THE RELATIONSHIP BETWEEN TUMOR SIZE AND THE NODAL STATUS: IN BREAST CANCER

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Abstract

Background: Patients having breast cancer, with increasing tumour size is associated with an increased of axillary lymph node involvement. Moreover, all this association to place altogether of all tumors smaller than 1.0 cm in a single category and all tumors larger than 5.0 cm in another category. This coarse classification may obscure a nuanced description of the effects of tumour size across the full range of possible sizes.

Methods: Here we have studied association between primary tumour size, lymph node status cohort study of 88patients whom have been diagnosed with first primary invasive breast cancer from 2014 - 2022 in SPSS method. All patients in the cohort had a known primary tumour size between 1 and 150 mm in greatest dimension. Primary tumour size was examined as continuous (1–150 mm) and categorical variable(10-mm intervals). For each 1 or 10-mm size group, we set on the corresponding of patients with positive lymph nodes at diagnosis.

Results: Amid 88 patients who is having invasive breast tumorsof size 1 and 150 mm in size, not any association of increasing tumour size and prevalence of lymph node metastases (% node-positive). For very small size of tumors (under 10 mm) and for very large size of tumors (larger than 60–90 mm) there was little correlation between

tumour size. Conclusions Association of tumour size and lymph node status in patients with breast cancer is not straightforward.

INTRODUCTION:-

Breast cancer usually progress by several stages: Hyperplasia—Intraductalcarcinoma—invasion and growth within the breast, Few cases by metastasis to the lymph nodes and distant sites. Breast cancer has potential of cause metastases to distance organ from primary site can be a lethal development. Usually acknowledged hypothesis that cancer grows, cells within tumour is having Potential of spread to survive and develop within theregional lymph nodes and other distant sites. This aspect built on explanation of well-established association between primary tumour size and the prevalence of metastases.

There has been belief that risk of developing metastases increases monotonically with tumour size,because if larger the cancer at diagnosis, the more tumor cells will be obtainable to metastasize.[1–3] But here this theory suggests other side of it. Crosssectional association between tumour size and metastasis is a graphical representation ofa sample of different patients at diagnosis, because Patients could not be followed for wardin time to record progression from non-metastatic stateto a metastatic state. Data which we collected also compatible with model that indicating slow-growing tumours are small and are intrinsically less prone to metastasize(i.e. tumour aggressiveness predicts tumour size).[4]

Almost all studies till now have been conducted have suggested that associations between primary tumour size and the probability of metastasis(to the lymph nodes or to distant sites) have treated all tumors smaller than 1.0 cm at diagnosis as a single category and those tumors larger than 5.0 cm at diagnosis as another category. There

is a clear and consistent linear Association between size and metastases in the size range between 1.0 and 5.0 cm, and it is assumed this curve can beextra polated in both directions to predict the proportions of patients with nodal metastases for very small size tumor and for very large size tumors. New hypothesis gaining popularity that risk of metastasis is toa large extent determined by the intrinsic biology of breast cancer rather than the timing of diagnosis within the clinicalwindow. That's-why studies are conducting that association between tumour size and prevalentmetastases, in order to gain insight into the early eventsin cancer progression. We have mentioned here comprehensive descriptive study of association between tumour size at diagnosi sand the prevalence of metastases (to the lymph nodes) in women with invasive breast cancer across the size range of 1–150 mm. By employing SPSS study, prevalence of lymph node metastases at diagnosis who is having breast cancer, of distantmeta stases at diagnosis.[5-7]

Materials and Methods

We have employed here SPSS version 22.0 to do a case listingsession and retrieved all cases of first primary invasivebreast cancer diagnosed from 2014to 2022 in the SPSS 22.0 registries research database. We choose cases that have pathologically confirmed and had primary tumour size of 1 and150 mm in greatest dimension. We did not includepatients with noprimary tumour found, primary tumour size not known, diffusedisease, Paget's disease of nipple, or in situ disease.For each of 88 remaining patients, we retrievedin formation on year of breast cancer diagnosis, age atdiagnosis, race/ethnicity, primary tumour size, lymph nodestatus, number of lymph nodes excised, {oestrogen receptor (ER) status, progesterone receptor (PR) status, HER2 status} Primary predictor variable was the size of tumor.[5-6]outcomes of interest were the prevalence of lymphnode metastases at diagnosis. Tumour size in

the SPSS database refers to the greatest dimension (usually the diameter)of the largest contiguous area of stromal invasion. In SPSS, patients with invasive breast cancer are assigneda tumour size of between 1 mm (microscopic focus only,or invasive focus no larger than 1.0 mm in greatest dimension)and 990 mm (99.0 cm); however, only sizes between1 and 150 mm are considered to be reliable. Tumour sizein this study was analyzed as both a continuous variable(1–150 mm) and a categorical variable (5- or 10-mm size intervals). For each 1-mm size measurement we calculated tumour volume assuming that the invasive focus is spherical and the greatest dimension (size measurement) is thediameter.We defined the prevalence of lymph node metastases atdiagnos is as the proportion of patients with positiveregional lymph node metastasis (AJCC classificationsN1, N2 or N3) among all patients for whom the regional lymph nodes were assessed (AJCC classifications N0, N1,N2 or N3). Patients with only isolatedtumour cells identified in regional lymph nodes (≤ 200 individualcells or focus ≤ 0.2 mm) were considered to be lymphnode-negative (N0).

To assess the association between primary tumour size and prevalence of lymph node metastases at diagnosis,we plotted the proportion of patients with lymph nodemeta stases at diagnosis according to primary tumour size(diameter and volume) for all patients in the cohort and then for patients stratified according to clinical sub-type{(ER+/HER2−; ER−/PR−/HER2−; HER2+).Data related to patients- name, age etc. Noted down. In all patients, side and location of tumour and histological types, tumour size, histological grade, skin, nipple and areola invasion noted down. Size of tumour was defined as the largest diameter of tumour reported on pathological examination following surgery. The number of nodes were pathologically evaluate and grading was done Scarff– Bloom–Richardson (SBR) system. Results were

systemized and subjected to statistical analysis. P value less than 0.05 was considered significant.

Results

We identified 88 patients who have diagnosed with invasivebreast cancer in INDIA(PUDUCHERRY) time spend of 2014 to 2022. Supplementary Table 1 to sum up all baseline characteristics in gender distribution out of 88 patient with 87 were female, it accounts approximate 98.90% of total patient and 1(1.10%) patient was male. Among patients of breast cancer-cohort study showing primary tumour of size 1and 150 mm;

Table-2 shows comparison of right to left side; Out of 88 cases right sided breast cancer more compared to left side its accounted 50 cases approximately 56.80% compared to 38(43.20%) is left sided breast cancer.

Table 3 explain if necrosis is present or not in those patients: 33 patient were shown necrosis , its around 37.50% and other 55 patient did not shows necrosis.

Table 4 gives explanation of about muscle infiltration , its shows that 10 patients shows not at all muscle infiltration, 61 patients shows 1 muscle involvement - so its accounted 69.30% and 9 patients shows 2 muscle infiltration.

Table 5 shows Modified Bloom- Richardson (MBR)grading and its divided according to this grading. MBR grading systems reflects predicts breast cancer recurrence risk reliability and there is acceptance concordance between MBR grade and onco-type diagnostic recurrence risk. It will shows 0-3 grading system. Grade1 : indicates more towards normal breast cells and is slow growing; Grade 2 not more

towards normal cells and growing faster compare to grade1; Grade 3 looks different to normal breast cells and fast growing. According to MBR grading grade 2 shows highest proportion and its counted 71.60%, so it will be 63 patient out of 88, grade 0

shows lowest ratio and accounted only 1 patient (1.10%), MBR grade-1 shows 14 patients- will be around 15.90%, MBR GRADE 3 shows there are 10 patient (11.40%).

Table 6 shows different histologic variant of breast carcinoma and it will be included Infiltrating Duct Carcinoma (IDC), Mucinous variant, Intracystic papillary variant and also shows Micro-papillary variants. Out of total 88 patient 73 patient shows IDC; So it will be around 83.00% and its the highest ratio compare to other variant , mucinous variant included 1 case(1.10%), intracystic papillary variant having 2 cases (2.30%), micro-papillary variant we got 2 cases (2.30%), fibrocystic variant we got 4 cases and its accounted 4.50%, phylloids showing 5 cases(5.70%). out of 88 cases mucinous is accounted only 1.10% and its shows lowest percentage among all.

In table 7 shows if there is lympho-vascular emboli(LVI) presents or absent. We found that out of all cases 47 cases shows LVI presents and its around 53.40% of all cases , other 41 cases LVI Were absent.

Table-1 : Gender Distribution:

Gender distribution	**No. of Patients**	**Percentage**
Male	1	1.10%
Female	87	98.90%
Total	**88**	**100%**

Table-2 : Side:

Side	**No. of Patients**	**Percentage**
Left	38	43.20%
Right	50	56.80%
Total	**88**	**100%**

Table-3 : Necrosis:

Necrosis	No. of Patients	Percentage
Present	33	37.50%
Absent	55	62.50%
Total	**88**	**100%**

Table-4 : MSL Infiltration:

MSL Infiltration	Frequency	Percentage
0	10	20.50%
1	61	69.30%
2	9	10.20%
Total	**88**	**100%**

Table - 5 : MBR Grade:

MBR Grade	Frequency	Percentage
0	1	1.10%
1	14	15.90%
2	63	71.60%
3	10	11.40%
Total	**88**	**100%**

Diagnosis:

Diagnosis	Frequency	Percentage
Idc	73	83.00%
Mucinous	1	1.10%
Intracystic Papillary	2	2.30%
Micropapillary	2	2.30%

Fibrocystic	4	4.50%
Physllodes	5	5.70%
Pagets	1	1.10%
Total	**88**	**100%**

Table- 7 : LV Emboli:

LV Emboli	No. of Patients	Percentage
Present	47	53.40%
Absent	41	46.60%
Total	**88**	**100%**

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age	88	29.00	83.00	49.2273	11.09388
largest m/s of tumor size	88	1.00	18.00	5.4023	3.03565
Tumor Size	88	.49	2639.00	137.20	332.53582
Largest Tumor Size	88	1.00	18.00	5.4023	3.03565
involved nodes	88	.00	25.00	2.8636	4.77345
Valid N (listwise)	88				

Nonparametric Correlations

Correlations

			Side	Necrosis
Spearman's rho	Side	Correlation Coefficient	1.000	-.036
		Sig. (2-tailed)	.	.742
		N	88	88
	Necrosis	Correlation Coefficient	-.036	1.000
		Sig. (2-tailed)	.742	.
		N	88	88

Correlations

			Side	Lymphnodes
Spearman's rho	Side	Correlation Coefficient	1.000	-.139
		Sig. (2-tailed)	.	.196
		N	88	88
	Lymphnodes	Correlation Coefficient	-.139	1.000
		Sig. (2-tailed)	.196	.
		N	88	88

Variables	**Spearman's Correlation value**	**P value**
Side vs Necrosis	-0.036	0.742
Side vs lymphnodes	-0.139	0.196

IMAGE – 1 : INVASIVE DUCT CARCINOMA WITH COMEDO NECROSIS

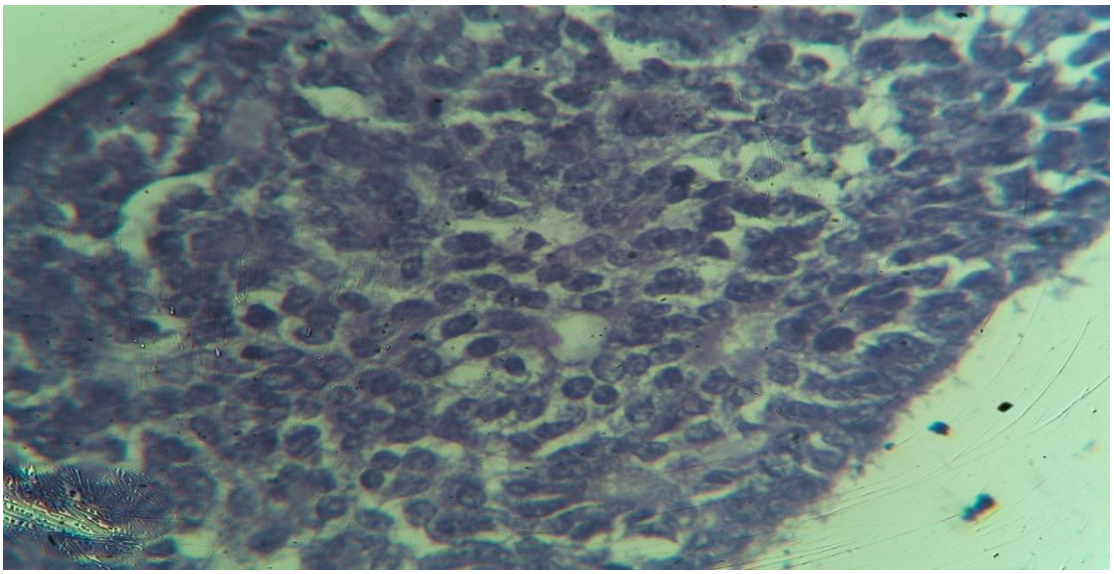

IMAGE – 2 : INVASIVE DUCT CARCINOMA – TUMOR CELLS IN HIGH POWER VIEW.

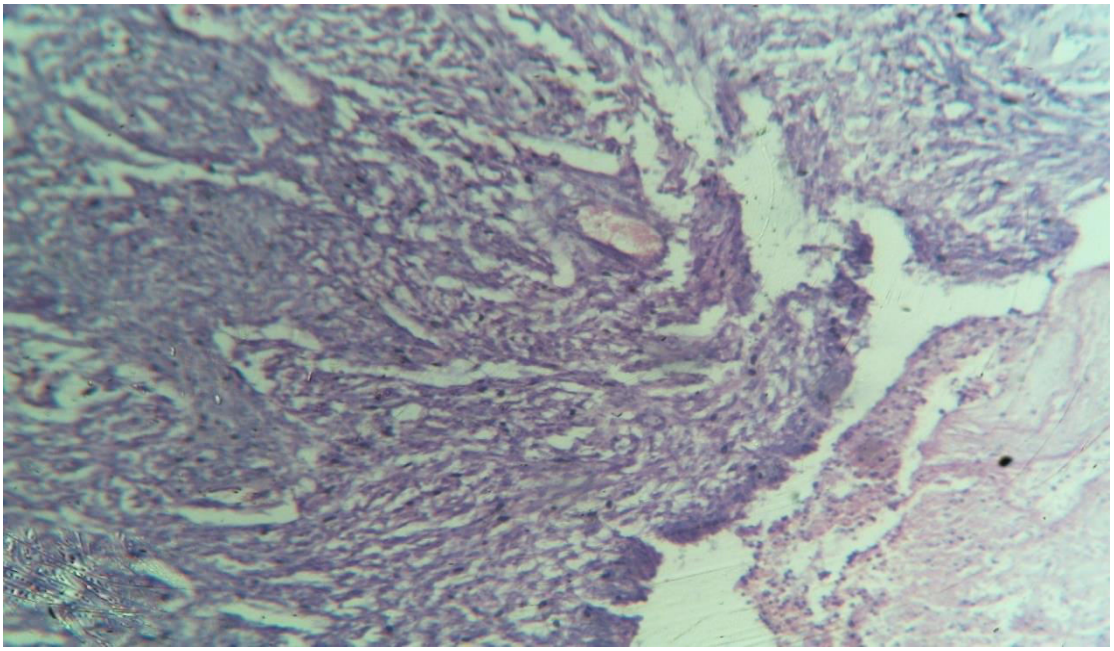

IMAGE – 3 : BODERLINE PHYLLOIDS.

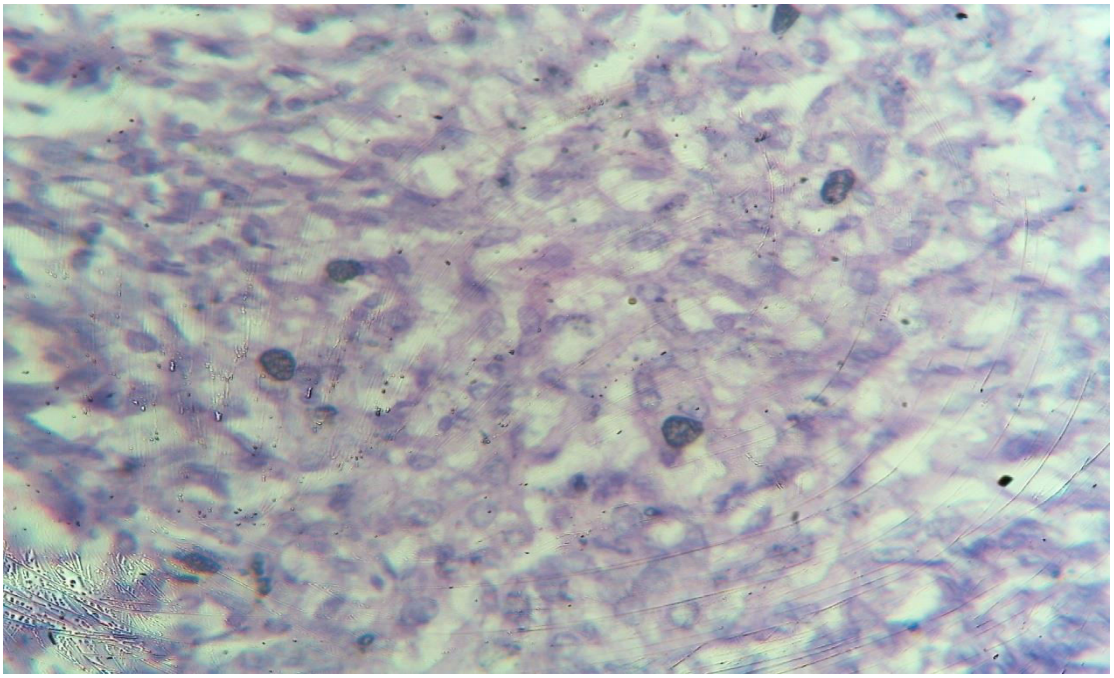

IMAGE – 4 : PHYLLOIDS IN HIGH POWER VIEW SHOWING TUMOR CELLS.

Discussion

We studied association between primary tumour size and the prevalence of metastases (to the lymph nodes) cohort of 88patients with invasive breast cancer. For cancers between approximately 0.4 and 18cm in size, straight correlation between tumour size

and the probability of nodal metastases; moreover, very small size cancers and large size cancers there were notable departures.

Ingender distribution out of 88 patient with 87 were female, it accounts approximate 98.90% of total patient and 1(1.10%) patient was male.

Among patients of breast cancer- cohort study showing primary tumour of size 1and 150 mm. There was a comparison between comparison between right to left side; Out of 88 cases right sided breast cancer more compared to left side its accounted 50 cases approximately 56.80% compared to 38(43.20%) is left sided breast cancer. In our study shows modified Bloom- Richardson (MBR)grading and its divided according to this grading. MBR grading systems reflects predicts breast cancer recurrence risk reliability and there is acceptance concordance between MBR grade and onco-type diagnostic recurrence risk. It will shows 0-3 grading system. Grade1 : indicates more towards normal breast cells and is slow growing; grade 2 not more towards normal cells and growing faster compare to grade1; Grade 3 looks different to normal breast cells and fast growing. According to MBR grading grade 2 shows highest proportion and its counted 71.60%, so it will be 63 patient out of 88, grade 0 shows lowest ratio and accounted only 1 patient (1.10%), MBR grade-1 shows 14 patients- will be around 15.90%, MBR GRADE 3 shows there are 10 patient (11.40%).

In our study we also shown that different histology variant of breast carcinoma and it will be included Infiltrating Duct Carcinoma (IDC), Mucinous variant, Intracystic papillary variant and also shows Micro-papillary variants. Out of total 88 patient 73 patient shows IDC; So it will be around 83.00% and its the highest ratio compare to other variant, mucinous variant included 1 case(1.10%), intracystic papillary variant having 2 cases (2.30%), micro-papillary variant we got 2 cases (2.30%), fibro-cystic

variant we got 4 cases and its accounted 4.50%, phylloids showing 5 cases(5.70%). out of 88 cases mucinous is accounted only 1.10% and its shows lowest percentage among alls. We have found that 53.40% of all cases , other 47% cases LVI Were absent.

The correlationin aggressiveness reflects the intrinsic growth properties of the underlying cancer stem cell population. In the conventional model, the lymph node metastases are markers of the aggressive nature of the in-breast cancer [1], under theparallel model this also holds true, but the size of the inbreast cancer is also a marker of the tendency to form nodalmetastases (i.e. is not a direct conduit of cancer spread) in the parallel model. Both the size of the breast cancer and the lymph node metastases are markers of the current (orsubsequent) occurrence of distant metastases. Only distantmeta stases are directly relevant in terms of mortality—in the absence of distant metastases, the patient cannot die of breast cancer, regardless of the number of nodes involved orthe size of the primary tumour. Under the parallel model, thepotential for distant metastases is an inherent property of thecancer stem cell population and neither the primary breast cancer nor the regional lymph nodes are source of metastases.This model is supported by recent molecular studies inbreast cancer [7] as well as in other cancer types such aspan creatic[8], colon[9] and skin (melanoma)[10].

Conclusion

In present study there are some cases were small tumors has metastasis to lymph nodes whereas big tumors has shown no metastasis. So lymph node involvement does not depend on tumor size but ability of particular tumor to metastasize. Even in small size of tumor which is mm in size can also show lymph node involvement.

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