

Application of scoring system in FNAC of thyroid lesions

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Abstract

Background: Assigning a score to cytology/FNA of thyroid lesions can provide important information regarding their neoplastic or non-neoplastic nature. The present study was undertaken to score thyroid lesions on aspirates based on various characteristics and correlating with standard cytological classification. Histopathology was done and the two cytological classification systems (Cytological scoring and Standard method) were compared.

Methods: 196 cases of thyroid lesions with preoperative cytologic diagnosis were assigned cytological score/classified. Histopathology diagnosis was compared and statistical analysis was performed; correlation between cytologic score and histopathology was established using Spearman correlation coefficient. Regression analysis was done to assess the significance of each cytological score.

Results: Multivariate analysis of cytologic features revealed that the amount of colloid, nuclear features and background pattern are the most influential features. There was high degree of correlation between the scoring methods on cytology with histopathology compared to standard cyto classification with histopathology. There was a significant association ($p < 0.001$) between the scores assigned to cytologic and histopathologic specimens.

Interpretation and Conclusion: Cytological scoring method can be used to assess the lesions of the thyroid as a significant relationship exists between both the classification systems and histopathology.

Keywords: FNAC, Cytological scoring, Statistical analysis

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Introduction

Fine needle aspiration cytology (FNAC), the history of which is dated up to 10 centuries back is now increasingly being used for preoperative diagnosis of thyroid lesions. It is minimally invasive, cost-effective, has minimal complications and is used to triage patients into those who require surgery and those who do not. Errors from sampling, screening and interpretation, still conceal some unpleasant results. Assessment using all the available characteristics would allow making it more valuable. Such scoring if applied could avoid inter-observer variation to a large extent. This scoring method could accurately assess cytological diagnosis in thyroid lesions, which is useful to clinician.⁽¹⁻⁴⁾

Further studies are needed to investigate and use all the available information on the smear, in order to classify the lesions on FNAC, to predict its possible histopathological diagnosis. Scoring system using morphometry has been applied in Vaginal Pap smears on a larger scale in developed countries, whereas in

relation to other cytological lesions is still at a research stage.^{1,5,6}

This study aims at evaluating the application of scoring system with standard cytological classification and its correlation with histopathology.

Method

This prospective 4 year study was conducted at Pathology department, Vinayaka Missions Kirupananda Variyar Medical Hospital, Salem during the year 2011-2014, which included 196 histopathology cases of thyroid lesions which had pre-operative cytological diagnoses. Cases in which both satisfactory cytological material and histopathology was available were included in the study. Cases in which histopathology was not available or cytology was unsatisfactory were excluded from the study. All the aspirate smears were stained by H&E, Papanicolaou smears and Giemsa stains.

Scoring system was done according to Table 1 and standard classification was based on National cancer institute thyroid fine needle aspiration guidelines committee IV and further categorized and converted into various grades (Table 2).

The cytological features by both methods were independently evaluated by two examiners. Measure of agreement between two examiners was determined by combining the diagnosis for scoring method, standard cytological method and histopathological diagnosis.

Statistical Analysis

Descriptive data was presented as numbers and percentages. Multiple regression analysis was done to assess the significance of different cytological features. Association between the different systems of grading was tested by Chi-square test. Agreement was assessed by kappa measure of agreement. Correlation between cytological and histological grading was examined by Spearman’s correlation coefficient. A p-value of 0.05 or less was considered for statistical significance.

Results

The study comprised of 140 female and 56 male patients in the age group of 22 to 58 years. Right lobe was predominantly involved. Size of lesions varied from 0.5cm to 5cm in the largest diameter. Out of 196 cases aspirated, majority were non-neoplastic lesions.

A high proportion of lesions were characterized as benign by standard classification (172) compared to scoring system (144). Histopathology revealed a higher proportion to be benign lesions (168). Follicular Neoplasm/atypia of undetermined significance were included in the category of indeterminate lesions and not considered under the benign category. Malignant lesions were very few in our study (8). (Table 3)

Multivariate analysis of components of scoring system revealed that the components such as colloid, nuclear pleomorphism and background pattern contribute to diagnosis independently.

A complete concordance in diagnosis by both methods was obtained in 90.3% of the cases. The overall correlation between the standard cytologic method and histopathology was 73.97%, where as in between scoring cytological method and histopathology was 90.81%. (Table 4, 5, 6)

Scoring system correlated positively with standard system. Scoring system showed a positive correlation with histopathology. The high value of co-efficient of correlation showed a significant and marked association between the diagnosis (P <0.001) on cytology and histopathology specimens. (Table 7)

A positive correlation was present between presence of benign diagnosis and 2 of features evaluated in scoring method i.e. colloid and background pattern.

The two observers assigned different grade for 2% of cases in Scoring-cyto method, 8% of cases in Standard-cyto method and 4% of cases in standard-histopathology diagnosis. Kappa measure of agreement, $\kappa = 0.89$ (p<0.001).

Table 1: Scoring system

Criteria	Score		
	1	2	3
a. Colloid	Thick and thin	Thin	Scanty to absent
b. Follicular cells	Scattered/sheets	Follicles/ Papillae/ overcrowding / overlapping	No follicular cells
c. Nuclear features	Small dark nuclei	Grooves	Inclusions / hyperchromatic nuclei
d. Nuclear pleomorphism	Monomorphic	Mild anisokaryosis	Pleomorphic
e. Background	Mild hemorrhage	Moderate hemorrhage	Severe hemorrhage

Other cells: Score 1 for each type

1. Hurthle cells
2. Macrophages
3. Lymphoid background
4. Giant cells

Grade 1: Score 5-9

Grade 2: Score 10-12

Grade 3: Score 13-16

Table 2: Standard classification: National cancer institute thyroid fine needle aspiration guidelines committee IV

Categories	Lesions included
Grade I	Benign lesions
Grade II	Atypia of undetermined significance / Follicular neoplasm
Grade III	Suspicious malignancy / Malignant

Table 3: Distribution of cases

Category	Scoring system	Standard classification	Histopathology
I	144 (73.46%)	111 (56.63%)	145 (73.97%)
II	39 (19.90%)	72 (36.73%)	33 (16.84%)
III	13 (6.64%)	13 (6.64%)	18 (9.19%)
Total	196 (100%)	196 (100%)	196 (100%)

Table 4: Comparison of cytological grade – scoring system with standard classification

Cyto Scoring	Cyto Standard			Total
	Non-neoplastic	Benign	Malignant	
Non-neoplastic	137	6	1	144
Benign	8	27	1	36
Malignant	2	1	13	16
Total	147	34	15	196

Spearman correlation: 0.376
 Standard error: 0.67
 Agreement: 90.3%
 P < 0.001 (Significant)

Table 5: Comparison of scoring system with histopathology

Cyto scoring	Histopathology			Total
	Non-neoplastic	Benign	Malignant	
Non-neoplastic	138	4	2	144
Benign	7	28	4	39
Malignant	40	1	12	13
Total	145	33	18	196

Spearman correlation: 0.465
 Standard error: 0.051
 Agreement: 90.81%
 P < 0.001 (Significant)

Table 6: Comparison of cytological grade – standard cyto system with histopathology

Cyto standard	Histopathology			Total
	Non-neoplastic	Benign	Malignant	
Non-neoplastic	104	5	2	111
Benign	41	28	3	72
Malignant	0	0	13	13
Total	145	33	18	196

Spearman correlation: 0.639
 Standard error: 0.076
 Agreement: 73.97%
 P < 0.001 (Significant)

Table 7: Test showing correlation and significance between various lesions

Paired Samples Correlations			
Categories correlated	N	Correlation	Sig.
C – Scoring & C – Standard	196	.603	.000
C – Scoring & Histopathology	196	.762	.000
C – Standard & Histopathology	196	.662	.000

Discussion

Thyroid cancer, still considered a rare cancer, comprising about 2 percent of all cancers, is now considered the fastest rising cancer among women in the United States, rising in incidence faster than lung or breast cancers. Part of the rise in incidence likely has to do with better screening and information about early signs of thyroid cancer. In the past, many patients with thyroid cancers were not diagnosed early enough, and some of these cancers were missed until they were very aggressive and hard to treat. The disparities in cytology and histopathology in some cases were chiefly due to low cellularity, increased hemorrhage and difficulty in identification of colloid in FNA smears.⁷⁻¹²

The practice of histopathology is very important to make a correct diagnosis. This trend has stimulated the development of numerous immuno markers, serology that actually represent biological continua.¹³⁻¹⁵

The value of histopathology is well established. Since diagnosis of thyroid lesions are often made by FNAC it would be more informative if scoring method is done in the management of the patient.^{16,17}

Colloid, follicular cell pattern and background were the most influential features in scoring system. Colloid especially if thick is easy to identify presenting as a crackling artifact and small amount of it can be seen in various lesions like thyroiditis, neoplasms, papillary carcinoma as well as goitre. Chewing gum colloid is the characteristic colloid seen in papillary carcinoma. Thick Colloid especially if appreciated macroscopically which appears as varnish on the slide is a reliable sign of benignity and not a feature reported to be associated with malignancy commonly.^{7,10}

Cellularity defines the adequacy of a smear, and is variable and not standardized. Various studies give different criterias. From the majority of the studies, in which adequacy is clearly defined and the follicular cells determined, the minimum criteria for adequacy is 5-6 follicle groups each with at least 10 cells, but each case needs to be evaluated in the context of clinical and radiological information available. Follicular cells were predominantly found in sheets. In cases with cystic change, they were scattered. Micro-follicles were appreciated in many cases which later turned out to be follicular adenoma. Microfollicles appear as glandular structures with well defined lumens that are either empty or contain inspissated colloid. Recognition of abundant colloid should override the requirement of a set number of follicular cells as the follicular cells might be zero in some cases.^{7,10,17}

Background pattern usually with mild hemorrhage usually indicates non-neoplastic lesion. Colloid rich background is commonly non-neoplastic, but care needs to be taken as neoplastic lesions can present with moderate amounts of colloid rarely. Difficulty in identification of colloid could be the reason in over-diagnosis on cytology. Colloid has variable density and takes different color with different stains. It usually

stains blue with MGG but can vary from pink to violet to blue and pale grey green to pink in Pap. When mixed with blood, in the absence of typical crackling artifact pattern, thin colloid is indistinguishable from serum and other proteinaceous material.^{8,10}

Colloid, follicles and nuclear features are the cytological features simultaneously used in histopathology to evaluate diagnosis of thyroid lesions. Serology could be useful to separate Hurthle cells lesions like Hashimoto's thyroiditis, and Hurthle cell adenoma. The use of immune-markers is expensive and not cost-effective at present. However its sensitivity and objectivity might be useful in future.^{14,15-18}

It was noted that more nuclear pleomorphic lesions (thyroid cancers) displayed greater hemorrhage. Hemorrhage is indicative of a neoplastic lesion and increased number of microfollicles in a background of hemorrhage should always point out towards a neoplastic lesion. Inexperienced hands and abysmally slow method can increase the blood in the smears and increase the chance of lesion being called neoplastic. The risk of neoplasia usually increases with the amount of hemorrhage if done by an experienced cytologist. Hemorrhage due to angiogenesis is an important finding. This might be useful for diagnosis of malignant lesions.^{8,9,19}

The main role of FNA is to differentiate malignant from benign lesions and triage the cases. Close cooperation and communication between pathologists and clinicians are essential to maximize the diagnostic sensitivity of this technique. For pathologists, it is imperative to carefully review the slides, discuss the benign tumors (by FNA) with the clinicians, and if warranted recommend biopsy or resecting the cystic lesions. We should acknowledge that the diagnostic accuracy of FNA is also dependent on the location of the mass, type of the lesion, and the expertise of both aspirator and cytopathologist as expressed by others as well.^{2,3,20}

The present study showed that it is possible to diagnose thyroid lesions on aspiration and cytological score correlates with histopathological diagnosis. Scoring system is simple, takes little time, is reproducible and with rare exceptions, depending on sample limitations correlates precisely with histopathology.

Our study recommends scoring system as this is simple reproducible and has greater degree of correlation with histopathology among the two systems. Cytological scoring is performed with ease, correlates well with histopathology, therefore cytology scoring is useful in predicting histopathological diagnosis pre-operatively should be included in FNAC reports as much as possible.

Conclusion

The most important service of FNAC we can render to our clinical colleagues is a near accurate cyto-

diagnosis. For practical purpose one pathologist cytological score must be able to predict another histopathological diagnosis, because in many practice situations the cytological and histopathological specimens will be signed out by different pathologists.

References

- Magiorkinis E, Diamantis A. Comments on the history of needle and fine-needle aspiration. *Diagn Cytopathol* 2009;37(8):625-7.
- Jing X, Michael CW, Pu RT. The clinical and diagnostic impact of using standard criteria of adequacy assessment and diagnostic terminology on thyroid nodule fine needle aspiration. *Diagn Cytopathol* 2008;36(3):161-6.
- Layfield LJ, Cibas ES, Gharib H, Mandel SJ. Thyroid aspiration cytology - current status. *Ca Cancer J Clin* 2009;59:99-110.
- ElHag IA, Kollur SM, Chiedozi LC. The role of FNA in the initial management of thyroid lesions: 7 years experience in district general hospital. *Cytopathology* 2003;14:26-30.
- Huang PC, Chan YK, Chan PC, Chen YF, Chen RC, Huang YR. Quantitative Assessment of Pap smear Cells by PC-Based Cytopathologic Image Analysis System and Support Vector Machine. In: Zhang D, editor. *Medical biometrics*. Berlin: Springer; 2007. p. 192-9 (Lecture series in Computer science. vol 4901).
- Stemberger-Papic S, Stankovic T, Vrdoljak-Mozetic D, Versa-Ostojic D, Krasevic M, Stifter S et al. Morphometry and digital AgNOR analysis in cytological imprints of benign, borderline and malignant serous ovarian tumours. *Cytopathology* 2006;17(6):382-9.
- Pitman MB, Abele J, Ali SZ, Duick D, Elsheik TM, Jeffrey RB et al. Techniques for Thyroid FNA: A Synopsis of the National Cancer Institute. *Thyroid Fine-needle Aspiration State of the Science Conference*. *Diagn Cytopathol* 2008;36(6):407-24.
- Yang GCH, Liebeskind D, Messina AV. Should cytopathologists stop reporting follicular neoplasms on fine needle aspiration of thyroid? Diagnostic and histopathologic follow up of 147 cases. *Cancer Cytopathol* 2003;99(2):69-74.
- Gu M, Ghafari Z. Follicular Neoplasm of the thyroid gland: Unique cytologic appearances in a Fine-needle aspiration biopsy. *Diagn Cytopathol* 2010;00:1-3.
- Orell RS, Philips J. Cellular and non cellular components of fine needle biopsy smears from the thyroid. Orell RS, editor. *The thyroid. Fine needle biopsy and cytological diagnosis of thyroid lesions*. Basel: Karger; 1997. p.37-60. (Monographs in Clinical cytology. vol 14)
- Ain K, Rosenthal MS. *Thyroid Cancer. The complete thyroid book*. New York: McGraw Hill; 2005. p. 127-41.
- Ravetto C, Colombo L, Dottorini ME. Usefulness of Fine-needle aspiration in the diagnosis of thyroid carcinoma – a retrospective study of 37,895 patients. *Cancer Cytopathol* 2000;90(6):357-63.
- Dobrinja C, Trevisan G, Liguori G, Romano A, Zanconati F. Sensitivity evaluation of fine needle aspiration cytology in thyroid lesions. *Diagn Cytopathol* 2009;37(3):231-4.
- Kumar N, Ray C, Jain S. Aspiration Cytology of Hashimoto's thyroiditis in an endemic area. *Cytopathology* 2002;13:31-9.
- Pagedar NA, Chen DH, Wasman JK, Savvides P, Schlucter MD, Wilhelm SM et al. Molecular classification of thyroid nodules by cytology. *Laryngoscope* 2008;118:692-6.
- Bakhos R, Selvaggi SM, DeJong S, Gordon DL, Pitale SU, Herrmann M, Wojcik EM. Fine-needle aspiration of the thyroid: Rate and causes of Cytopathologic Discordance. *Diagn Cytopathol* 2000;23(4):233-7.
- Oertel YC. Cytologic analysis of follicular lesions of the thyroid gland. Online. 2003;[6]. Available from URL: www.thyroid.org/ann_mtg/2003_75th/documents/011_Oertel.pdf
- Shi Y, Ding X, Klein M, Sugrue C, Matano S, Edelman M et al. Thyroid fine needle aspiration with atypia of undetermined significance. *Cancer cytopathol* 2009;117:298-304.
- Watanabe I, Matsuura K. Angio architecture of thyroid carcinoma. *Japanese journal of clinical Oncology* 1985;15:77-85.
- Moatamed NA, Naini BV, Fathizadeh P. A correlation study of diagnostic fine-needle aspiration with histologic diagnosis in cystic neck lesions. *Diagn Cytopathol* 2009;37:720-6.