ORIGINAL ARTICLE

Diagnostic Accuracy of Ultrasound U Classification System of Thyroid Ultrasound in Predicting Thyroid Malignancy by Using Histopathology as Gold Standard

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Author`s Contribution

[1,3]Conception, planning of research and writing of manuscript,
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ABSTRACT

Objective: The objective of this study is to determine the diagnostic accuracy of ultrasound U classification system of thyroid ultrasound in predicting thyroid malignancy by using histopathology as gold standard.

Methodology: This was a cross sectional study conducted in the Fatima memorial Hospital, Lahore in a duration of one-year January 2017 to January 2018. All the patients irrespective of age and gender were taken. Patients were segregated with the presence of thyroid nodules. Lateron the patients were subjected to US and ultrasound guided FNAC. Correlation of the histopathology reports was made with the u classification system. Sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, predictive value, negative predictive value and accuracy were calculated in a conservative and non-conservative method.

Results: It was observed that out of 100 nodules examined 11 were malignant. The sensitivity of the ultrasonography was 80% and specificity was 34%. Moreover, positive predictive value was 100% and negative predictive value was found to be 90%.

Conclusion: The u classification system is a reliable tool for the detection of the thyroid nodules and predicting malignancy which is proved by histopathology. More research however is necessary for widespread acceptance and application of this tool.

Key word: Ultrasonography, thyroid nodules, Fine needle aspiration cytology, thyroid carcinoma.

Introduction

A thyroid nodule is a specific lesion with in the normal thyroid. Such nodules are a common occurrence in the general population and a frequent incidental finding on computed tomography (CT) and magnetic resonance imaging (MRI). Autopsy studies have reported incidental thyroid nodules in up to 50% of subjects.[1] Most nodules are benign, but between 3 and 7% of cases are found to be malignant.[2] Ultrasound (US) has become an unavoidable diagnostic tool in the assessment of thyroid nodules. It is highly sensitive for detecting nodules, and the sonographic features of the nodules can be used to determine the need for further investigation.[3] A number of studies have investigated both benign and malignant sonographic features of thyroid nodules. [1]

[4–7] However, because it is impossible from an economic and patient anxiety point of view to biopsy every thyroid nodule in order to exclude malignancy, a reliable guideline was necessary to specifically target nodules that require biopsy. Based on current evidence, the British Thyroid Association (BTA)recently produced a US classification (U1–U5) of thyroid nodules to facilitate the decision-making process regarding the need to perform fine-needle aspiration cytology (FNAC) in suspicious/ unequivocal cases.[8] The aim of this paper is to analyze the results we got from our practice here in a tertiary care hospital, in Lahore, and prove the accuracy of this classification using histopathology as a gold standard and thereby reduce the number of

unnecessary FNACs which is both a problem to the patients and waste of valuable energy and resources at our end. Apart from that it will help the radiologists and clinicians to readily recognize the sonographic patterns and classify nodules into categories of U1 to U5.

Methodology

We chose all patients who presented to us in the radiology department with request of thyroid scan including all ages groups both male and female. Some of the nodules were palpable while others were not. We included all the nodules that were solitary, multinodular goiters were excluded to reduce the confusion. Also, patients having a previous history of partial or total thyroidectomy or radioactive ablation were excluded from the study.

Ultrasound imaging protocol: All of the ultrasounds of thyroid gland were performed by a single radiologist on Toshiba xario 100 ultrasound machine equipped with 3.5-5MHz Curvilinear and 7.5-15 MHz Linear probe. Both transverse and longitudinal images were taken. A cross-sectional analytical study was designed to prospectively collect data from the department of Radiology, Fatima memorial hospital, Lahore, from January 2017 to January 2018 via nonprobability consecutive sampling technique

Nodule classification: The thyroid nodules were given a U1-U5 score based on the features that were described in the BTA Guidelines i.e. normal(U1), benign (U2), equivocal/indeterminate (U3), suspicious (U4) and malignant (U5). As U-classification system classify the patients into five different classes on basis of type of tumor, we categorized the class 2 as benign and class 4, 5 as malignant cases. While class 3 cases were placed in the respective groups as their level of significant closeness to the malignancy o benign type of tumor.

Ultrasound Guided Fine Needle Aspiration and Histopathology: All of the thyroid nodules were aspirated using (22) gauge disposable needles using standard procedures[7] after informed consent. The aspirated contents of the needle were expelled onto glass slides. With the help of the pathology department four slide smears were made for each case and immediately fixed in 95% ethyl alcohol for about 30 min. All the slides were stained with Papanicolaou stain. Diagnosis of cytological smears was done according to standard criteria defined by various authors.[2] The cytopathology reports were classified as benign, indeterminate, suspicious of malignancy, malignant, or inadequate. Histopathology reports were obtained for cases that were cytologically reported as inadequate, indeterminate or suspicious of malignancy.

Statistical Analysis: Statistical analysis was performed with the SPSS software package IBM version 23. There were conservative and non conservative methods of analysis of the U classification. For a conservative method, only U2 was classified as negative test whereas only U5 was classified as a positive test. For the non conservative method, both U2 and U3 were classified as negative test whereas both U4 and U5 were classified as positive test. A significant difference was defined as a p-value

less than 0.05.A receiver operating characteristic (ROC) curve analysis was used to examine the diagnostic performance of the U Classification in determining a malignant result.

Results

Mean age of the study samples was 41.64 years (11.57). Majority of the cases were female with frequency of 73(73%) while male were 27(27%). On ultrasonographical evaluation it was noted that most of the cases were with U-3 classification 59(59%), U-2 with frequency of 29(29%), 11(11%) were classified in U-4 category and 1(1%) in U-5. While it was noted that benign cancer was in 89(89%) and malignant was 11(11%) on evaluation of histopathology. It was observed that there was non-significant difference between the US and histopathology for the detection of the carcinoma and it's a particular type as mentioned in the (Table I). It was noted that there were 29(100%) who were in U-2 and predicted for the benign type of tumor, 51(86.4%) were predicted benign and confirmed same from the histopathology and 8(13.6%) were benign which were predicted for benign but in actual was malignant. (Table II) There was no significant impact was noted on the diagnostic difference between US and histopathology when the analysis was specified taking age and gender specific. (Table III).

Table I: Evaluation of the accuracy of the US for detection of the Tumor type

	Histopathological classification of tumor			P-Value	
	Benign	Malignant	Total		
Benign	69 89.2%	8 10.8%	77 100.0%	0.001	Sensitivity 80%
Malignant	12 65.2%	8 34.8%	23 100.0%		Specificity 34%
	PPV	82%	NPV	50%	Accuracy=77%

Table II: Comparison of categories of u classification by US and FNAC

		Histopathological classification of tumor		Total
		Benign	Malignant	
Ultra-sonographic classification of tumor	U-2	29	0	29
		100.0%	.0%	100.0%
	U-3	56	3	59
		94.9%	5%	100.0%
	U-4	4	7	11
		36.4%	63.6%	100.0%
	U-5	0	1	1
		.0%	100.0%	100.0%

Discussion

Thyroid nodules are quite common particularly in females and ultrasound is often the first radiological examination asked. Ultrasound was believed to be useful just in separating solid from cystic nodules, but higher resolution probes and doppler scanning has carried ultrasound to a higher level by denoting certain factors which have become better appreciable by the new machinery. Because no single sonographic feature is dependable in separating benign from malignant thyroid nodules and an over lap exists between them.[9] So British thyroid association, in 2014, came up with a U classification system which compiled all the research done on thyroid nodules and classified the nodules based on their knowledge of features associated with proven cases of benign and malignant nodules into five categories U1 being normal and U5 containing features which were most consistently associated with malignancy. This tool will help the radiologist to further guide for the need of FNAC on selected patients as it is not possible to target all the nodules to aspiration which can be both a financial and physical burden. So, nodules classified into U2 were always benign so they just needed to be reported as such, no intervention was needed. But categories U4 and U5 had features which either in solitude or multitude were associated with malignancy, so had to be aspirated. U3 however was the class which although was the commonest yet hardest to predict, as the risk of malignancy in this class was low but nonetheless not ignorable,

Table III: Impact of age and gender for on the diagnosis of the tumor

Group of Age			Carcinoma type on US		P-value
			Benign	Malignant	
21-40 years	Histopathological classification of tumor	Benign	31(93.9%)	2(6.1%)	0.01
		Malignant	7(58.3%)	5(41.7%)	
>40 years	Histopathological classification of tumor	Benign	40(97.6%)	1(2.40%)	0.04
		Malignant	11(78.6%)	3(21.4%)	
Male	Histopathological classification of tumor	Benign	23(95.8%)	1(4.2%)	0.02
		Malignant	1(33.3%)	2(66.7%)	
Female	Histopathological classification of tumor	Benign	48(96%)	2(4.0%)	0.01
		Malignant	17(73.9%)	6(26.1%)	
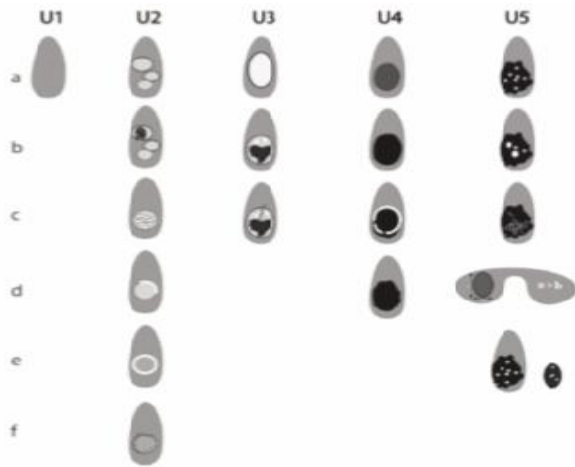
So we carried out this study in our department to assess the diagnostic accuracy of this classification system in our set up and thus benefit from the study reducing both the patient anxiety and morbidity. We found that the sensitivity of the classification system was good in correctly classifying the nodules especially the u2 nodules and U 5 nodules which were 100% accurately predicted as benign and malignant respectively. In U4 class 63% were malignant which was also considered as malignant and had good sensitivity in recording that. So U4 and U5 nodules should be subjected to FNAC. Out of 12 nodules, which were classified as U4 and U5, 4 turned out to be benign giving a few false positives. U3 category showed 59 nodules out of which 56 were benign and 3 showed atypia rendering them false negatives. So this means the safest practice would be to do FNAC on them.

In a previous study it was noted that sensitivity and specificity with 95%CI of ultrasound in differentiating malignant thyroid nodule from benign thyroid nodule calculated to be 91.7% (95%CI, 0.72-0.98) and 78.94% (0.68-0.87) respectively. Reported positive predictive value and negative PV were 57.9% (0.41-0.73) and 96.8% (0.88-0.99) and overall accuracy was 82% which was lower as compared to the result of in this study. But it may be due to use of the fact that only two options in histopathology as gold standard were considered.[13] This also makes room for more research here.

It was noted that sensitivity and specificity may also be low because of peripheral calcification of the nodule rendering the nodules hypoechoic and results

in the placement of some of these nodules into U-4 class that should be in U-2 category otherwise.

We have classified the patients on the basis of U-classification into two groups. Group one consisted of U-2 nodules and partially U-3 nodules defined as benign cases and U4 and U5 classified nodules were considered as malignant cases. cy. Limitation of this study involved the smaller sample size and clinically more accurate patients were considered. There is need to conduct this study on a larger sample size with the general population having any type of abnormal growth at the thyroid region.

Conclusion

Taking everything into account, Ultrasound U-classification system has a high indicative precision in distinguishing and segregating thyroid nodules on premise of features like echogenicity, edges, small scale calcifications shape and vascularity. Radiologists' must be acquainted with these signs on ultrasound that guide to separate benign from malignant lesions and for right application of FNAC. So that, diagnosis can be made more cost effective even for the low socio economic population and avoid unnecessary aspirations but expedite them when needed.

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