%)	12(34.28%)	3(8.57%)	14(40%)	35
T3	0	1(16.66%)	2(33.33%)	3(50%)	6
T4	0	1(50%)	0	1(50%)	2
Total	7	17	7	19	50

There was no statistically significant correlation between T stage and molecular subtypes (p-0.126).

Table 6: Molecular subtype vs n stage

N stage	Luminal A	Luminal B	Her 2 Neu Enriched	Triple negative	Total
N0	4(12.5%)	11(34.37%)	5(15.62%)	12(37.5%)	32
N1	1(14.28%)	2(28.57%)	0	4(57.14%)	7
N2	1(12.5%)	4(50%)	1(12.5%)	2(25%)	8
N3	1(33.33%)	0	1(33.33%)	1(33.33%)	3
Total	7	17	7	19	50

- There is no statistically significant correlation between nodal status and molecular subtype (p-0.857)

Table 7: Molecular subtype vs pathological type

Type	Luminal A	Luminal B	Her 2 Neu Enriched	Triple negative	Total
Ductal with NOS	412.90%)	11(35.48%)	4(12.90%)	12(38.70%)	31
Lobular	2(40%)	1(20%)	1(20%)	1(20%)	5
Ductolobular	1(16.66%)	2(33.33%)	2(33.33%)	1(16.66%)	6
Ductal others	0	3(37.5%)	0	5(62.5%)	8
Total	7	17	7	19	50

- There is no statistical significance between pathological type and molecular subtypes (p -0.136)

Table 8: molecular subtype vs histological grade

Grade	Luminal A	Luminal B	Her 2 Neu Enriched	Triple negative	Total
I	1(11.11%)	4(44.44%)	2(22.22%)	2(22.22%)	9

Grade	Luminal A	Luminal B	Her 2 Neu Enriched	Triple negative	Total
II	6(21.42%)	12(42.85%)	4(14.28%)	6(21.42%)	28
III	0	1(7.69%)	1(7.69%)	11(84.61%)	13
Total	7	17	7	19	50

➢ In this study Most of the Triple negative subtype were associated with Histological Grade III and the p -value was found to be significant (<0.000)

Table 9: Molecular subtype vs mitotic index

Mitotic index	Luminal A	Luminal B	Her 2 Neu Enriched	Triple negative	Total
I	2(20%)	4(40%)	2(20%)	2(20%)	10
II	5(18.51%)	12(44.44%)	4(14.81%)	6(22.22%)	27
III	0	1(7.69%)	1(7.69%)	11(84.61%)	13
Total	7	17	7	19	50

➢ In this study Most of the Triple negative subtype were associated with Mitotic Index III and the p -value was found to be significant (< 0.000).

Table 10: molecular subtype vs lymph vascular invasion.

Invasion	Luminal A	Luminal B	Her 2 Neu Enriched	Triple negative	Total
Present	1(6.66%)	6(40%)	4(26.66%)	4(26.66%)	15
Absent	6(7.14%)	11(31.42%)	3(8.57%)	15(42.85%)	35
Total	7	17	7	19	50

➢ In This study Most of the Triple negative subtype were found to have No invasion and the correlation between Triple negative molecular subtype with Negative Lympho-vascular invasion was found to be statistically significant (p-0.03).

Table 11: molecular subtype vs ki 67

Grade	Luminal A	Luminal B	Her 2 Neu Enriched	Triple negative	Total
High	2(6.89%)	9(31.03%)	4(13.79%)	14(48.27%)	29
Borderline	0	5(55.55%)	2(22.22%)	2(22.22%)	9
Low	5(41.66%)	3(25%)	1(8.33%)	3(25%)	12
Total	7	17	7	19	50

- In This study Most of the Triple negative subtype were found to have High Ki-67 index and Most of the Luminal B and Luminal A subtypes were found to have Borderline and Low Ki-67 Index. The correlation between molecular subtype with Ki-67 index was found to be statistically significant (p -0.000).

Discussion

Age

Most of the patients in this study be longed to age range 50-59 years, and the mean age of patients was found to be 54 years which was similar to the study done by Widodo I et al., and Chuthapisith et al., 2012 where the mean age was 52.5 years (5,6).

Distribution of subtypes

In our study triple negative was the most common molecular subtype which was similar to study done by Carey et al., in which most of the study group were triple negative(7).

Molecular Subtype Vs Menopausal Status

Most of the women in study belonged to post-menopausal age group,in which Luminal B and Triple negative were the most common subtype. In our study most of the pre -menopausal women were found to have triple negative/basal like molecular subtype. Similar results were found in a study conducted by Fernando et al.,in which they concluded that triple negative tumors were common in younger age group and pre -menopausal status (8).

Molecular Subtype Vs T Stage

Most of the patients in our group were T2 stage and triple negative was the most common subtype in T2 tumors.

However, there was no statistically significant correlation between molecular subtypes with T stage. Similar results were found in a study conduct ed by Onitilio et al.,and concluded no significant difference was noted in regard to tumor size in comparison with Molecular subtypes (9).

Molecular Subtype Vs N Stage

Most of the patients in the study were found to be node negative (64%). Majority of patients belonging to Node negative group -N0 were found to be triple negative.However, there was no statistically significant correlation between N stage and molecular subtypes. Similar results were found in a study conducted by Liu N et al., in which they concluded that triple negative tumors are not associated frequently with higher number of involved nodes (10).

Molecular Subtype Vs Pathological Type

Most of the patients in the study belonged to the pathological type -ductal carcinoma (NOS) type. Specific types of ductal carcinoma like Papillary, Medullary, Tubular, Mucinous were found to be more common in Triple negative subtype.

There was no correlation between molecular subtypes and pathological type of tumors.

Molecular Subtype Vs Histological Grade

Most of the patients in our study were Grade II (57.4%) in which Luminal B was the most common molecular subtype. 87.5% of Grade III tumors were found to be Triple negative suggesting that Triple negative tumors were associated with higher grade. The correlation was found to be statistically significant.

Similar results were noted in a study done by Eun Sook Ko et al.,where they concluded that triple negative tumors were found to have higher grade (11).

Molecular Subtype Vs Mitotic Index

Most of the patients were found to have Grade II mitotic index in which Luminal B was the most common subtype.

Triple negative subtype was found to have high mitotic index whereas Luminal B had low mitotic index. The correlation was found to be statistically significant.

Similar results were noted in a study done by Boyle et al., where triple negative tumors were found to have higher mitotic index (12).

Molecular Subtype Vs Lymphovascular Invasion

Lympho-vascular invasion was absent in most of the patients in our study. Most of the Luminal A and Triple negative subtypes were found to have no lympho-vascular invasion and the correlation was found to be statistically significant.

Similar results were found in a study conducted by Ugras et al., where Lympho-vascular invasion and nodal metastases were least frequent in Triple Negative cancers compared with other subtypes. This suggests Triple Negative cancers spread via lymphatics is less frequent than other subtypes (13).

Molecular Subtype Vs Ki-67

Most of the patients in the study were found to have High Ki-67 proliferation index. Most of the Triple negative tumors were found to be associated with high Ki 67. Luminal A and Luminal B subtypes were associated with low Ki 67 and the correlation was found to be statistically significant.

Similar results were noted in a study conducted by Aman et al., in which they concluded that triple negative tumorswere found to have high Ki-67 score (14).

Conclusion

- The correlation is found to be statistically significant with a p value < 0.0000, On comparing of molecular subtypes with Histological grade and mitotic index -Triple negative was associated with higher histological grade and mitotic index
- Lympho-Vascular invasion with -Most of the Triple negative subtype patients were found to have no lympho -vascular invasion
- Ki-67 index -Triple negative patients were found to have High Ki-67 index Whereas Luminal A and Luminal B were found to have Low Ki-67 index.
- However, There is No statistically significant correlation of molecular subtypes with Age, Menopausal status, T stage, N stage and Pathological type.

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