

Comparative Evaluation of Three Cytological Grading Systems for Carcinoma Breast

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Abstract

Background: Fine needle aspiration cytology is an important tool in the diagnosis, prognosis and management of breast carcinoma. It has been recommended that cytological grading should be included in the FNA reports to know the tumor aggressiveness and prognostication. Among the many cytological grading systems existing, there is still no agreement on the most reliable system. *Aim:* The study was undertaken to evaluate three cytological grading systems and correlate with histological grading by Nottingham modification of Scarff Bloom Richardson (SBR) method. *Materials and Methods:* Cytological grading by Robinson's grading, Fisher's modification of Black nuclear grading and Howell grading systems was done on 50 carcinoma breast cases. Histological grading by Nottingham modification of SBR grading was done. Cytohistologic grading correlation was done by testing concordance, association and correlation. *Results:* The three cytological grading systems correlated well with histological grading. Fisher's modification of Black nuclear grading system demonstrated the best correlation ($\rho = 0.61$; $P < 0.001$) and concordance (Percent of agreement=70%) with the SBR's grading system. *Conclusions:* Fisher's modification of Black nuclear grading system is simple, reproducible and showed the best concordance with histological grading.

Keywords: Breast Carcinoma; Cytological Grading; Fine Needle Aspiration Cytology; Prognosis.

Introduction

Carcinoma breast is one of the commonest malignancies in females. Great advancement has been noticed in its diagnostic and management modalities like mammography, neoadjuvant therapy and breast conservation surgery. FNAC is a simple, reproducible and feasible method, with a role in prognostication of tumor. The conference at National Cancer Institute, Bethesda suggested that tumor grade should be included in the cytology reports [1]. Preoperative chemotherapy and tamoxifen are the treatment modalities for early cancers of breast. The morbidity due to overtreatment of low grade tumors can be avoided by preoperative cytological grading [2].

Robinsons, Black, Mouriquand, Taniguchi, Howell et al, Khan et al cytological grading systems have been comparatively evaluated in various studies. But till now, there is no consensus regarding the most effective cytological grading system. In the present study, comparative evaluation of three cytologic grading systems and correlation with the histopathology grading was done.

Materials and Methods

The study included 50 cases of carcinoma breast diagnosed on both cytology and histology. The study was conducted in Dept of Pathology, from January 2015 to December 2016. FNAC was done using a 22 gauge needle and 10ml syringe with aseptic precautions. Wet fixed smears were stained by Papanicolaou and Haematoxylin and Eosin (H&E) stain. Air dried smears were stained with Giemsa stain. Cytology smears were evaluated and carcinoma

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breast was graded using three cytological grading systems- Robinsons, Fisher's modification of Black and Howell modification of SBR grading systems by two pathologists.

In the Robinson's grading system, six cytological parameters including cell dissociation, cell size, cell uniformity, nuclear margin, nuclear chromatin and nucleolus were used to grade the tumors (Figure 1-a,b,c). Each parameter was scored 1 to 3 and the tumor was graded as Grade I with score of 6 to 11, Grade II with score of 12-14 and Grade III with score of 15-18 [3,4].

By Fisher's modification of Black's nuclear grading system (Figure 1- d,e,f) , smears were graded I,II,III considering the nuclear characteristics - nuclear size, chromatin, anisonucleosis, nuclear membrane and nucleoli [5, 6, 7,8].

SBR grading was done on cytology using the three parameters - tubule formation, nuclear pleomorphism and mitotic count, similar to that of histology grading. Howell modification for mitotic count scoring was followed (Figure 2- a,b,c). Microacini and branching elongated three dimensional tubular clusters were considered as tubule formation in smears [9].

Breast wide excision specimen and modified radical mastectomy were included. Nottingham modification of SBR grading was done on H&E stained sections using the 3 parameters - tubule formation, nuclear pleomorphism and mitotic count. Each parameter was given a score of 1 to 3 and total score was graded. Grade I - Score 3 -5, grade II - 6-7, grade III- 8-9 (Figure 2-d,e,f). Mitotic figures were scored using Labomed CXR3 with a high power field diameter of 0.45 mm [2].

Statistical analysis was done after tabulating the results. Chi-square test was done to know the association between different grading systems. P value <0.05 was considered statistically significant. Strength

of association was assessed by Kappa value of agreement. Correlation of different cytological grading systems and histopathology grading was done by Spearman's correlation coefficient, considering the grades only. Correlation using scores were not done, as Fisher's modification of Black grading does not give scores. Concordance analysis was done.

Results

In the present study, 46 out of 50 cases were diagnosed as Infiltrating duct carcinoma- NOS on histopathology. Other cases included two medullary carcinomas, one mucinous carcinoma and one infiltrating papillary carcinoma. Both the pathologists assigned the same grade in majority of cases. In other cases, discrepancy was discussed and the grade was assigned. Case distribution in different grades in three cytology grading systems and SBR grading is shown in Table 1. In all the grading systems, clustering of cases in grade II is seen. Comparison and concordance of different cytology grading methods and SBR grading are shown in Tables 2 and 3.

Chi-square test showed significant association between cytological grading systems and histopathology grading, with a p value of <0.001 for Fisher grading and <0.05 for Robinson and Howell grading. Kappa value of agreement between cytological grading and histologic grading was maximum for Fisher grading (0.41- moderate agreement). Spearman correlation coefficient revealed strong correlation for Fisher's modification of Black grading with SBR grading ($\rho=0.61$). Concordance analysis showed maximum percent agreement of 70% in Fisher's modification of Black grading (35 out of 50 cases) whereas in Robinson and Howell grading, it was 60% (30 out of 50 cases).

Table 1: Distribution of cases according to cytology and histopathology grades (percentage in parenthesis)

Grade	Robinson	Fisher	Howell	Histopathology
I	12(24%)	03(6%)	12(24%)	10(20%)
II	29 (58%)	34(68%)	33(66%)	33(66%)
III	09 (18%)	13(26%)	05(10%)	07(14%)

Table 2: Correlation of different cytological grades and histopathology grade

Histopathology grading		Distribution of cases in cytology grading								
Grade	No of cases	Robinson			Fisher			Howell		
		I	II	III	I	II	III	I	II	III
I	10	6	4	0	3	7	0	6	4	0
II	33	6	21	6	0	26	7	6	23	4
III	07	0	4	3	0	1	6	0	6	1

Table 3: Correlation and concordance analysis of different cytological grades and histopathology grade

Grading System	Robinson	Fisher's	Howell
Correlation coefficient ρ	0.47 (moderate correlation)	0.61 (Strong correlation)	0.41 (Moderate correlation)
Concordance analysis	60%	70%	60%

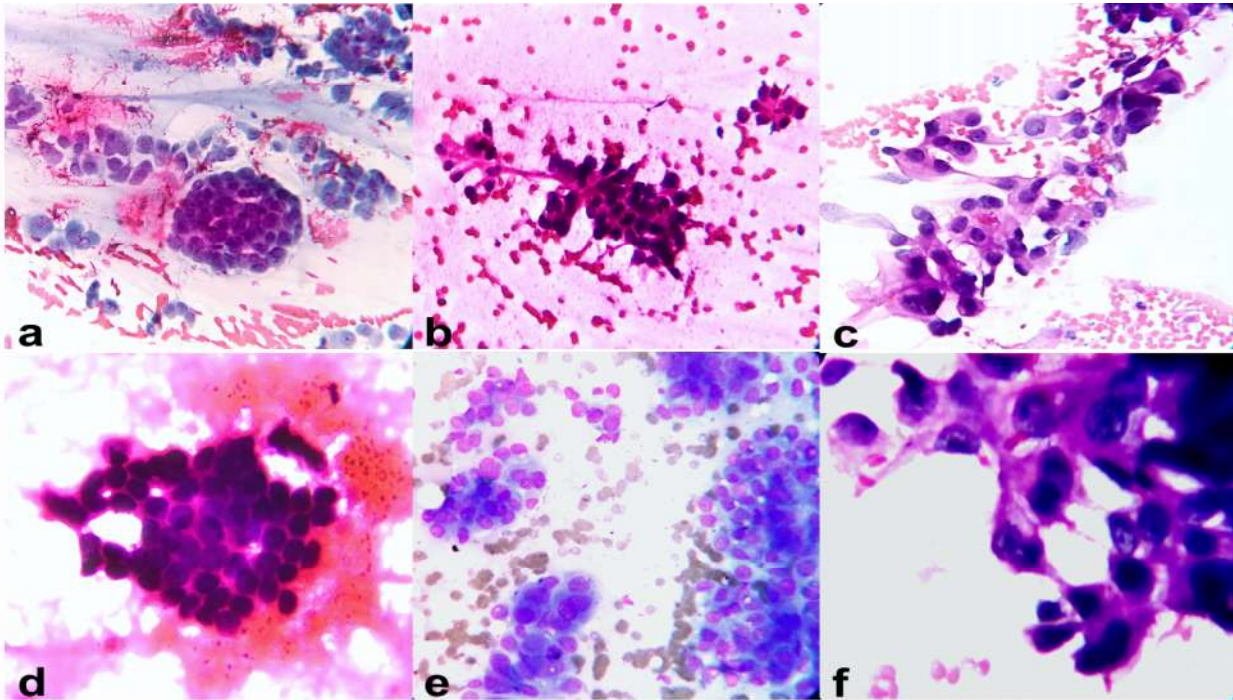


Fig. 1.a: Robinson grade I(PAP x 400). b and c. Robinsons grade II and III(H &E, x400). d-Fisher's modification of Black nuclear grade I- smooth nuclear border, no anisonucleosis, fine chromatin (H&E x400), e - Fisher grade II - moderate anisonucleosis, uniform chromatin, inconspicuous nucleoli (Geimsa x400), f- Fisher grade III- shows anisonucleosis, irregular nuclear membrane, prominent nucleoli (H&E x1000).

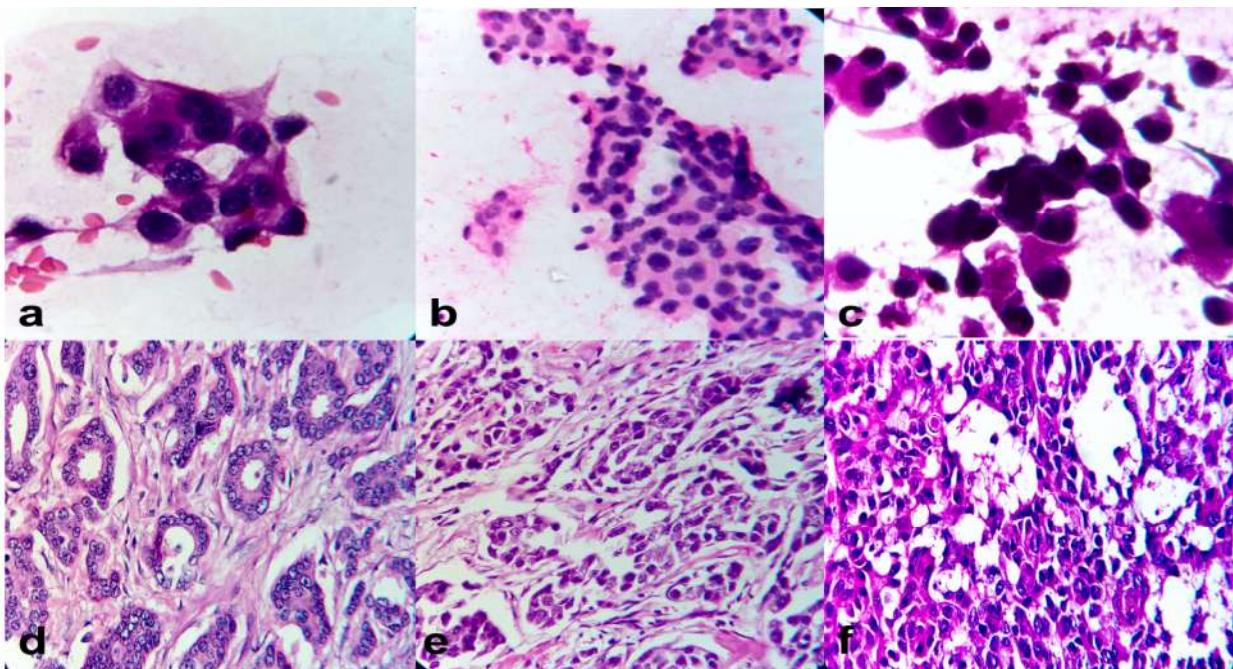


Fig. 2a: Howell grade I-Microacini, uniform nuclei (H&E x1000), b- Howell grade II - Vague acini, moderate anisonucleosis (H&E x400), c - Howell grade III- single cells, marked anisonucleosis (H&E x400), d- Histopathologic SBR grade I- tubules, uniform cells with bland chromatin (H&E x400), e and f - SBR grade II and III (H&E x400).

Discussion

FNAC is a very useful, rapid, accurate, cost effective diagnostic test for carcinoma of breast. Beyond diagnosis, its role as a prognostic indicator and thus aiding in management of carcinoma cases is established. Histopathological grade, axillary lymph node status, hormone receptor status, cell proliferation index are the proven prognostic markers for carcinoma breast [10]. By cytological grading, high grade tumors that are more likely to respond to chemotherapy are identified. Low grade tumors are likely to respond to tamoxifen pretreatment [11,12]. Even though histologic grading and hormone receptor studies on trucut biopsy have overshadowed the role of FNA in prognostication, in developing countries, maximum possible information from FNAC report including tumor grade may aid in plan of management. Core needle biopsy carries the risk of complication like pain, hematoma, bleeding and infections [13,14,15]. The conference held at National Cancer Institute, Bethesda recommended that in carcinoma breast cases, tumor grading should be incorporated in FNAC reports for prognostication.

Of the various grading systems for carcinoma breast, Robinsons, Fisher's modification of Black, Mouriquand, Taniguchi, Howell et al, Khan et al grading systems have been comparatively evaluated [16,17,18]. Different studies have showed varied concordance results between different cytology grading systems and histopathology grade. In our study, Fisher modification of Black's grading showed maximum strength of association with histopathology SBR grading. By Spearman correlation analysis, it showed strong correlation with SBR grading as compared to moderate correlation in Robinson and Howell systems. Concordance analysis among the 3 cytological grades and SBR grade showed highest concordance of 70% for Fisher's grading.

Different studies have observed different results on comparison of Fisher's modification of Black's nuclear grading with SBR grading system. Concordance was 95% by Dabbs et al. [19], 70.37% by Zoppi et al. [20], 77.78% by Bhargava et al. [21], 70.18% in Saha et al. [22] and 70% in the present study. The present study result is comparable with previous study results.

For Robinson grading, the concordance was 57% by Robinson et al. [3], 71.2% by Das et al. [23], 65% by Chhabra et al. [12], 77.19% by Saha et al. [22], 88.89% by Bhargava et al. [21], 88% by Khan et al. [17], 64% by Lingegowda et al. [24], and 60% in the present study. The present study results are similar to that of studies by Robinson et al and Chhabra et al.

We observed concordance of 60% for Howell cytological grading with the histological SBR grading. Previous studies have shown concordance values of 57.1% by Howell et al. [9], 50% by Bhargava et al. [21], 63.16% by Saha et al. [22], 82% by Lingegowda et al. [24], and 87% by Dabbs and Silverman studies [25]. Discordance between the cytologic and SBR grade in certain cases could be explained by heterogeneity of tumor and observer subjectivity. In previous few studies, Robinson's grading was considered as better choice amongst cytologic gradings, because of its simplicity and better reproducibility. Subjectivity in cases of mild nuclear pleomorphism and minimal dyscohesion could be the reason for grade discrepancies by Robinson grading. Appearance of chromatin on cytology smears are influenced by the smear preparation and fixation. Mitotic figures and tubules, that are not easily discernable in cytology, could be the limitations of Howell modification of SBR grading. Mitotic figures are relatively sparse in cytology as these cells are fragile and do not survive smear preparation [9].

Conclusion

The present study revealed that cytologic grading of breast carcinoma by three grading systems correlated well with the histopathologic grading. In the present study, Fisher's modification of Black's nuclear grading, being a simple, reproducible and objective grading system, showed the best concordance with histopathologic grade. FNAC being a simple, feasible, outpatient department procedure and less invasive when compared with core biopsy, cytological grading can be useful in prognostication and management of carcinoma breast cases.

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