Annals of Thyroid Research

Open Access

Austin Publishing Group

Research Article

New Score for Risk Stratification and Sub-classification of Bethesda III Thyroid Nodule for Optimum Management; CUC Score (Cytological, Radiological, and Clinical Scoring System)

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Received: March 05, 2019; **Accepted:** April 12, 2019; **Published:** April 19, 2019

Abstract

Background: Thyroid swelling is a common clinical problem. The Bethesda classification of FNAC of the thyroid swelling is very helpful in decision making and choosing the optimum management policy. However, Bethesda III is still a problem with a wide recommendation in the management. Histologically, Bethesda III is a heterogeneous group with considerable cytological variations that proved to be of variable malignant risk. Accordingly, there is a need to subcategorize the Bethesda III into subgroups of variable malignant risk and clear recommendation in the management in order to avoid unnecessary surgery or omit necessary one.

Materials and Methods: The study assumed a score system that includes the cytological and ultrasongraphic features in addition to the clinical risk factors in the assessment and getting subcategories for Bethesda III. The study is a retrospective one that was delivered from May 2016 to January 2019. The cytological features were further subdivided into follicular lesion of undetermined significance or atypia of undetermined significance, while the ultrasound features were standardized by TIRABS. The patients were also assessed for the age, gender, and family history of thyroid cancer, in addition to the red flag sings in the clinical data The latter includes hard consistency, fixed nodule, and or rapid growth or recent onset of the swelling within four to six months. The patients were classified according to the CUC (cytological, ultrasongraphic & clinical) score into three groups; group CUC I; which includes patients with score three or less. Group CUC (2) includes patients with score four or five, and group CUC (3) which includes patients with score six or more. The study assessed the malignant risk in each group. Results: Five hundred and sixty-nine (569) patients were presented in the study and with Bethesda III constituted 23% (131/569). (9/131) Patients (7%) with Bethesda III were sent for repetition of FNAC and 18% (24/131) were observed. While 106 (81%) patients sent for surgery. The total cases with reported malignancy after thyroidectomy were 14 patients (13%). The malignant cases were two (5.5%) in CUC (1) group and four cases (9.5%) in CUC (2) and eight cases (28%) in group CUC (3). On comparisons the three groups, a significant difference was present in the rate of malignancy. Group CUC (3) has the highest risk for malignancy with five folds more than group CUC (I) and three folds more than group CUC (2).

Conclusion: CUC score is a scoring system that utilizes the cytologic and ultrasongraphic features in addition to the demographic & clinical characteristics in determining the malignant risk and sub-categorized Bethesda III. The score provides three groups with variable malignant risk and management policy. CUC (1) group (low risk group) had the lowest malignant risk (5.5%) where ultrasound follow up is recommended as management policy. The CUC (2) groups (intermediate risk group) had an intermediate risk (9.5%) where cytological follow up by repletion of FNAC is recommended. While CUC (3) (high risk group) carries the highest risk (28%) and surgical treatment is recommend.

Keywords: Thyroid nodule; Bethesda classification; Bethesda III subgroups; Thyroid swelling; Cancer thyroid; CUC score for Bethesda III

Introduction

Most thyroid diseases occur in a nodular form and can reach a prevalence of up to 68% in adult women [1]. Bethesda classification of FNAC is very helpful in decision making of the optimum management

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Citation: Elsaady A, Abdelgawad W. New Score for Risk Stratification and Sub-classification of Bethesda III Thyroid Nodule for Optimum Management; CUC Score (Cytological, Radiological, and Clinical Scoring System). Annals Thyroid Res. 2019; 5(1): 188-195.

Table 1: CUC score (Cytological, radiological and clinical scoring system) for sub-classification of Bethesda III patients.

Risk Factor	Definition	Details	Score; point
Bethesda III	Bethesda III A	follicular lesion of undetermined significance (FLUS)	1
	Bethesda III B	atypia of undetermined significance (AUS)	3
TIRADS	TIRADS 0	Normal thyroid gland	0
	TIRADS 1	Purely cystic nodule, no solid component.	1
	TIRADS 2	Spongiform or partially cystic nodule without any of the sonographic features described in TIRADS 3,4 or 5	2
	TIRADS 3	Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid areas, without micro-calcification, irregular margin or ETEc (extra-thyroid extension), or taller than wider.	3
	TIRADS 4	Hypoechoic solid nodule with smooth margins without micro-calcification, ETEc, or taller than wider.	4
	TIRADS 5	Solid hypoechoic nodule, or solid hypoechoic component of a partially cystic nodule with one or more of the following features; - irregular margin (infiltrative, micro-lobulated) - micro-calcification, - taller than wider shape, - rim calcifications with small extrusive soft tissue component, - evidence of ETE (extra-thyroid extension),	5
Clinical Data	Age	Less than 14 years, or more than 65 years	
	Gender	Male	
	Family History	family history of thyroid carcinoma in a first degree relative,	
	Duration	Recent onset or rapid growth within four month in a previously diseased thyroid gland	
Clinical signs		Hardness & or fixation of the nodule.	
		Every item takes 0.5 if present	
			Total 11

[2]. However, Bethesda III is still a hazy area, with unclear recommendations for the management. It is very variable from just follow up to surgical treatment (lobectomy or total thyroidectomy). It represents a heterogonous group in the cytological features with wide range in the malignant risk. The limitations of FNA cytology imply that other diagnostic options may be valuable to delineate risk further and assist clinicians in choosing the best management. Accordingly the study assumed a score (CUC Score) involving cytological & ultrasound features as well as the risk factors in the demographic and clinical data to subcategorize Bethesda III into three sub-groups according to the degree of risk and malignant potentiality. The study is a retrospective one that aims at assessment of the significance of the CUC score (cytological, ultrasound & clinical score) in determining the degree of the malignancy risk among patients with Bethesda III and accordingly the optimum management.

Materials & Methods

The study is a retrospective one that was delivered from May 2016 to January 2019). All patients presented with thyroid diseases and sent for fine needle aspiration cytology were involved in the study, to assess the prevalence of Bethesda III among them. Patient with Bethesda III were re-assessed by cytological, ultrasound & clinical score system (CUC score) shown in (Table 1). This score sub-classifies the Bethesda III category into three groups according to the cyto-pathologic, radiologic and clinical risk characteristic in order to determine the approximate risk for malignancy more precisely than the mere use of Bethesda classification. The cytological features were further subdivided into Bethesda III A (follicular lesion of undetermined significance) that given one point in the score, and Bethesda IIIB (atypia of undetermined significance) that given three points in the score. The ultrasound features (standardized by TIRABS) were assessed with increasing the score according to the TIRABS category (as in Table 1). The patients were assessed for age, gender, family history of thyroid cancer, or syndromes associated with thyroid cancer as in (Table 2), in addition to the red flag sings in the clinical data which entail hard consistency, fixed nodule, rapid growth or recent onset of the swelling within four to six months. For

Table 2: Thyroid cancer syndrome; inherited syndromes associated with thyroid cancer.

• Familial adenomatous polyposis
• Gardner's syndrome
• PTEN hamartoma tumor syndrome
• Carney complex
• Multiple endocrine neoplasia (MEN 2A and 2B)
• Familial medullary thyroid cancer
• Cowden's syndrome
• Werner's syndrome

Table 3: Comparisons between the assumed three CUC subgroups of Bethesda III.

Items	CUC (1)	CUC (2)	CUC (3)
Prevalence (from 131)	36 (34%)	42 (40%)	28 (26%)
Age (in years)	46	45	48
Gender	Females 36 (100%)	Females 40/42 (95%)	Females 26/28 (93%)
Reported Malignancy	2 (5.5%)	4 (9.5)	8 (28.5%)

Figure 1: Female patient with huge goiter, Bethesda III in FNAC and colloid nodular hyperplasia after thyroidectomy.

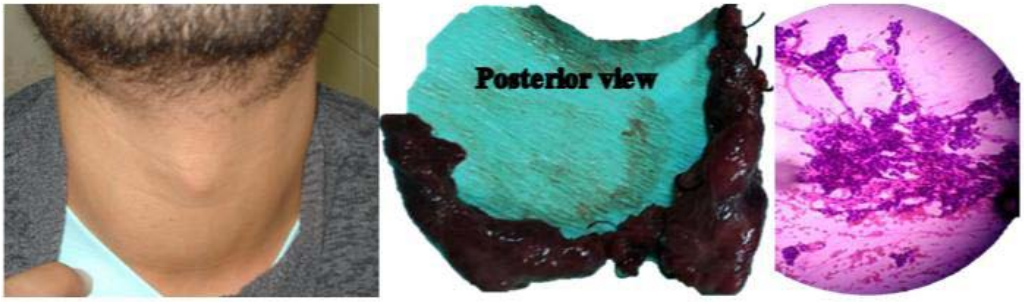

Figure 2: Male Patient with right thyroid nodule (STN) & Bethesda III on FNAC. Total thyroidectomy was done and papillary thyroid carcinoma was reported in biopsy.

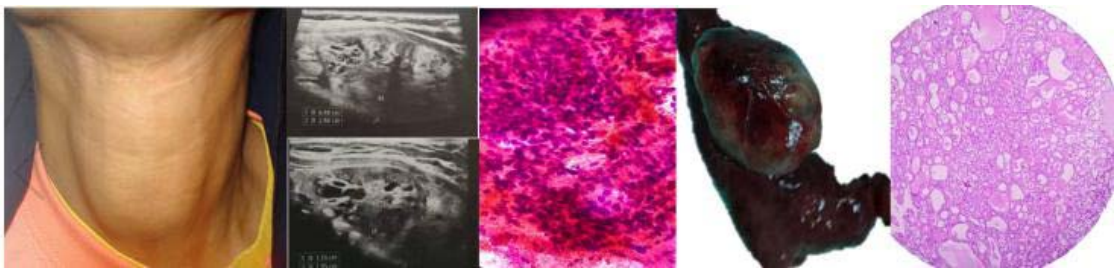

Figure 3: Female patient with thyroid swelling, TIRADS 2, Bethesda III with follicular lesion of undetermined significance. Right hemi-thyroidectomy was done and adenomatous colloid multi-nodular goiter reported in biopsy.

each clinical risk factor present 0.5 was given in the score assessment as in (Table 1). According to the patient data, every patient was given a score according to assumed risk mention in (Table 3). The patients were classified according to the CUC score into three groups; CUC (1) group; which includes patients with score three or less, that assumed to have low risk for malignancy. CUC (2) group; which includes patients with score four or five, and assumed to have intermediate risk for malignancy, and CUC (3) group which includes patients with score six or more, and assumed to have high malignant risk. Every group was assessed for the rate of malignancies reported after operative interference.

Results

Five hundred and sixty nine (569) patients were presented in the study and with Bethesda III constituted 23% (131/569), while Bethesda II 57% (327/569), Bethesda I 0.9% (5/569), Bethesda IV 12% (69/569), Bethesda V 4% (23/569) & Bethesda VI 3% (17/569). Patients with Bethesda III were prepared for surgery in 75% (98/131), while 7% (9/131) sent for repetition of FNAC and 18% (24/131) were observed. Two patients from the group of repetition of FNAC were sent for surgery while six patients in the observed group were sent for surgery after follow up. Thus the total number of patients sent for surgery was 106 (81%). Eight patients in the observation group were lost in follow up. (Figures 1,2,&3) show cases presented with Bethesda III on FNAC and different pathology after excision biopsy.

The total cases with reported malignancy after thyroidectomy were 14 patients (13%).

On assessment of CUC (1) group (assumed low risk group), which included patients with score three or less; 36 patients (34%) were presented, the mean age was 46 years and all patients were female (100%). The malignant cases were two (5.5%).

While CUC (2) group (assumed intermediate risk group)m that included patients with score 4 or 5, contained 42 patients (40%), the mean age was forty five years, forty patients were females (95%). The malignancy was reported in four cases (9.5%).

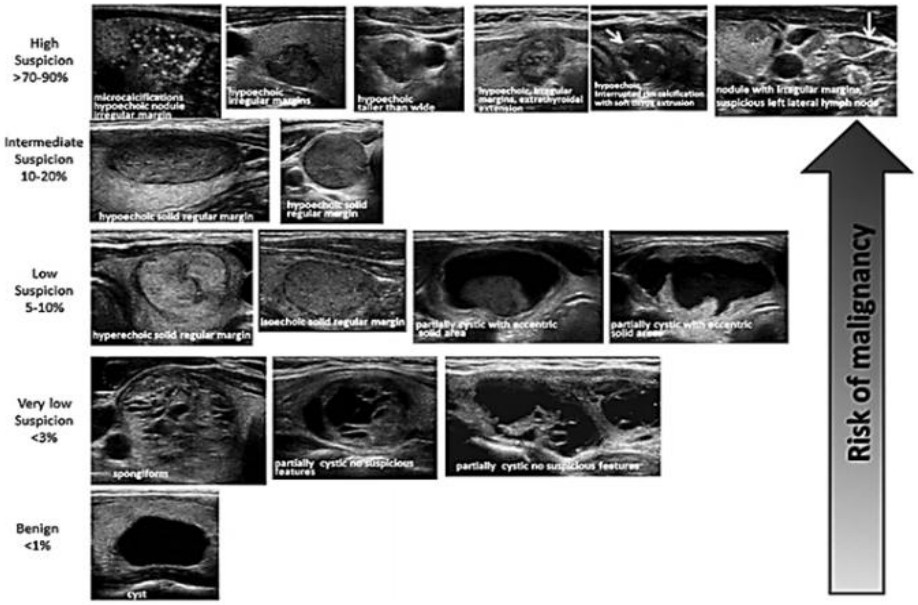

Figure 4: TIRADS for sonographic assessment of thyroid nodule and risk of malignancy. (ATA (American thyroid association) guidelines in the management of thyroid nodule, 2015).

Table 4: Bethesda System for Reporting Thyroid Cytopathology.

Bethesda category	Cytopathologic category	Approximate expected frequency	Malignancy rate	Suggested treatment (Prior to availability of molecular testing)
I	Non-diagnostic/Inadequate	5-11%	1-4%	Repeat FNA
II	Benign	55-74%	0-3%	US follow-up
I I I	Atypia/fdlioular lesion of undetermined significance	5-15%	5-15%	Repeat FNA or US follow-up or Lobectomy
I V	Follicular neoplasm/ St-ISPiCiOLJS for FN	2-25%	15-30%	Lobectomy
V	Suspicious for malignancy	1-6%	60-75%	Lobectorny or Thyroidectomy
VI	Malignant	2-5%	97.99%	Near-total thyroidectomy

FNA: Fine-needle aspiration; FN: Follicular neoplasm; US: Ultrasonographic

The CUC (3) group (assumed high risk group),which included patients with score 6 or more, has 28 patients (26%), with the mean age was forty eight, and twenty six patients were females (95%). The malignancy was reported in eight cases (28%).

On comparisons the three groups (Table 4); there is no significant difference in the mean age or gender. But a significant difference was present in the rate of malignancy. CUC (3) group has the highest risk for malignancy with five folds more than CUC (1) group and three folds more than CUC (2) group.

Discussion

Thyroid disease is a common clinical problem. Most of thyroid diseases occur in a nodular form. The prevalence of thyroid nodules in adults is reported between 4 to 8% [1], and up to 67% by ultrasound, while in autopsies up to 49–57% [3]. Although most of these nodules are benign, the possibility of malignancy is a major concern [4]. In fact, the differential diagnosis of a thyroid nodule is the most common endocrine problem [3]. Fine Needle Aspiration Cytology (FNAC) is the corner stone in decision making in the management of thyroid nodules especially after the FNAC reports had been standardized by the Bethesda System for Reporting Thyroid Cytopathology according to the suspected rate of malignancy [5]. Bethesda system consists of six categories that usually provide clear decision in the management of the patients as shown in (Table 4).

However, the category of Bethesda III is still a major problem with no clear recommendation or cut off for surgical interference. They represent a considerable ratio of cases, that is variable in different studies as shown in (Table 5) [6]. However, a recent large study reported a prevalence of more than 35% of the all Bethesda categories [7].

The expected malignancy rates for the Bethesda III category range from 5 to 15% according to relevant published studies [7]. Some recent papers have shown higher malignancy rates in lesions associated with nuclear atypia [8] and even the risk may exceed category Bethesda IV [9], suggesting that the heterogeneity of lesions within Bethesda III may have relevant impacts on the diagnosis and management of patients [10]. The current recommendation for the management of Bethesda III includes repetition of FNAC, ultrasound follow up or surgical interference (lobectomy) [11].

Table 5: Comparison of percentages of cases in each Bethesda Category and risk of malignancy between different studies.

Study	Year Country	Total FNAC cases	Percentage of cases in each Bethesda category						FNAC with follow-up*	Risk of malignancy in each Bethesda category (X)					
			I	II	III	IV	V	VI		I	II	III	IV	V	VI
TEtSPTC[14]	2010		2-20	60-70	3-7	-	2-8	3-7		1.4	0-3	5.15	15.3	60-75	97-99
				Middle East											
Present study	2017 Bahrain	681	10.1	68.8	12.4	2.9	2.6	4.1	126	6.67	Is	28	22.2	72.7	100
Mufti and Mola[3]	2012 KSA	250	11.6	77.6	0.8	4	2.4	3.6	84	20	3.1	SO	20	80	100
Al Dawish et al. [14]	2017 KSA	1433	3.2	75.3	9.1	5	2.2	5.1	124	25	8.9	14.3	47.2	69.7	96.7
Kapita et al. [17]	2015 Kuwait	374	4.8	30.5	15.8	4.5	21.4	23	374	33.3	11.4	18.6	35.3	61.3	96.5
Sinna and Exaatl[18]	2012 Egypt	296	7.1	33.1	13	16.5	10.1	19.5	220		2		32.7	96.7	96
				Other countries											
Bongiovanni et al. [13]	2012 Meta-analysis	2.5.445	12.9	59.3	9.6	10.1	2.7	5.4	6.362	16.8	3.7	15.9	26.1	75.2	98.6
Wu et al. [3]	2012 USA	1382	20.1	39	27.2	8.4	2.6	2.7	221		3	6	22	56	100
Kiernan et al. [11]	2014 USA	777	3	36	26	9	8	18	777	4	4.3	IS	26	65	97
Jo et al. [9]	2010 USA	3080	18.6	59	3.4	9.7	2.3	7	892	8.9	1.1	17	25.4	70	98.1
Sarkis et al. [1]	2014 Australia	2076	12.8	74.7	4.7	4.7	0.8	2.3	425	4.2	0.26	9.3	15.3	79	100
Melo-Uribe et al. [2]	2015 Colombia	196	4.1	23	5 2	16.8	37.2	16.3	196	75	13	75	39	90	100
Mondal et al. [4]	2013 India	1020	1.2	87.5		4.2	1.4	4.7	323	0	4.5	20	30.6	75	97.8

*FNAC with follow-up: Cases of FNAC underwent surgical treatment and correlation was done between cytology and histology result. KSA: Kingdom of Saudi Arabia; USA: United States of America; FNAC: Fine needle aspiration cytology.

Table 6: Cytologic substratification of Bethesda III nodules.

AUS/FLUS cases with surgery	Benign[a]	Malignant
AUSIFLUS—NOS (n=218)	41.3% [CI 36.0-46.6]	36.2% [CI 29.4-42.5]
AUS/FLUS—favor benign (n=13)	76.9% [CI 69.2-84.6]	7.7% [CI 1.9-36.0]
AUS/FLUS—cannot exclude FTC (n=28)	28.6% ICI 9.4-47.8)	53.6% [CI 33.9-72.1]
AUSiFLUS—cannot exclude Hiinhle cell neoplasm (n=44)	341% [CI 20.5-47.7]	29.5% [CI 16.8-45.2]
AUS/FLUS—cannot exclude follicular neoplasm (n=78)	24.4% [CI 11.9-36.9]	56.4% [CI 443-67.6]

[a]Excludes nonmalignant neoplasms.
CI: Confidence Interval; PTC: Papillary Thyroid Carcinoma; NOS: Not Otherwise Specified.

Table 7: Thyroid Imaging Reporting and Data Systems (TIRADS).

Sonographic Pattern	Ultrasound Features	Estimated Risk of Malignancy
High Suspicion **(TIRAB V)**	Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule with one or more of the following features: Irregular margins (infiltrative, microlobulatecl), microcalcifications, taller than wide shape, rim calcifications with small extrusive soft tissue component, evidence of ETE	>70% to 90%°
Intermediate **(TIRAB IV)**	Hypoechoic solid nodule with smooth mar- gins without microcalcifications, ETE, or tatter than wide shape	10% to 20%
Low Suspicion **(TIRAB III)**	Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid areas, without microcalcification, irregular margin or ETEc, or taller than wide shape.	5%-10%
Very Low Suspicion **(TIRAB II)**	Spongiform or partially cystic nodules without any of the sonographic features described in low, Intermediate, or high suspicion patterns	
Benign (**TIRAB I)**	Purely cystic nodules (no solid component)	<1%
Normal **(TIRAB O)**	Norm thyroid gland	

Some modifications of the Bethesda III have been developed to be subcategorized according to cytopathological characteristics to get more precise malignant risk.

Leticia et al subcategorized Bethesda III into; Bethesda IIIA which entails Follicular Lesion of Undetermined Significance (FLUS), and Bethesda IIIB that consists of lesion with Atypia of Undetermined Significance (AUS) [7]. They reported significantly higher malignancy rates for Bethesda Class IIIB than those for Bethesda Class IIIA and even Bethesda Class IV [7]. Other study has divided Bethesda III into; cases presenting common characteristics of papillary carcinomas and cases without features of papillary carcinoma. This study showed increased malignancy rates associated with the papillary features [5]. On the other hand Renshaw subdivided Bethesda III into four groups, and reported a difference in the malignancy risks that reached to 38% higher risk in lesions with papillary carcinoma characteristics

Table 8: CUC Scoring System for Bethesda III and selection of the management policy.

CUC Scoring System	Score	Risk for malignancy	Recommendation for management
CUC (1)	1,2,3	5.5%	Follow up after 4 months (clinical & ultrasound) and reassessment and Re-scoring.
CUC (2)	4,5	9.5%	Repetition of FNAC after 4 -6 months With re assessment clinical & ultrasound, and re-scoring
CUC (3)	6 or more	28.5%	Lobectomy or total thyroidectomy.

[12]. Others have divided Bethesda III nodules into those with low cellularity with a micro-follicular pattern and those showing nuclear atypia with significant increase in the malignant risk in atypia group [13]. Some studies have suggested that nuclear atypia is an independent risk factor [14]. Kelman et al. found that up to 60% of thyroid nodules with nuclear atypia were related to malignant disease, while only 7% of those without atypia had the same diagnosis [14].

Similarly, other authors re-evaluated the sub classification of Bethesda III and considered two categories: architectural atypia and nuclear atypia and concluded that; patients with nuclear atypia had a malignancy rate of 35% compared to a rate of 10% for other Bethesda III cases [15]. Again, Bethesda III is re-classified in another study into four groups; nonspecific, favor benign , papillary cancer cannot be excluded, Hurthle cell neoplasm can`t be excluded, & follicular neoplasm can`t be excluded as in (Table 6) with variable malignancy risk among these groups [16]. Other published cohorts of smaller size have suggested wide-ranging malignancy risk for Bethesda III [16]. Parengi et al. observed an incidence of 16% [17], while Vander Laan et al. reported a prevalence of 46% [18]. These and other outcomes have been confounded by study periods predating the Bethesda System for Reporting Thyroid Cytopathology, an incidence of AUS/FLUS diagnoses that is higher than the 7% expected, and, in some cases, inflation of the malignancy rate with incidental cancers [19].

A large study was done at Memorial Sloan–Kettering Cancer Center to determine the risk of malignancy in Bethesda iii and concluded that; the risk of malignancy in Bethesda III group is higher than estimated, with an estimated prevalence of 26.6-37.8%. Repetition of FNAC may not have clear utility in clinical decision-making and the guidelines recommending repeat FNA or observation merit reconsideration [16]. In addition the study added The limitations of FNA cytology imply that other diagnostic options may be valuable to delineate risk further and assist clinicians in identifying low-risk patients who may not require surgery [16].

Accordingly this Bethesda III category represents a heterogeneous group in terms of lesion characteristics, and wide range in both the malignancy rates, and the assumed management policy [15]. Consequently, Bethesda III need to be further reassessed in order to reach a clear guideline in the management.

On the other hand many sonographic characteristics of a thyroid nodule associated with a higher likelihood of malignancy include hypo echogenicity, increased intra-nodular vascularity, irregular margins, micro calcifications, absent halo, and a taller-than-wide shape measured in the transverse dimension [20]. Accordingly, ultrasound assessment and participation in decision making in the management of thyroid nodules is progressively increasing and well established. Similarly, the sonographic data and reports are recently standardized by Thyroid Imaging Reporting and Data Systems (TIRADS), that have been proposed for risk stratification of thyroid nodules (demonstrated in figure 4) [15]. The terminology of TIRADS was first used by Horvath et al. [21]. The initial purpose of TIRADS was to improve patient management and cost-effectiveness by avoiding unnecessary FNA Biopsies in patients with thyroid nodules (Table 7), with a sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 88, 49, 49, 88, and 94%, respectively [22]. However, its clinical use is still very limited and its practical application in clinical practice is questioned [22]. Some modifications of TIRAB were developed to improve the accuracy, such as Kwack that further subcategorized TIRAB categories [23]. However, large study has reported that TIRADS described by Horvath is not practicable due to numerous unclassifiable nodules, while the revised TIRADS published by Kwak is feasible and suitable to assess the prevalence of malignancy, but it cannot replace scintigraphic imaging and still of limited value compared to Bethesda in recommendation for the best management [24]. Moreover, till now FNAC is the most accurate method for determining malignancy, and is a fundamental part of current thyroid nodule evaluation [22].

In addition some demographics of the patients are important and should not be ignored in assessment of the malignant potentiality. The risk of cancer is higher with extremes of age (< 14 or >65) and male gender [3]. Also, family history of thyroid carcinoma in a first ¬degree relative, and positive family history of syndromes that are associated with differentiated thyroid cancer (Figure 4) constitute considerable risk factors that should be considered [3]. Clinical data such as hardness or fixation of the nodule as well as recent onset or rapid growth within four month in a previously diseased thyroid gland are considered one of the red flag signs for malignancy [25]. Subsequently, this study assumed a scoring system (CUC scoring system) for risk scarification of Bethesda III category considering the cytopathologic, ultrasound, and clinical characteristics (Table 8), to get a clear surgical decision in these cases. Cytologicaly, the study re-classified Bethesda III into Bethesda III A which entails Follicular lesion of Undetermined Significance (FUS) giving it a point in the score and Bethesda III B which consists of lesion of an Atypia of Undetermined Significance (AUS), giving it three points in the score. This based on the data from different studies that reported risk of malignancy three fold or more in cases presented with nuclear atypia than those with undetermined follicular lesions. Shrestha et al. showed a 36.8% malignancy rate for patients with nuclear atypia compared to rate of 10.8% in those without nuclear atypia [8]. Similary, Rosario PW et al, reported a malignancy rate of 41.5% in patients with nuclear atypia, while those with architectural atypia or others had a malignancy rate of 15.5% [26]. The CUC scoring system incorporate the ultrasonographic features that were standardized by TIRADS in the assessment giving the lesion scoring from zero to five according to the ultrasound findings. The CUC scor also consider the red flag signs in the clinical data in its assessment of the malignant potentiality

of the lesion. For each clinical risk factor present, 0.5 was given in the score assessment as in (Table 1). The Cytological, ultrasound & clinical score system (CUC score) sub-classifies the Bethesda III into three groups according to the degree of malignant risk.

Bethesda III low risk group (CUC 1): Which has score three point or less, this has a low risk for malignancy (5.5%), and the study suggested follow up management poly for these patient with clinical and ultrasound re assessment after four months and re scoring again.

Bethesda III Intermediate risk group (CUC 2): Which has score of four or five points, this has a intermediate risk for malignancy (9.5%), and the study suggested cytological follow up by repetition of FNAC re-assessment.

Bethesda III High risk group (CUC 3): Which has score six points or more, this has a high risk for malignancy (~28.5%), and the study suggested surgical management for this patients with lobectomy or total thyroidectomy.

Although further studies may be needed for more evaluation of the significance of CUC score, but there no doubt in the necessity of sub categorizing the Bethesda III category for better risk assessment and precise choice of the optimum management.

Conclusion

The differential diagnosis of a thyroid nodule is the most common endocrine problem with the Fine Needle Aspiration Cytology (FNAC) standardized by Bethesda system is the corner stone in decision making & management. However, Bethesda III is still a problem that needs to be subcategorized for better risk assessment and consequently the optimum management. The Cytological, ultrasound & clinical score (CUC score) is a scoring system that utilizes the cytologic and ultrasongraphic features in addition to the risk factors in the clinical data in determining the malignant risk. The score provides three groups with variable malignant risk and management policy. The study subcategorized the Bethesda III category into three groups. Low risk group (CUC 1) that has a low malignant risk (5.5%) where ultrasound follow up is recommended as management policy. Intermediate risk group (CUC 2) group; that has an intermediate risk (9.5%) where cytological follow up by repetition of FNAC is recommended. And High risk group (CUC 3) that carries a high malignant risk (28%) and surgical treatment is recommend in this group.

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Citation: Elsaady A, Abdelgawad W. New Score for Risk Stratification and Sub-classification of Bethesda III Thyroid Nodule for Optimum Management; CUC Score (Cytological, Radiological, and Clinical Scoring System). Annals Thyroid Res. 2019; 5(1): 188-195.