

Malignancy risk for fine-needle aspiration of thyroid nodules according to the Bethesda system for reporting thyroid cytopathology, at King Abdul-Aziz National Guard Hospital

Abstract

Introduction: The Bethesda System was introduced to help us in risk of malignancy in reporting thyroid cytopathology. The Bethesda system is high predictive value of thyroid fine needle aspirates. FNA of the thyroid gland is an accurate method in our approach to manage our patient.

Aim: The aim of this study was to determine the rates of malignancy of thyroid nodules in each standard cytologic diagnostic category of Bethesda system in our hospital.

Materials and methods: A retrospective cross-sectional study in which all cases of thyroid nodules, presented to the OPC between September 2009 and August 2015 at King Abdulaziz NGH. All preoperative cytologic examination by FNA and concurrent postoperative histopathologic examination were included. All FNA diagnoses were reclassified using the thyroid FNA Bethesda reporting system, including non-diagnostic, benign, atypical follicular lesion of undetermined significance, follicular/hurthle cell neoplasm, suspicious for malignancy and malignant categories, the rate of malignancy based on final histopathologic evaluation was analyzed for each of these cytologic groups.

Results: We reviewed 237 thyroid FNA samples and recorded interpretations according to the proposed standardized 6 categories and pursued follow-up cytology and histology. Of the 237 FNAs, 4.2% were nondiagnostic, 39.2% were benign, 15.6% were AFLUS, 8.9% were SFN, 16.9% were SM, and 15.2% were malignant.

The rates of malignancy in histology were as follows: nondiagnostic, 0.0% benign, 4.3%; AFLUS, 18.9%; SFN 34%: SM 95.0% and malignant, 94.4%

Conclusion: The Bethesda system is a standardized system of reporting thyroid cytopathology, improving communication between cytopathologists and clinicians leading to ideal management approaches.

Keywords: Bethesda system, cyto-histological correlation, fine needle aspiration cytology, rate of malignancy

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Abbreviations: FNA, fine-needle aspiration; NCI, national cancer institute; TBSRTC, the Bethesda system for reporting thyroid cytopathology;

Introduction

Thyroid nodules occur commonly and can be detected by ultrasound in 60% of the general population.¹⁻³ The Surveillance Epidemiology and End Results Registry (SEER Registry) shows increasing prevalence of differentiated thyroid cancer in the world^{4,5} mostly due to the increased detection of small papillary carcinomas.⁶ For initial evaluation of patients with thyroid nodules, fine-needle aspiration (FNA) of the nodules is safe, simple, accurate, cost effective, and widely accepted.⁷ FNA of the thyroid allows 70-80% of lesions to be classified as benign or malignant, with a 92% negative predictive value for benign nodules and a 100% positive predictive value for malignancy.⁸ FNA reduces the rate of unnecessary thyroid surgery for patients with benign lesions and appropriately triages patients with thyroid malignancy for appropriate management.⁹

The literature is deficient with regard to the precise frequency of thyroid nodules and the associated rate of malignancy in Saudi Arabia.

Nodular thyroid diseases are common in mountainous areas of the eastern region of the country,¹⁰ and thyroid cancer is the second-most common cancer among females (10.2%).¹¹ In the United States, seven percent of the population has a palpable thyroid nodule,¹² but only one of 20 clinically identified nodules is malignant.¹³ An estimated 30 million individuals in the United States have thyroid nodules larger than one cm. With the high prevalence of thyroid nodules, 30,000 patients are diagnosed yearly with thyroid malignancy.^{13,14}

Given the high prevalence of nodules, FNA is an important screening test.⁸ Every patient with a palpable or incidental nodule is a candidate for FNA. A thyroid nodule that is either iso- or hypo-functioning, according to a radionuclide scan, should be considered for FNA.¹³⁻¹⁵ Incidental lesions detected by ultrasound have a 10-15% cancer risk and should undergo sonographic evaluation.¹⁶ A thyroid nodule of any size and shape that is determined sonographically should also be evaluated by FNA.^{17,18}

Currently, confusion surrounds the reporting of FNA for thyroid nodules, because of differently named lesion categories, unclassified descriptive reports, and varying surgical and pathological terminology.¹⁶ This confusion has led to wide variance in the sensitivity

and specificity of what can be considered true or false positive or negative results, which has led to uncertainty among clinicians on how to manage patients with thyroid nodules that do not have a clear, informative result in thyroid FNA.¹⁸

In 2007, the National Cancer Institute (NCI) held the NCI Thyroid Fine Needle Aspiration State of the Science Conference, wherein the terminology and morphologic criteria for reporting thyroid FNA were decided, forming a framework for The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). This solved much of the confusion.^{16,17}

The Bethesda system improves communication among cytopathologists and surgeons. This allows reliable sharing of data and comparison between laboratories, nationally and internationally, by establishing a common language and reliable conclusions.¹⁷⁻¹⁹

Few studies have validated the utility and diagnostic accuracy of FNA of thyroid nodules across Saudi Arabia, reported the risk of thyroid malignancies among the Saudi population, or provided feedback on TBSRTC after it was implemented in Saudi Arabia. In contrast, several international studies and reviews have been published on these topics in other countries.²⁰⁻²⁷

The purpose of this study is to categorize thyroid lesions by FNA using the Bethesda FNA classification system, including the following categories:

- a. Non-diagnostic, benign, atypical follicular lesions of undetermined significance
- b. Follicular/Hurthle cell neoplasm
- c. Suspicious for malignancy
- d. Malignant sub-categories

The purpose is also to determine the rate of malignancy in each cytological category by correlating the results with histopathologic diagnoses on the resected specimens.

Materials and methods

A retrospective cross-sectional study was conducted on the

charts in which all cases of thyroid nodules, presented to the OPC between from September 2009 to August 2015 at King Abdul-Aziz National Guard Hospital. All cases of thyroid nodules that underwent preoperative cytological examination by FNA and concurrent postoperative histopathologic examination were included. The FNA diagnoses were reclassified using TBSRTC, including:

- i. Non-diagnostic
- ii. Benign
- iii. Atypical follicular lesion of undetermined significance
- iv. Follicular/hurthle cell neoplasm
- v. Suspicious for malignancy
- vi. Malignant categories
- vii. The rate of malignancy based on final histopathological evaluation was analyzed for each of these cytological groups.

Results and discussion

Our demographic of our study sample set, divided in to age, gender, family history, main presenting symptoms, Bethesda grading, pathology and type of pathology as shown in Table 1, The mean age of our study group was 44.59years, with a range from 14-96years among 237 patients and majority of cases clustered in fourth decade. Of these patients, 40 (16.9%) were males and 197 (83.1%) were females, we found there were more percentage females in the study compare to male's gender and the malignancy rate higher in the 4, 5, 6 grading in each gender as shown in Table 2, we found only (5.1%) had family history of thyroid disease, thyroid symptoms were examined by the visual examination of neck. It was observed that (45.1%) patients had neck swelling with compression symptoms while (54.9%) had neck swelling without compression symptoms as shown in Table 1.

The Age distribution of thyroid lesion based on FNAC according to Bethesda System and correlation with pathology type, the majority of our patient were between age (35-45)years 75 patient and age (45-55)years 55 patient, the Bethesda grading is very significantly related with the pathology results given that it is highly sensitive on determining pathology according to that age as shown in Table 3.

Table 1 Characteristics of Study Sample Set

Demographics (N = 237)		Min	Max	Mean	SD
Age		14	96	44.59	13.3
	N		%		
Gender	Male	40	16.9		
	Female	197	83.1		
Family History	Positive	12	5.1		
	Negative	225	94.9		
Main Presenting Symptom	Neck swelling with compression	107	45.1		
	Neck swelling without compression	130	54.9		
Bethesda Grading	Non-diagnostic or unsatisfactory	10	4.2		
	Benign	93	39.2		
	Atypia of undetermined significance or follicular lesion	37	15.6		
	Follicular neoplasm or suspicion of a follicular neoplasm	21	8.9		
	Suspicion of malignancy	40	16.9		
Pathology	Malignant	36	15.2		
	Benign	135	57		
Type of Pathology	Malignant	102	43		
	A benign follicular nodule (includes adenomatous nodule, colloid nodule)	119	50.2		

Table Continued...

Demographics (N = 237)		Min	Max	Mean	SD
	Lymphocytic (Hashimoto) thyroiditis	5	2.1		
	Granulomatous (subacute) thyroiditis	6	2.5		
	Hurthle cell (oncocytic)	17	7.2		
	Papillary thyroid carcinoma	84	35.4		
	Poorly differentiated carcinoma	1	0.4		
	Medullary thyroid carcinoma	3	1.3		
	Metastatic carcinoma	2	0.8		

Table 2 The Age distribution of thyroid lesion based on FNAC according to Bethesda System and correlation with pathology type

Bethesda grading		Total	Pathology N (%)		p value
			Benign	Malignant	
Age less than 35 years	Non-diagnostic or unsatisfactory	3	3 (100.0%)	0 (0.0%)	<0.001e
	Benign	26	26 (100.0%)	0 (0.0%)	
	Atypia of undetermined significance or follicular lesion	5	4 (80.0%)	1 (20.0%)	
	Follicular neoplasm or suspicious for a follicular neoplasm	6	0 (0.0%)	6 (100.0%)	
	Suspicious of malignancy	8	2 (25.0%)	6 (75.0%)	
	Malignant	11	0 (0.0%)	11 (100.0%)	
35–45 years	Non-diagnostic or unsatisfactory	2	2 (100.0%)	0 (0.0%)	<0.001e
	Benign	23	23 (100.0%)	0 (0.0%)	
	Atypia of undetermined significance or follicular lesion	15	11 (73.3%)	4 (26.7%)	
	Follicular neoplasm or suspicious for a follicular neoplasm	5	0 (0.0%)	5 (100.0%)	
	Suspicious of malignancy	15	0 (0.0%)	15 (100.0%)	
	Malignant	15	1 (6.7%)	14 (93.3%)	
45–55 years	Non-diagnostic or unsatisfactory	3	3 (100.0%)	0 (0.0%)	<0.001e
	Benign	22	20 (90.9%)	2 (9.1%)	
	Atypia of undetermined significance or follicular lesion	11	9 (81.8%)	2 (18.2%)	
	Follicular neoplasm or suspicious for a follicular neoplasm	6	1 (16.7%)	5 (83.3%)	
	Suspicious of malignancy	7	0 (0.0%)	7 (100.0%)	
	Malignant	6	1 (16.7%)	5 (83.3%)	
56 years and older	Non-diagnostic or unsatisfactory	2	2 (100.0%)	0 (0.0%)	<0.001e
	Benign	22	20 (90.9%)	2 (9.1%)	
	Atypia of undetermined significance or follicular lesion	6	6 (100.0%)	0 (0.0%)	
	Follicular neoplasm or suspicious for a follicular neoplasm	4	1 (25.0%)	3 (75.0%)	
	Suspicious of malignancy	10	0 (0.0%)	10 (100.0%)	
	Malignant	4	0 (0.0%)	4 (100.0%)	

e-significant using chi-square test at less than 0.05

Table 3 Bethesda Grading by gender

Variables		Total	Pathology		p-value
			Benign	Malignant	
Bethesda Grading	Non-diagnostic or unsatisfactory n (%)	2	2(100.0%)	0(0.0%)	<0.001c
	Benign n (%)	21	20(95.2%)	1(4.8%)	
	Atypia of undetermined significance or follicular lesion n (%)	4	4(100.0%)	0(0.0%)	
	Follicular neoplasm or suspicious for a follicular neoplasm n (%)	5	1(20.0%)	4(80.0%)	
	Suspicious of malignancy n (%)	5	1(20.0%)	4(80.0%)	
	Malignant n (%)	3	0(0.0%)	3(100.0%)	
Bethesda Gradingb	Non-diagnostic or unsatisfactory n (%)	8	8(100.0%)	0(0.0%)	<0.001c
	Benign n (%)	72	69(95.8%)	3(4.2%)	
	Atypia of undetermined significance or follicular lesion n (%)	33	26(78.8%)	7(21.2%)	
	Follicular neoplasm or suspicious for a follicular neoplasm n (%)	16	1(6.3%)	15(93.8%)	
	Suspicious of malignancy n (%)	35	1(2.9%)	34(97.1%)	
	Malignant n (%)	33	2(6.1%)	31(93.9%)	

Gender: ^a-Male

^b-Female

^c-significant using Chi-Square test @ <0.05 level.

We reviewed 237 thyroid FNA samples and recorded interpretations according to the proposed standardized 6 categories and pursued follow-up cytology and histology. Out of the 237 FNAs 4.2% were non diagnostic, 39.2% were benign, 15.6 % were atypia of undetermined significance or follicular lesion, 8.9 % were follicular neoplasm or suspicious for a follicular neoplasm, 16.9% were suspicious of malignancy, and 15.2% were malignant as shown in Table 1, the rates of malignancy in histopathology were as follows: non diagnostic, 0.0% benign, 4.3%; Atypia of undetermined significance or follicular lesion 18.9%; Follicular neoplasm or suspicious for a follicular neoplasm 34%: Suspicious of malignancy 95.0% and malignant 94.4% as shown in Table 4.

The type of pathology has a significant relationship with Bethesda

grading, especially results is mainly coming from a benign follicular nodule, hurthle cell and papillary thyroid carcinoma. When patient was categorized under a benign follicular nodule (119) patient, 68% were under category 2 (benign) and 27% were under category 3 (atypia of undetermined significance or follicular lesion).

When patient was categorized under hurthle cell (17) patient, 100 % were under category 4 (Follicular neoplasm), When patient was categorized under the papillary thyroid carcinoma (84) patient, 3, 6%, were fall under category 2 (benign), category 5 (Suspicious of malignancy), 6 (malignant) and 3 (atypia of undetermined significance or follicular lesion) which had 37, 34 and 7 patients respectively and covered around 36% of total patients as shown in Table 5.

Table 4 Correlation between Bethesda grading and pathology type

Variables	Total	Pathology N (%)		p value
		Benign	Malignant	
Total	237	135 (57.0%)	102 (43.0%)	N/A
Bethesda Grading				
Non-diagnostic or unsatisfactory	10	10 (100.0%)	0 (0.0%)	<0.001a
Benign	93	89 (95.7%)	4 (4.3%)	
Atypia of undetermined significance or follicular lesion	37	30 (81.1%)	7 (18.9%)	
Follicular neoplasm or suspicious for a follicular neoplasm	21	14 (66%)	7 (34%)	
Suspicious of malignancy	40	2 (5.0%)	38 (95.0%)	
Malignant	36	2 (5.6%)	34 (94.4%)	

Table 5 The correlation between the type of pathology with Bethesda grading

		Non-Diagnostic or Unsatisfactory	Benign	Atypia of undetermined Significance or follicular Lesion	Pathology	Total	Bethesda Grading N (%)	pvalue
Total	237	10 (4.2%)	93 (39.2%)	37 (15.6%)	21 (8.9%)	40 (16.9%)	36 (15.2%)	N/A
A benign follicular nodule (includes adenomatous nodule, colloid nodule)	119	10 (8.4%)	81 (68.1%)	27 (22.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	<0.001a
Lymphocytic (Hashimoto) thyroiditis	5	0 (0.0%)	2 (40.0%)	3 (60.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Granulomatous (Subacute) Thyroiditis	6	0 (0.0%)	6 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Hurthle cell (Oncocytic)	17	0 (0.0%)	0 (0.0%)	0 (0.0%)	17 (100.0%)	0 (0.0%)	0 (0.0%)	
Papillary thyroid Carcinoma	84	0 (0.0%)	3 (3.6%)	7 (8.3%)	3 (3.6%)	37 (44.0%)	34 (40.5%)	
Poorly differentiated Carcinoma	1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	
Medullary Thyroid Carcinoma	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (100.0%)	0 (0.0%)	
Metastatic Carcinoma	2	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)	

a-significant using chi-square test at less than 0.05

Conclusion

Our study concluded that FNAC reporting using TBSRTC highly correlated with histopathological diagnosis. The Bethesda system is a standardized system of reporting thyroid cytopathology, improving communication between cytopathologists and clinicians leading to ideal management approach. The Bethesda system for reporting thyroid cytopathology can estimate the risk of malignancy and have important prognostic information regarding the cancer type, variant, and risk of recurrence.

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Conflicts of interest

Author declares there are no conflicts of interest.

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