Original Article ▌

COMPARATIVE EVALUATION OF ROBINSON'S CYTOLOGICAL GRADING WITH ELSTON AND ELLIS' NOTTINGHAM MODIFICATION OF BLOOM RICHARDSON HISTOPATHOLOGY GRADING FOR BREAST CARCINOMA

Pandya Amrish N[1], Shah Neelam P[2]

Author's Affiliation:
[1] Professor & Head, IHBT department, [2] 4th year resident pathologist, Pathology department, Government Medical College, Surat

Correspondence:
Dr. Amrish N Pandya
Professor & Head, IHBT department, Government Medical College, Surat
E-mail: dramrish21@gmail.com; dr_amrish21@yahoo.com

ABSTRACT

Background: Cytological grading of mammary carcinoma provides useful information about prognosis. It also helps in selecting therapy. Aim: This study has been carried out to compare correlation of Robinson's cytological grading with modified Bloom Richardson grading system of infiltrating ductal carcinoma in histology.

Material and method: 59 FNAC smears of, invasive breast carcinoma, were graded according to the Robinson's grading system. Corresponding histology sections were graded according to Elston and Ellis' Nottingham modification of Bloom Richardson method.

Result: On cytology, there were 24, 26 and 9 cases of grade I, II and III tumor respectively while on histology 25, 24 and 10 cases of grade I, II and III tumor respectively. The concordance rate between cytology and histology grades were 79.16%, 73.07% and 66.66% for grade I, II and III tumor respectively. Absolute concordance rate was 74.57%.

Conclusion: Apart from being simple and non-invasive, cytologic grading method is comparable with histologic grading system. It might provide information about aggressiveness of tumor and is useful parameter while selecting neo adjuvant chemotherapy in patients of breast carcinoma.

Key words: breast cancer, FNAC, Elston and Ellis's Nottingham modification of Bloom-Richardson method, infiltrating ductal carcinoma, mammary carcinoma, Robinson's cytology grading.

INTRODUCTION

Breast cancer is the commonest cancer of urban Indian women and the second commonest cancer in the rural women next to cervical cancer. Owing to the lack of awareness of this disease and in absence of a breast cancer screening program, the majority of breast cancers are diagnosed at a relatively advanced

stage.[1] For primary diagnosis FNAC becomes standard method in recent years.

The standard prognostic factor recognized by National Cancer Institute in 1990, include lymph node status, tumor size, nuclear grade, steroid receptor content, tumor type and cellular proliferation rate.[2]

Now a days Grading of breast cancer on fine needle aspiration material is being attempted because of the changing modalities for treatment of breast carcinoma such as preoperative neo adjuvant chemotherapy. Knowledge of the grade of the tumor would help in judicious use of chemotherapy. In India many patients still come with advanced disease requiring preoperative chemotherapy and/or radiotherapy. As the grade become higher, it gives more response to neo adjuvant therapy. The cytologic grade may provide information about aggressiveness/biological behavior of tumor, and also provides possibility of lymph node metastasis.[3] Assigning a tumor grade to breast cancer provides important prognostic information and guides optimal therapy.[4]

Histological grading of breast carcinoma using the Nottingham method described by Elston and Ellis (Elston's modified Bloom and Richardson method) is a widely accepted tumor grading system and has been found to have good prognostic correlations.[5] Nowadays, attempts have been made to determine various prognostic parameters on FNA materials.[3,5] Ideally, criteria for nuclear grading as prognostic parameter should include following: 1.ease of use, 2.high reproducibility, 3.consistency whether using surgical or cytopathology material, 4.universal availability and applicability, 5.inexpensive application, 6.verification through a large database of patient with breast cancer who have followed up long period.[6]

In present study, Robinson's cytological grading was done on cytology and compared with modified Bloom and Richardson system on histopathology sections.

MATERIALS AND METHODS

This study was ethically approved by concerned authority.

This was cross-sectional study. In this study, 530 patients with palpable breast lump, including 47 had bilateral breast lumps. So, total 577 FNACs were performed from 530 patients. Both females and males were included in this study and metastasis in breast was excluded. Out of 577 FNAC cases, 110 cases were found cytologically mammary carcinoma, 68 of them were correlated histologically. Remaining was not correlated in histology because they lost to follow-up for further management. Comparison of Robinson's grading with modified Bloom Richardson grading was possible only in 59 cases because remaining 9 cases were either ductal carcinoma in situ or received neo adjuvant chemotherapy.

Each patient was subjected to FNAC of breast lump under aseptic precautions after explaining the procedure and taking written consent.

FNA was performed by using a 10ml disposable syringe and 22/23-gauge needle. No local anesthesia was given during the procedure. FNA smears were stained with H & E, Pap and MGG stains. Tissue sections obtained from mastectomy specimens were stained with H & E stain. FNAC smears were evaluated for cytological grading according to Robinson's grading system (table 1) and histologic sections were evaluated for grading according Elston and Ellis modification of Bloom Richardson grading system (table 2). Comparison was done between these two grading systems and concordance rates were calculated between each grade separately and absolute concordance was calculated between all three corresponding grades. Kappa (κ) coefficient was calculated for each grade to compare the agreement.

Table 1: Robinson's cytologic grading system

Cells	Score 1	Score 2	Score 3
Dissociation	Mostly in cluster	Mixture of single & cell Clusters	Cells mostly Single
Cell size	1-2 x RBC size	3-4 x RBC size	>5 x RBC size
Cell uniformity	Monomorphic	Mildly Pleomorphic	Pleomorphic
Nucleoli	indistinct	Noticable	Prominent
Nuclear margin	smooth	Folds	Buds/Clefts
Chromatin	vesicular	Granular	Clumped and Cleared

Grade 1- score 6-11, grade 2- score 12-14, grade 3- score 15-18

Table 2: Elston and Ellis modified Bloom-Richardson grading system

Feature	Score 1	Score 2	Score 3
Tubule formation	>75%	10-75%	<10%
Nuclear pleomorphism	Small, regular uniform cells	Moderate variation in size/shape	Marked nuclear pleomorphism
Mitosis per 10 hpf in 44mm field diameter	0-5	6-10	>/=11

Histologic grade: Grade I – score 3-5 well differentiated; Grade II- score 6-7 moderately differentiated; Grade III – score 8-9 poorly differentiated.

RESULTS

Distribution of cases, according to cytologic Robinson's grading, modified bloom Richardson histologic grading and comparison between both grading systems were shown in table 3. In this study, cytologically, 24 (40.68%), 26 (44.07%) and 9 (15.25%) cases were in grade I, II and III respectively. In grade I(fig 1) ductal cells are small, in cluster with smooth nuclear membrane. In grade II (fig 2), ductal cells are both in cluster and scattered along with some pleomorphism. In grade III (fig 3) cells are large, pleomorphic with clumped nuclear chromatin and prominent nucleoli. Histologically, 25 (42.37%), 24 (40.68%) and 10 (16.95%) cases were in grade I, II and III respectively. Concordance rate between grade I tumors in cytology and histology was 79.16% (19 cases), for grade II tumors, was73.07% (19 cases) and for grade III tumors it was 66.66% (6 cases).The absolute concordance rate between all three corresponding grades was 74.57% (44/59).

Table 3: Distribution of cases according to cytology and histology grading along with comparison between two grading system

Cytologic grade (CG)	Number of cases in cytologic grading (%)	Cases in histologic garding			Concordance rate (%)
		Grade I	Grade II	Grade III	
I	24 (40.68)	19	4	1	79.16
II	26(44.07)	4	19	3	73.07
III	9(15.25)	2	1	6	66.66
Total	59	25(42.37%)	24(40.68%)	10(16.95%)	
Absolute concordance					44/59 (74.57%)

Table 4 shows strength of agreement between cytological and histologic grades by statistical analysis using kappa statistics. Kappa value for grade I tumors is 0.61 which indicates substantial agreement between cytological and histological grading systems. Kappa value for grade II and III tumors are 0.58 and 0.56 respectively which indicates moderate agreement between cytological and histological grading systems.

Therefore it can be stated that cytologic grading is comparable to histology grading of tumors to assess the tumor behavior and prognosis.

Table 4: Agreement between cytological and histologic grades by statistical analysis (kappa statistics)

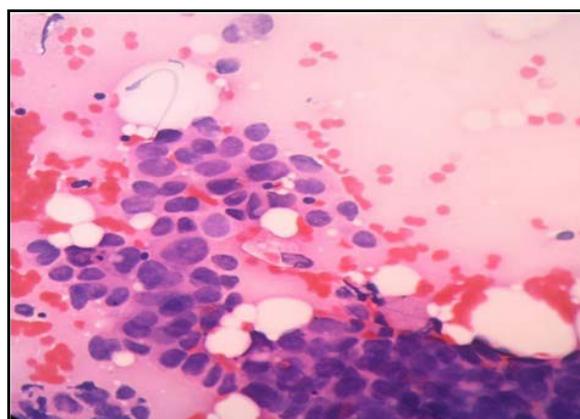| Grade	Kappa value (95% CI) for concordance	Standard error	Strength of agreement
I	0.61 (0.412-0.820)	0.104	substantial
II	0.58 (0.374-0.793)	0.106	moderate
III	0.56 (0.271-0.850)	0.147	moderate

Figure 1: Cytology of carcinoma breast with cytologic grade I showing loosely cohesive cluster of mild pleomorphic ductal cells with smooth nuclear membrane and indistinct nucleoli (H & E 400 x)
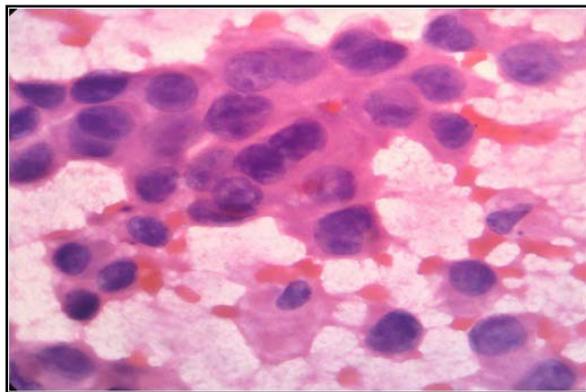
Fig 2: Cytology of carcinoma breast with cytologic grade II showing loosely cohesive cluster as well as single cells with moderate pleomorphism, slighty irregular nuclear membrane and noticable nucleoli (H & E 1000 x)
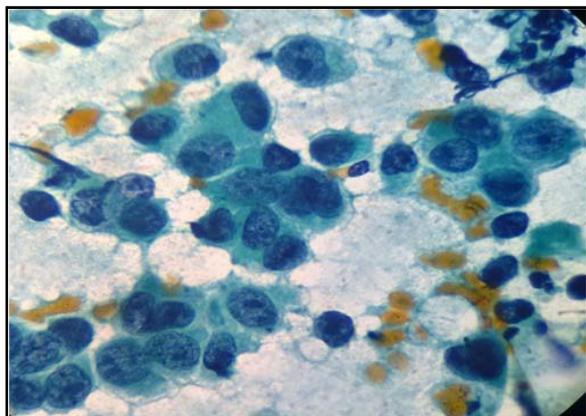

Fig 3: Cytology of carcinoma breast with cytologic grade III showing markedly pleomorphic ductal cells irregular nuclear margin and prominent nucleoli coarse chromatin (PAP 1000 x)

DISCUSSION

A palpable breast lump, whether benign or malignant, is a cause of anxiety to patient. Therefore accurate pathological diagnosis is crucial for further treatment and estimation of an outcome. The rising incidence of breast cancer continues to concern. There are three main objectives for investigations in breast carcinoma, to establish correct diagnosis and staging the disease, to detect breast cancer in very early stage & to predict the prognosis. Combination of clinical examination, mammography, and FNAC 'triple diagnosis' in parallel lead to improved diagnosis. If all three investigations are in agreement, diagnostic accuracy is over 99%.[7] Definitive treatment is often based on cytological diagnosis without histological confirmation, unless there is

disagreement between cytology and clinical and/or mammographic assessment.[7]

Cell dissociation is indicator of cell cohesion and loss of cohesion facilitates vascular infiltration by tumor cells and increases incidence of lymph node metastasis.[3] A number of studies have shown that neoplasm with greater cell dissociation show higher incidence of regional lymph node metastasis.[8, 9] There are many cytologic grading system for mammary carcinoma and they have good correlation with Elston and Ellis grading system.[10] Robinson's method was considered better because of its more sensitivity, simplicity and more objective set of criteria and easy reproducibility.[11,12]

Table 5: Comparison of concordance rates reported in different series

Authors	Concordance rate (%)
Robinson et al (1994)[17]	56.9
Das et al (2003)[12]	71.2
Chabbra et al (2005)[18]	65.0
Meena et al (2005)[19]	59.1
SK Sinha (2009)[20]	69.5
Nazoor Khan et al (2009)[3]	89.1
TS Rekha et al (2011)[19]	82.0
Present study (2010-2011)	74.57

There were many studies showing prognostic value of histologic grading system for infiltrating ducal carcinoma.[10] Thus FNAC is helpful in predicting histologic grade and thus also predict biologic behavior and useful parameter in selecting neo adjuvant therapy. High cytologic score also predict higher potential for lymph node metastasis.[10]

Some studies show association of tumor grade with ER/PR content.[13, 14] Low cytoprognostic scores are associated with positive ER and PR. High cytoprognostic score is associated with positive expression of her2/neu, p53, and ki-67.

Utility of cytologic grading is to detect fast growing grade III tumors which are more likely to respond to chemotherapy than low grade (slow growing) tumor. Slow growing tumor may be better suited to pretreatment with tamoxifen.[3] Preoperative neo adjuvant chemotherapy is becoming common for treatment of breast cancer. So, it is desirable to grade tumor before surgery. So, most appropriate regime can be selected.[15]

In present study, the absolute concordance rate between all three corresponding grades was

74.57% (44/59 cases). Discordance was found in five cases in grade I, seven cases in grade II, and three cases in grade III. Thus total discordance was seen in 15 cases out of 59 cases. Concordance rate between Robinson's grading and histologic grading in different studies was shown in table 3.

We also used kappa statistical analysis to find out strength of agreement between cytological and histologic grades. As shown in table 4 Kappa values for grade I, II and III tumors were 0.61, 0.58 and 0.56 respectively. Kappa values were interpreted according to Landis and Koch classification, which indicates substantial agreement for grade I tumors between cytological and histological grading systems. While Kappa value for grade II and III tumors indicate moderate agreement between cytological and histological grading systems. Stronger correlation was noted between grade I tumors than grade II and III tumors.

Thus besides from having minimal subjective discomfort, insignificant complications, negligible risk of tumor spread, rapidity of diagnosis, utility for multiple lesions, readily repeatability, high accuracy of FNAC; FNAC grading is comparable with histology grading and is useful in assessing the tumor behavior and prognosis and guiding neo adjuvant chemotherapy. Now-a-days, attempts have been made to determine various prognostic parameters on FNA materials.[4,6] The National Cancer Institute (NCI), Bethesda, sponsored conference had also recommended that tumor grading on FNA material should be incorporated in FNA reports for prognostication.[16]

CONCLUSION

Apart from being simple and non-invasive cytologic grading method is comparable with histological grading system and might provide information about aggressiveness of tumor and is useful parameter while selecting neo adjuvant chemotherapy in patients of breast carcinoma.

REFERENCES

1. Agarwal G, Ramakant P. Breast Cancer Care in India: The current scenario & the challenges for future. Breast Care (Basel). 2008; 3(1): 21-7.
2. Shahla Masood. Assessment of prognostic factor in breast FNA: Am J Clin Pathol 2000; 113 (suppl 1), s84-s96
3. Khan,N., Afroz, N., Rana,F., Khan, M.A. Role of cytologic grading in prognostication of invasive breast carcinoma: journal of cytology. 2009;26(2):65-8
4. Lingegowda, JB, MuddeGowda, PH, Ramakantha CK, Chandrasekar, HR. Cytohistological correlation of grading in breast carcinoma. Diagn. Cytopathol.2011; 39: 251–7.
5. Elston CW, Ellis IO.Pathological prognostic factors in breast cancer: I: The value of histological grade in breast cancer: Experience from a large study with long-term follow-up. Histopathology.1991; 19: 403–10.
6. Dabbs DJ. Prognostic information from fine needle aspiration biopsy of breast carcinoma. Am J Clin Pathol. 2000 May; 113(5 Suppl 1):S76-83.
7. Svante R.Orell, Gregory F. Sterrett, Darrel Whitaker. Fine needle aspiration cytology. 4th ed. New Delhi: Reed Elsevier India Private Limited, 2005:148.
8. Yu GH, Cajulis RS, DeFrias DVS. Tumor cell (dys) cohesion as a prognostic facto in aspirate smears of breast carcinomas. Am J Clin Pathol 1998; 109 ;315-9.
9. Yu, G. H., Lawton, T. J., Pasha, T. L. and Reynolds, C.Intercellular adhesion molecule expression in ductal carcinoma of the breast. Diagn. Cytopathol, 2000; 23: 73–76.
10. Antonio RF, Ricardo GC, Diego MP, Maria Jose, et al. Robinson cytologic grading of invasive ducal breast carcinoma correlation with histologic grading system and regional lymph node metastasis. Acta cytol 2005; 49:149-53.
11. Wani FA, Bhardwaj S, Kumar D, Katoch P. Cytological grading of breast cancers and comparative evaluation of two grading systems. J of Cytology.2010; 27(2):55-8.
12. Das AK, Kapila K, Dinda AK, Verma K. Comparative evaluation of grading of breast carcinomas in find needle aspirates by two methods. Indian J Med Res 2003; 118:247-50.
13. Ruibal A, Arias JI. Histologic grade in breast cancer: association with clinical and biological features in a series of 229 patients. Int J Biol Markers 2001;16;56-61.
14. Thike Aa,Chng MJ. Immunohistochemical expression of hormone receptors in invasive breas carcinoma:correlation of results of H-score with pathological parameters. Pathology 2001; 33:21-5.
15. Vidhi bhargava, Manjula Jain, Kiran Agarwal, Thomas S, Smita singh.Critical appraisal of cytological nuclear grading in carcinoma of breast and its correlation with ER/PR expression. Journal of cytology 2008;25(2):58-61.
16. Abati A, Abele J, Bacus SS, Bedrossian C, Beerline D, Bibbo M, et al. The uniform approach to breast fine-needle aspiration biopsy. Diagn Cytopathol. 1997; 16(4):295-311.
17. I.A. Robinson, G. McKee, A. Nicholson, P.A. Jackson, M.G. Cook, J. D'Arcy, et al. Prognostic value of cytological grading of fine needle aspirates from breast carcinomas. Lancet.1994; 343: 947–9.
18. Chhabra S, Singh PK, Agarwal A, Bhagoliwal A, Singh SN: Cytological grading of breast carcinoma - A multivariate regression analysis. Journal of Cytology 2005; 22(2):62-5.
19. TS Rekha, NM Nandini, Murali Dhar. Validity of Different Cytological Grading Systems of Breast Carcinoma - a Hospital-based Study in South India. Asian Pacific J Cancer Prev, 12, 3013-16.
20. Sinha SK, Sinha N, Bandyopadhyay R, Mondal SK (2009). Robbinson's Cytological grading on aspirates of breast Carcinoma: Correlation with Bloom Richardson's histological grading, J Cytol. 26; 4: 140-3.