Original Article

Diagnostic Accuracy of Ultrasonography in Classifying Thyroid Nodules Compared with Fine-Needle Aspiration

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Abstract

Background: Classifying thyroid lesions is challenging; nonetheless, using ultrasonography may allow for accurate diagnosis, differentiation and management of thyroid lesions and help avoid unnecessary biopsy.

Objectives: The main objective of the study is to determine the diagnostic accuracy of ultrasonography in classifying thyroid nodules compared with fine-needle aspiration.

Materials and Methods: This retrospective study included all 68 patients diagnosed with thyroid nodules at King Fahd Hospital of the University, Al Khobar, Saudi Arabia, between June 1, 2014, and November 30, 2016. Parameters were selected based on the Society of Radiologists in Ultrasound criteria. Ultrasonographic features, namely, nodule margins, echotexture, vascularity and calcifications, and fine-needle aspiration cytology (FNAC) results were reviewed by two radiologists blinded to each other's findings and validated by another experienced interventional radiologist. Ultrasonography results were compared against that of FNAC to calculate sensitivity and positive- and negative-likelihood ratios, and the nodule types were compared using Fisher's exact test.

Results: Of the 68 nodules analyzed, 59 were reported as benign using FNAC (specificity = 95%; $P < 0.001$). Of these 59, 56 were also reported as benign using ultrasonography. The specificity of ultrasonography in determining benign nodules was 94.9%, and the positive- and negative-likelihood ratios were 13.0 and 0.35, respectively. Six of the nine suspicious nodules were confirmed as malignant using FNAC, and the ultrasonography and FNAC findings were strongly associated ($P = 0.001$). According to the Society of Radiologists in Ultrasound criteria, FNAC and ultrasonography findings were significantly associated for nodule calcification ($P = 0.001$) and echogenicity ($P = 0.001$).

Conclusion: The diagnostic specificity of ultrasonography and FNAC in this study are consistent with those reported previously, indicating that ultrasonography reliably classifies thyroid nodules, and thus can assist in the decision-making regarding need for biopsy.

Keywords: Cytology, diagnostic accuracy, fine-needle aspiration, thyroid gland, thyroid nodule, ultrasonography

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INTRODUCTION

The incidence of thyroid nodules has been on the rise in the Saudi population, with women more likely to develop thyroid cancer than men. In fact, thyroid cancer is the second most common malignancy among Saudi women.[1] Similarly, in the Gulf countries, thyroid cancer is the fifth most common cancer among women, and the rates of thyroid malignancies are significantly higher in women from these countries than in those from the United States.[2-4] Therefore, it is crucial to differentiate between benign and malignant thyroid nodules in this population.

Ultrasonography (US) is considered as the primary method for evaluating thyroid nodules because of its acceptability, cost-effectiveness and safety.[5-7] However, being an operator-dependent method, its use is limited by the technical skill of the operator. In contrast, fine-needle aspiration cytology (FNAC) is considered the gold standard diagnostic test for evaluating thyroid nodules.[8,9]

The Society of Radiologists in Ultrasound (SRU) recommends avoiding unnecessary tests and surgeries in patients with benign nodules.[10] Therefore, to diagnose clinically significant thyroid cancers, the SRU recommends the use of FNAC only when the nodules are ≥10 mm in size and with microcalcifications; ≥15 mm and solid or with coarse calcifications; ≥20 mm and mixed solid and cystic or for nodules that significantly increase in size since the last US. However, despite these guidelines, the use of US-guided FNAC is globally increasing to avoid missing cases of malignancy.[10,11]

The current study was conducted to determine the diagnostic accuracy of US in differentiating benign, suspicious and malignant thyroid nodules compared with fine-needle aspiration (FNA), and thus, determine if US can be used as a viable alternative to the more invasive, expensive and time-consuming FNAC. Similar previous studies have been conducted but were inconclusive and were limited by small sample sizes.[12,13] This study will add to the existing literature and help substantiate the findings of previous studies. In addition, to the best of the authors' knowledge, despite the high rates of thyroid malignancies, no study has been conducted from the Gulf region to analyze the diagnostic accuracy of US in classifying benign and malignant thyroid nodules.

MATERIALS AND METHODS

Study design, setting and subjects

This retrospective cohort study analyzed the reports and images of all patients who had been diagnosed with thyroid nodules at the Radiology Department of King Fahd Hospital of the University (KFHU), Al Khobar, Saudi Arabia, between June 1, 2014, and November 30, 2016. KFHU is a tertiary, academic, governmental hospital with a capacity of 600 beds. KFHU is the largest government hospital in Al Khobar. In addition, its Radiology Department is considered one of the largest in the area and serves as one of the main referral centers. Therefore, the sample size would be representative of the area.

The keyword "thyroid nodule" of the International Classification of Diseases-9 coding system, under codes 241.0, 242.1, 226, 193, 258.03 and 258.02, was used to retrieve medical file reports from the hospital's electronic medical filing system. Patients with solid or partly solid nodules were included in the study. Patients with only cystic nodules or with nodules of complete watery content without evidence of complex components on sonography were excluded, as these nodules were considered benign. Patients with any missing US or FNAC data were not included in this study.

Ethical approval for this study was obtained from the Institutional Review Board of Imam Abdulrahman Bin Faisal University (approval number: IRB-2016-01-148) on October 16, 2016.

Imaging studies

Ultrasound image acquisition and analysis

US had been performed using an Esaote US machine (MyLab™ ClassC, Esaote, Genoa, Italy) and electronically focused near-field probes with a bandwidth of 7–12 MHz. Data collection was performed by two board-certified radiologists who reviewed the stored US images and written reports. A radiology consultant with 10 years of experience in diagnostic and interventional radiology reviewed this data by checking and validating the collected findings; these findings were found to be in agreement. For assessing the interrater reliability, the kappa test was conducted, and the kappa value was >80%, indicating adequate reliability.

The US parameters evaluated were based on the consensus conference statement of SRU, without delineating regions of interest and with a focus on nodules requiring US-guided FNAC and FNAC. The included parameters were nodule margins, echotexture, vascularity and calcifications.[10] Unfortunately, electrical impedance was excluded because it was not routinely performed in practice. Margins and echotexture were assessed using qualitative measures. In

patients with multiple nodules, only the most dominant nodule in terms of size and suspicious sonographic features was included in the analysis, in line with the SRU consensus. The mean sonographic size criteria of the study nodules were 3.14 ± 0.72 cm along the longest axis; as size is not a specific criterion of malignancy according to the SRU consensus, this sensitive measure was not included for comparison in this study.[10,14] Nodules were defined under US as either benign, unlikely to be benign (i.e., suspicious with imaging features not pathognomonic to a certain category) or malignant.

Fine-needle aspiration procedures

The purpose and procedure had been explained to the patients and informed consent was obtained. For US-guided FNAC, patients were placed in a supine position with the neck slightly extended backward. Then, the lesion was identified and anatomically localized, the covering skin was cleansed and sanitized with a 10% povidone-iodine solution, and the surgical site was draped. A high-resolution (7.5–15-MHz) linear-array sonographic transducer with a sterile cover placed over its headpiece was used for US. US gel was not always necessary because the povidone-iodine antiseptic solution used for skin sterilization could serve as a primary coupling agent. A local anesthetic agent is normally utilized during this process to reduce a patient's discomfort. Approximately 1–2 ml of 1% lidocaine hydrochloride solution (a voltage-gated Na^+ channel blocker of nerve conduction) was typically interjected into the skin and superficial subcutaneous tissue at the predetermined site. In terms of needles, mostly 20–27G needles (Echo-Coat US needle; STS Biopolymers Inc., Henrietta, NY, USA) were used for FNA with an attached 2–20-mL syringe.

For fine-needle aspiration, the transducer was positioned immediately over the lesion, scanning was performed for lesion localization, followed by color Doppler imaging to detect blood vessels in and close to the nodule, to avoid vascular injury during the procedure. A freehand biopsy technique was used with careful monitoring of the needle's tip. When the needle hit the targeted lesion, the biopsy was completed. Four aspirations were performed on each nodule.

The SRU criteria for biopsy selection were followed, and tissues for biopsy were obtained from multiple sites of a solid lesion, including the center and the peripheral aspects of the lesion with existing microcalcification. If there was a cystic component in the nodule, it was usually aspirated for cytology.

Classification

Cytological classifications were either positive, negative or indeterminate for malignancy, according to the histopathological analysis performed by the assessors blinded to the US results. For indeterminate nodules, a complementary diagnostic assessment using thyroid core needle biopsy was considered. The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was not implemented because it correlates the estimated risk of malignancy with proper management, which was outside the scope of this study and lacked uniformity in the reporting terminology. Moreover, the current study had a small sample size, and thus, a limited number of diagnostic categories and subcategories of thyroid FNAC specimens were encountered in this study, whereas the TBSRTC requires multiple diagnoses for implementation.[15]

Statistical analysis

Statistical analysis was performed using the SPSS Statistics for Windows version 21.0 (IBM Corp., Armonk, NY, USA) and Minitab 17 Statistical Software (Minitab Inc., State College, PA, USA). Results from US were compared against that from FNAC to calculate the sensitivity as well as positive- and negative-likelihood ratios. Chi-square test was used for categorical variables and *t*-test for continuous variables. Comparisons between nodule types were performed using Fisher's exact test. Statistical significance was set at $P < 0.05$.

RESULTS

A total of 68 patients were included in this study, of which 78% were female. The mean age of the participants was 39 ± 13 years (range: 8–82 years). As KFHU is a tertiary, government hospital that provides free health care, the referred patients were from diverse ethnicities: 82.35% patients were Arab, 5.88% were far-East Asian, 5.88% were South Asian (Indian) and 5.89% were African.

In FNAC, 59 of the 68 nodules analyzed were reported as benign; 56 of these were also designated as benign with US. Therefore, the specificity of US in determining benign nodules was 94.9% (95% confidence interval [CI] = 85.9%–98.9%), the positive-likelihood ratio was 13.0 (95% CI = 1.1%–7.2%), and the negative-likelihood ratio was 0.35 (95% CI = 0.1%–0.9%). There was no inadequate sampling or indeterminate cytology of the lesions. Of the nine suspicious nodules, six were found to be malignant using FNAC, with histology revealing papillary adenocarcinoma. The US and FNAC findings were strongly associated ($P = 0.001$) [Table 1]. In addition, the diagnostic specificity of FNAC was 95% ($P < 0.001$)

Table 1: Specificity of ultrasound in classifying benign and malignant tumor compared with fine-needle aspiration

Type of tumor	FNAC finding	US finding	Specificity of US (95% CI)
Benign	59	56	94.9 (85.9–98.9)
Malignant	6	9	100.00 (54.07–100.00)

FNAC – Fine-needle aspiration cytology; US – Ultrasonography; CI – Confidence interval

when benchmarked against the histological findings, indicating that it is a reliable diagnostic modality for thyroid nodules.

According to the SRU criteria, FNAC and US findings were significantly associated for calcifications ($P = 0.001$), margins ($P = 0.031$) and echogenicity of the nodules ($P = 0.001$), while the association for vascularity was nonsignificant ($P = 0.058$), indicating that US aids in identifying malignant thyroid nodules [Figures 1-3 and Table 2].

DISCUSSION

The SRU consensus statement had been developed to provide physicians with specific recommendations for US-detected nodules that should undergo FNAC. Adoption of these recommendations would help in avoiding unnecessary biopsies. Despite these guidelines, US-guided FNAC is increasingly being used to avoid missing cases of malignancy.[11,16] In this study, US had a 94.9% specificity in diagnosing benign thyroid nodules. Therefore, US may be useful for the assessment and classification of thyroid nodules and may help avoid unnecessary FNAC. In addition, the use of diagnostic US can be maximized by applying the prescreening risk stratification and using the SRU consensus criteria for nodule biopsy [Figures 1-3]. It should be noted that no single sonographic feature can classify benign and malignant thyroid nodules. Further, with US being an operator-dependent modality, it increases the importance of the technical skills an operator develops after years of working with US.

Shape, orientation, size, margins, acoustic transmission, calcifications, echogenicity and vascularity are some of the US parameters that were identified in previous studies as being useful for the classification of thyroid nodules.[14,15,17,18] In a recent study that evaluated the diagnostic value of Thyroid Imaging Reporting and Data System classification in conjunction with ultrasonic elastography for assessing the risk of malignancy in thyroid nodules, high accuracy was reported in evaluating the potential risk of malignancy in thyroid nodules with a high elastography ratio, with a sensitivity of 88.9% and a specificity of 91.8%, that was confirmed by histological examination.[19]

In another recent study, Ní Mhuircheartaigh *et al*.[20] evaluated the use of thyroid nodule size on US as a standard parameter for primary surveillance of thyroid nodules and correlated its size with those on imaging modalities such as computed tomography, magnetic resonance imaging and positron emission tomography. The findings of that study indicated that cross-sectional imaging underestimates

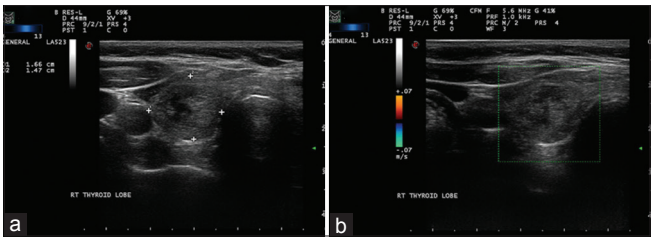

Figure 1: (a) Grayscale ultrasound image of the right thyroid lobe showing a well-defined, predominately iso- to low-echogenic lesion with distal acoustic enhancement. (b) The contour of the lesion is regular and no vascularity is visible on color Doppler imaging. These features are consistent with a benign thyroid nodule. Fine-needle aspiration interpretation revealed few polymorphs and occasional macrophages, negative for malignant cells

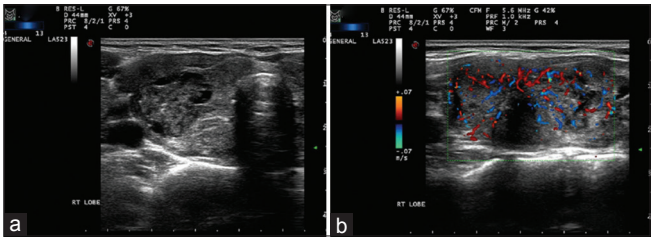

Figure 2: (a) Grayscale ultrasound image of the right thyroid lobe showing a well-defined, predominately low echogenic lesion with multiple minute cysts located peripherally. There are multiple echogenic foci with distal acoustic shadows representative of calcifications. (b) The contour of the lesion is regular and shows hypervascularity on color Doppler imaging. These features are consistent with a suspicious thyroid lesion. Fine-needle aspiration interpretation revealed several papillary clusters of follicular cells that are suspicious for papillary thyroid carcinoma

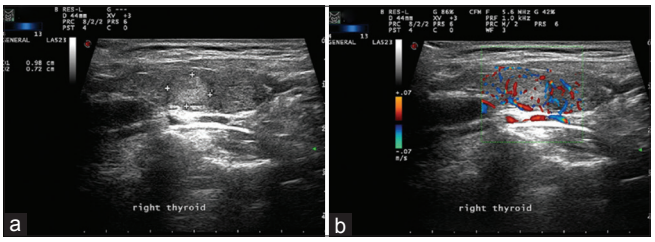

Figure 3: (a) Grayscale ultrasound image of the right thyroid lobe showing a well-defined echogenic lesion with distal acoustic enhancement. (b) The contour of the lesion is regular with a peripheral anechoic halo and shows hypervascularity on Doppler imaging. These features are consistent with a malignant thyroid lesion. Fine-needle aspiration interpretation revealed Bethesda category (6) consistent with papillary thyroid carcinoma

Table 2: Cancer risk in thyroid nodules with regard to calcification, margins, vascularity and echogenicity, as per the Society of Radiologists in Ultrasound criteria

Parameter	Type of tumor and method	Characteristics		*P*
		Macrocalcification	Microcalcification	
Calcification	Benign	56	3	0.001
	Cytology (%)	96.6	30.0	
	US (%)	94.9	5.1	
	Suspicious	2	7	
	Cytology (%)	3.4	70.0	
	US (%)	22.2	77.8	
Parameter	**Type of tumor and method**	**Regular**	**Irregular**	***P***
Margins	Benign	55	4	0.031
	Cytology (%)	93.2	44.4	
	US (%)	93.2	6.8	
	Suspicious	4	5	
	Cytology (%)	6.8	55.6	
	US (%)	44.4	55.6	
Parameter	**Type of tumor and method**	**Normal**	**Increased**	***P***
Vascularity	Benign	41	18	0.058
	Cytology (%)	93.2	75.0	
	US (%)	69.5	30.5	
	Suspicious	3	6	
	Cytology (%)	6.8	25.0	
	US (%)	33.3	66.7	
Parameter	**Type of tumor and method**	**Regular**	**Irregular**	***P***
Echogenicity	Benign	55	4	0.001
	Cytology (%)	93.2	44.4	
	US (%)	93.2	6.8	
	Suspicious	4	5	
	Cytology (%)	6.8	55.6	
	US (%)	44.4	55.6	

The cytology percentages are calculated vertically. US – Ultrasonography

the size of thyroid nodules and lacks valuable clinical significance.

In the current study, the SRU diagnostic criteria were used for classifying thyroid nodules based on calcification, margins, echogenicity and vascularity, as they have the strongest correlation with malignancy.[21] This is one of the strengths of our study, in that the analysis was not limited to only a single criterion, such as nodule size.

In this study cohort, the use of US features for differentiating benign from suspicious lesions was found to be useful and efficient. These results showed that the presence of features such as regular margins, normal vascularity and homogeneity as well as the absence of macrocalcifications on US [Figure 1] were strongly associated with benign thyroid lesions, which was a finding similar to the findings from various studies.[14,17,18,22] In fact, the FNAC and US findings were significantly associated, and thus presence/absence of these features in US would indicate that no further evaluation might be necessary for benign nodules. Our findings are in agreement with those of previous studies reporting that US performed in conjunction with FNAC can aid in accurate diagnosis.[12,13,23-25] In addition, the diagnostic specificity of FNAC (95%; $P < 0.001$) in our study reflects the validity of FNA as an advanced modality for the surgical and pathological examination of thyroid nodules.

Most previous studies have found that papillary thyroid carcinoma was the most common type of thyroid tumor;[26] in the current study, all encountered malignant lesions were diagnosed as papillary thyroid carcinoma based on the histopathology. A small percentage (2%) of the investigated benign nodules had features such as microcalcifications, irregular margins or internal vascularity on US, which were not sufficient for the exclusion of malignancy, similar to the findings from other studies.[13,23,25]

Thyroid core-needle biopsy exhibits higher diagnostic sensitivity and accuracy, especially with papillary and follicular thyroid carcinomas. Further, it also enables a better assessment of the histological architecture and relation to the adjacent thyroid tissue and may lower the rate of inconclusive FNA results. Therefore, core-needle biopsy is considered in cases where FNA only obtained specimens of grossly scant-appearing cellularity after

several passes or in patients who return for a repeat biopsy after a nondiagnostic initial FNA biopsy.[27,28]

It should be noted that core-needle biopsy has several disadvantages compared to FNA; it can cause more patient discomfort, necessitates local anesthesia and needs more experience in image-guided thyroid interventions, and thus, has a higher operator dependency. In addition, it is considered relatively more invasive, with larger tissue samples being obtained, and it may be technically unfeasible or difficult in some cases.[11,28] Therefore, in the current study, this technique was considered for use only in the complementary diagnosis of indeterminate nodules.

Recent studies concluded that enlarged cervical lymph nodes in conjunction with thyroid nodules are highly suggestive of thyroid cancer. However, the precise estimation of the risk of thyroid cancer when encountering cervical lymphadenopathy and presence of suspicious thyroid lesions remains unknown.[29] Moreover, we believe that the presence of abnormal lymph nodes overrides the US features of thyroid nodule(s) and is most suggestive of metastasis and should prompt further diagnostic investigations.[10] Nonetheless, tissue elasticity (elastography) has recently been proposed to detect malignancy in thyroid nodules; unfortunately, the US machines in our institution do not support the feature of strain- and shear-wave elastography.[30,31]

There are several limitations to our study. First, its retrospective nature renders it at risk of selection bias. Second, the study had a relatively small sample, which may have led to over- or under-estimation of the study findings. Third, most of the lesions were found to be benign, and thus, the analysis of the study was limited.

CONCLUSION

The findings of this study indicate that thyroid nodules with the potential risk of malignancy can be recognized by identifying several sonographic features including calcifications, margins, vascularity and echogenicity. This approach is imperative to anticipate the cancerous risk of nodules, which can help avoid unnecessary FNA. The present study demonstrates that the US criteria provide substantial guidance pertaining to the requirement of biopsy, and thus, the authors recommend inclusion of these criteria in the reporting systems used by radiologists. Further prospective studies with larger cohorts are warranted to confirm the findings of this study.

Ethical considerations

This study was approved by the Institutional Review Board of Imam Abdulrahman Bin Faisal University (approval number: IRB-2016-01-148) on October 16, 2016. As this study is a retrospective chart review, patients were deidentified and the need for informed consent was waived.

Peer review

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Conflicts of interest

There are no conflicts of interest.

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