International Journal of Clinical and Diagnostic Pathology

ISSN (P): 2617-7226
ISSN (E): 2617-7234
www.patholjournal.com
2020; 3(3): 158-162
Received: 10-06-2020
Accepted: 12-07-2020

Dr. Varadharajaperumal
Assistant Professor, Department of Pathology, Aarupadai Vedu Medical College & Hospital, Puducherry, India

Dr. K Siva
Assistant Professor, Department of Pathology, Aarupadai Vedu Medical College & Hospital, Puducherry, India

Dr. R Jawahar
Professor and HOD Department of Pathology, Aarupadai Vedu Medical College & Hospital, Puducherry, India

Dr. Dharmistha N Kapadiya
Assistant Professor, Department of Pathology, Mahatma Gandhi Medical College and Research Institute, Puducherry , India

Dr. Jeya Shambavi
Associate Professor, Department of Pathology, Aarupadai Vedu Medical College & Hospital, Puducherry, India

Corresponding Author:
Dr. K Siva
Assistant Professor, Department of Pathology, Aarupadai Vedu Medical College & Hospital, Puducherry, India

A comparative study of conventional anatomic staging with new prognostic staging of the American joint committee on cancer (AJCC) 8th edition on breast carcinoma in a tertiary Heath care centre of Puducherry

Dr. Varadharajaperumal, Dr. K Siva, Dr. R Jawahar, Dr. Dharmistha N Kapadiya and Dr. Jeya Shambavi

DOI: https://doi.org/10.33545/pathol.2020.v3.i3c.274

Abstract
The American joint committee on cancer (AJCC) eighth edition staging system integrates clinical laboratory testing for a more comprehensive and personalized prognostic staging criteria. This study aims to revaluate the clinic pathological character of tumour and prognostic staging system. Retrospective analysis was conducted on patients with invasive breast carcinoma for the period of four years from August 2016 – July 2020, conventional anatomic staging were restaged to prognostic staging. total 77 cases 23 (29.9%) cases stage unchanged, 18 (23.4%) cases Down staged and 36 (46.7%) cases upstaged. 36.5% cases of grade II were down staged, as it is ER, PR positive and Her 2 Neu negative, 90.5% of grade III were upstaged all cases were triple negative. More sample size and survival rate estimation along with present study will provide more insight toward the changes and impact on tumour biology and predictive value of prognostic staging of 8th edition AJCC.

Keywords: Breast carcinoma, hormone receptor, AJCC, anatomic staging, prognostic staging

1. Introduction
Breast cancer is the most common carcinoma, of all cancers in women globally. It is more than twice as common as cancer at any other site [1]. Breast cancer stage provides a concise summary of the disease at the time of diagnosis and/or surgery. It conveys how much cancer is present, where it is located, and highlights important tumour characteristics. It also allows for efficient communication between clinicians and provides a framework for assessing and relaying prognostic information based on the sum of the tumour and disease features [2]. Traditional, the American Joint Committee on Cancer (AJCC) anatomical staging system were used based on TNM (tumour size (T), nodal status (N), metastases (M)) staging system categorizes the extent and location of a breast cancer tumour without needing clinical laboratory testing [3]. Although the anatomic extent of disease alone may not define the entire prognosis, it has remained a key prognostic factor in breast cancer [2]. In addition to anatomic staging guidelines the utility of several biologic markers such as estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor-2 (HER2) and Histological grades are also included in the eighth edition the American Joint Committee on Cancer (AJCC) breast cancer staging system. Consequently, breast cancer patients are assigned a prognostic stage based on information gathered from TNM classification and the four above said biomarkers. The AJCC eighth edition staging system integrates clinical laboratory testing for a more comprehensive and personalized prognostic staging criteria [3]. This study aim to revaluate the clinical value of clinic pathological character of tumour and prognostic staging system.

2. Material Methods
After obtaining institutional review board and ethical committee approval, a retrospective analysis was conducted to patients with invasive breast carcinoma who underwent surgery as primary modality of treatment for the period of four years from August 2016 – July 2020.

clinical data and pathological information such as tumour size, tumour histology, tumour grade, Lymph vascular invasion (LVI), perineural invasion (PNI), no of lymph node dissected, lymph node tumour positivity, Extra nodal extension (ENE). Immunohistochemistry (IHC) on Hormonal receptor such as oestrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor-2 (HER2) were retrieved from medical records department. Previous Tumour anatomical stage pTNM were restaged to new prognostic staging system of AJCC based on Tumour size (pT), nodal status (pN), ER, PR, Her 2, receptor status Nottingham histological tumour grade [4].

3. Observation and Result

A total of 77 patients diagnosed as carcinoma Breast who underwent surgery as primary modality of treatment were included in the study.

Table 1: Clinical and Pathology Characteristics of Studied Breast Carcinoma (N= 77)

Parameter	Variables	No (%)
Age (yrs.)	< 40	7 (10%)
	≥40	70 (90%)
Menopausal Status	pre-menopausal	19 (24.7%)
	post-menopausal	58(75.3%)
Laterality	left	39(50.6%)
	Right	38(49.4%)
Tumour histology	Invasive carcinoma NST	70(90.9%)
	Mucinous carcinoma	3(3.9%)
	Metaplastic carcinoma	2(2.6%)
	invasive lobular carcinoma	1(1.3%)
	Neuroendocrine Carcinoma	1(1.3%)
Nottingham histology grade	Grade I	4(5.2%)
	Grade II	52(67.5%)
	Grade III	21(27.3%)
Insitu component	Present	32(41.6%)
	Absent	45(58.4%)
DCIS nuclear grade(N=32)	low	2 (6.25%)
	intermediate	14(43.75%)
	High	16(50%)
DCIS pattern (N=32)	Papillary	3(9.4%)
	Cribriform	06 (18.8%)
	Solid	04 (12.5%)
	Comedo	19(59.3%)
LVI	Identified	32 (41.6%)
	Not identified	45(58.4%)
PNI	Identified	04 (5.2%)
	Not identified	73 (94.8%)
Lymph node metastasis	Identified	36 (46.8%)
	Not identified	41 (53.2%)
ENE	Identified	08 (10.4%)
	Not identified	69 (89.6%)
Tumour size pT	T 1	27 (35%)
	T 2	47 (61%)
	T 3	02 (2.6%)
	T 4	01 (1.4%)
Node status pN	N0	42 (55.3%)
	N 1	24 (31.1%)
	N 2	08(10.2%)
	N 3	03 (3.4%)

All the subjects were female and majority of the cases were observed in 5th decade (35.0%) followed by 7th decade (33.7%). The age of subjects ranged from 30 to 80 years , with mean age of 54 years; 7 (10%) cases were of < 40 years of age and 70 (90%) cases were of ≥ 40 years of age. 19(24.7%) cases were premenopausal and 58 (75.3%) were post-menopausal.

Out of 77 cases 39 (50.64%) were on left side and 38 cases (49.36%) were of right sided. Tumour size ranges from 0.2 cm to 6 cm and average size of 2.6 cm, predominant tumour histology were invasive carcinoma NST 70 cases (91%) of which 5 cases were EIC component were observed, followed by 3(3.9%) cases of Mucinous carcinoma of which 2 cases presented with micro papillary pattern and one case of type A Mucinous carcinoma, 2 cases of Metaplastic carcinoma and 2(2.6%) cases each of invasive lobular carcinoma and Neuroendocrine carcinoma (chromogranin and synaptophysin positive). Predominant Nottingham histological grade observed were grade 2 , 52(67.5%)cases, followed by 21(27.3%) cases of grade 3 and 4(5.2%)cases of grade I. Insitu DCIS component observed in 32(41.6%) cases with high nuclear grade with Comedo pattern(grade 3 – 19 (59.3%) cases) as predominate observation, in all the cases surgical margins were negative. Average no of lymph node dissected out were 20 and 36 (46.8%) cases showed lymph node metastasis and 32 (41.6%) lymph vascular invasion and of which 08 (10.4%) cases showed ENE. In 04 (5.2%) cases PNI observed. Predominant Tumour stage was pT2 47 (61%) cases followed by 27 (35%) cases of P T2 , 02 (2.6%) cases pT3, and 01 (1.4%) of pT4.Predominat Node staging observed was 42 (55.3%) cases of pN0, followed by 24 (31.1%) cases of pN1, 08(10.2%) cases of pN2, and 03 (3.4%) cases of pN3.

Table 2: Observation on hormone receptor status

IHC ER, PR, Her 2 receptor status (n=77)		
ER status		N (%)
	Positive	43 (55.8%)
	Negative	34 (44.2%)
PR status		
	Positive	35 (45.5%)
	Negative	42 (54.5%)
Her 2 Neu		
	Positive	27 (35%)
	Negative	50 (65%)

Immunohistochemistry was performed on all 77 cases of which individual hormone receptor status as follows, 43 (55.8%) cases were ER positive, and 34 (44.2%) cases were ER negative, 35 (45.5%) cases were PR positive, 42 (54.5%) cases were PR negative, 27 (35%) cases were Her 2 Neu positive, 50 (65%) cases were PR negative.

Table 3: Observation based on anatomic and prognostic staging.

Anatomic staging	No (%)	Prognostic staging	No (%)
I A	17 (22%)	I A	10 (13%)
II A	32 (41.7%)	I B	22 (28.5%)
II B	17 (22%)	II A	9 (11.7%)
III A	7 (9.1%)	II B	7 (9.1%)
III B	1 (1.3%)	III A	19 (24.7%)
III C	3 (3.9%)	III B	5 (6.5%)
		III C	4(6.5%)

Based on original anatomic staging out 77 cases predominant cases staged as stage II A 32(41.7%), followed by equally distributed 17 (22%) cases among stage IA and IIB,7(9.1%) cases of stage IIIA, 3 (3.9%) cases of stage IIIC and 1 (1.3%) case of stage IIIB, all the 77 cases were restaged as per 2018 AJCC Prognostic staging including Tumour histological grade, Hormone receptor status such as ER, PR, Her 2 along with anatomic staging. Observations as follows predominate no of cases were of stage IB- 22 (28.5%), followed by 19 (24.7%) cases of IIIA, 10 (13%) cases of stage IA, 9 (11.7%) IIA, 7 (9.1%) II B, 5 (6.5%) and 4 (6.5%) cases of stage III B, III C.

Table 4: Comparison between AJCC anatomic staging and prognostic staging.

Anatomic staging	No (%)	Prognostic staging	No (%)
I A	17	I A	10 (58.9%)
		I B	05 (29.5%)
		II A	02(11.7%)
II A	32	I B	12 (37.5%)
		II A	05 (15.6%)
		II B	03 (9.4%)
		III A	12 (37.5%)
II B	17	I B	05 (29.5%)
		II A	01 (5.9%)
		II B	02(11.7%)
		III A	06 (35.3%)
		III B	02(11.7%)
		III C	01 (5.9%)
III A	7	II A	01 (14.3%)
		II B	02 (28.6%)
		III A	01 (14.3%)
		III B	02 (28.6%)
		III C	01 (14.3%)
III B	1	III B	01 (100%)
III C	3	III B	01 (33.3%)
		III C	02 (66.7%)

Out of total 77 cases 23 (29.9%) cases stage unchanged between anatomical staging and prognostic staging, 18 (23.4%) cases were Downstaged and 36 (46.7%) cases were upstaged.

Table 5: Correlation between histological grading and prognostic staging system

Tumour histological grade No (%)(N=77)	Stage unchanged N (%)	Downstaged N (%)	Upstaged N (%)
I - 4 (5.2%)	2 (50%)	2 (50%)	00
II - 52 (67.5%)	17 (32.7%)	19 (36.5%)	16 (30.8%)
III - 21 (27.3%)	2 (9.5%)	00	19 (90.5%)

Out of 77 cases predominant Nottingham histology grade observed was Grade 2 - 52 (67.5%) cases, followed by 21 (27.3%) cases of grade 3, and 4 (5.2%) cases of grade 1. Out of 52 (67.5%) cases of grade 2, 19 (36.5%) cases were down staged, 17 (32.7%) cases stage without any change and 16 (30.8%) cases were upstaged. Out of grade 3 of III - 21 (27.3%) cases, 19 (90.5%) cases were upstaged and 2 (9.5%) cases were without any change in staging. Out of 4 (5.2%) cases of grade 1, 2 (50%) cases down staged and 2 (50%) were without any change in staging.

Table 6: Correlation between Hormone receptor status and prognostic staging

IHC ER, PR, Her 2 Status (N=77)		Stage unchanged N (%)	Downstaged N (%)	Upstaged N (%)
ER Positive ,PR Positive ,Her 2 Positive	07 (9%)	1 (14.3%)	5 (71.4%)	1 (14.3%)
ER Positive ,PR Positive ,Her 2 Negative	28 (36.4%)	12 (42.8%)	15 (53.6%)	1 (3.6%)
ER Positive ,PR Negative ,Her 2 Negative	04 (5.2%)	2 (50%)	2 (50%)	0
ER Positive ,PR Negative ,Her 2 Positive	04 (5.2%)	2 (50%)	0	2 (50%)
ER Negative ,PR Negative ,Her 2 Positive	15 (19.5%)	4 (26.7%)	0	11 (73.3%)
ER Negative ,PR Negative, Her 2 Negative	19 (24.7%)	0	0	19 (100%)

Out of 77 cases majority of the cases fall under the group of ER, PR positive, and Her 2 negative 28 (36.4%) cases out of which 15 (53.6%) cases were down staged, 12 (42.8%) cases were without any change in stage, 1 (3.6%) case was upstaged as it is histological grade 3. Second predominant group includes triple negative 19 (24.7%) cases, all the cases were upstaged. Third group 15 (19.5%) cases of ER Negative, PR Negative, and Her 2 Positive in which 11 (73.3%) cases were upstaged as both ER and PR negative and 4 (26.7%) cases were stage unchanged.

Fourth group 07 (9%) cases of all three, ER, PR, Her 2 positive in which 5 (71.4%) cases were down staged 1 (14.3%) case each of stage unchanged and upstaged. Fifth and sixth group share 04 (5.2%) cases each in which ER Positive, PR, and Her 2 Negative group 2 (50%) cases each stage unchanged and down staged as in this group ER

positive and Her 2 negative. Next group in which ER Positive, PR negative, and Her 2 positive group 2 (50%) cases each stage unchanged and up staged as in this group and Her 2 positive.

4. Discussion

In present study total 77 cases of diagnosed breast carcinoma subjects who underwent surgery as primary modality of treatment were included and retrospectively analysed. In present study the mean age of subjects ranged from 30 – 80 years, mean age of 54 years, 70 (90%) cases were ≥ 40 years of age and predominantly postmenopausal patients 58(75.3%) [3, 56, 7, 9, 13]. clinical characteristics of tumour observed were left side dominance 39 cases (50.64%) [9, 13], tumour size ranged from 0.2 to 6 cm with average size of 2.6 cm, predominant tumour histology and tumour grade observed was invasive carcinoma NST 70 (90.9%) [9], cases. with grade 2 was 52 cases (67.5%) [3, 6, 7, 9, 10]. Insitu component were observed in 32 (41.6%) cases with nuclear grade of 3 in 19 cases 59.3%). Average no of lymph node dissected was 20 [13] Predominant tumour size and nodal stage was pT2 47 (61%) cases [5, 13] and pN0 42 (55.3%) cases [3, 5, 10]. Regarding hormone receptor status, predominate cases were ER positive 43 (55.8%) [3, 5, 7, 9, 10, 13], PR negative 42 (54.5%) cases and Her 2 negative 50 (65%) cases [3, 5, 7, 9, 10, 13], ER positive , PR positive and her 2 negative 28 (36,4%) cases combination was most observed followed by tripe negative combination 19 (24.7%) cases [6]. Based on original anatomic staging out 77 cases predominant cases staged as stage II A 32(41.7%) [5], followed by equally distributed 17 (22%) cases among stage IA and IIB [5], prognostic staging as follows stage IB- 22 (28.5%) [5], followed by 19 (24.7%) cases of IIIA, 10 (13%) cases of stage IA, 9 (11.7%) IIA, 7 (9.1%) II B, comparison between anatomic and prognostic staging results observations were 23 (29.9%) cases stage unchanged between anatomical staging and prognostic staging, 18 (23.4%) cases were Down staged as cases were ER ,PR positive and 36 (46.7%) [3, 13] cases were upstaged as these cases were grade 3 and triple negative. based on correlation between tumour histological grade with stage change, 52 (67.5%) cases of grade 2, 19 (36.5%) cases were down staged, 17 (32.7%) cases stage without any change and 16 (30.8%) cases were upstaged. Out of grade 3 of III - 21 (27.3%) [3, 5, 7] cases, 19 (90.5%) cases were upstaged and 2 (9.5%) cases were without any change in staging. Out of 4 (5.2%) cases of grade 1, 2 (50%) cases down staged and 2 (50%) [3, 5, 7] cases were without any change in staging. under the group of ER, PR positive, and Her 2 negative 28 (36.4%) cases out of which 15 (53.6%) [3, 5, 7-11, 13] cases were down staged, triple negative 19 (24.7%) cases, all the cases were upstaged [3, 5, 7-11, 13]. 15 (19.5%) cases of ER Negative, PR Negative, and Her 2 Positive in which 11 (73.3%) cases were upstaged as both ER and PR negative, 07 (9%) cases of all three, ER, PR, Her 2 positive in which 5 (71.4%) cases were down staged [3,5-11, 13].

5. Conclusion

Introduction of tumour histological grade and ER, PR, Her 2 receptor status in AJCC 8th edition give more insight on tumour biology and helps in personalizing the treatment. It helps in avoiding unnecessary treatment complication for Downstaged cases and proper treatment for upstaged cases. More sample size and survival rate estimation along with present study will provide more insight toward the changes and impact on tumour biology and predictive value of prognostic staging of 8th edition AJCC.

6. Acknowledgement

I acknowledge surgery department faculty, Radio diagnosis faculty and medical record department faculty.

7. References

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