Combined ultrasound criteria with ultrasound-guided fine-needle aspiration cytology in assessment of single thyroid nodule in Radiodiagnosis Department, Assiut University Hospital: a prospective study

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Background
Solitary thyroid nodule (STN) is a common clinical condition. There are several pathologic conditions including neoplastic, hyperplastic, and inflammatory diseases that can lead to focal enlargement of the thyroid gland.
Ultrasound (US) is the most sensitive imaging technique available for assessment of the thyroid gland. Thyroid fine-needle aspiration cytology (FNAC) under US guidance is a well-established test for preoperative diagnosis of thyroid diseases.

Objective
The aim of our study is to correlate the role of combined sonographic criteria and US-guided FNAC with postoperative histopathological examination in assessment of STN.

Patients and methods
A total of 30 patients (20 females and 10 males in different age groups) with STN were recruited from the Radiology Department, Assiut University Hospital, from May 2017 to May 2019. Their age ranged from 19 to 74 years, with a mean age of 41.50 ± 15.16 years. All our patients underwent US assessment of the STN and FNAC for cytological evaluation using Bethesda system before surgery to decide the type of surgery to be undertaken. Data were collected and analyzed using SPSS, version 20, and statistical significance was set at *P* value less than 0.05.

Results
Based on US findings, benign nodules presented in 21 (70%) patients, whereas nine (30%) patients had malignant nodules. However, regarding the results of cytology, 20 (66.7%) patients had benign nodules, whereas eight (26.7%) patients had malignant nodules, and only two patients in whom samples were taken by FNAC were unsatisfactory. US findings had 100% sensitivity and 84% specificity and FNAC had 100% sensitivity and 87.5% specificity for prediction of malignant thyroid nodules.

Conclusion
FNAC is considered the gold standard diagnostic test and has an important role in differentiating between benign and malignant lesions of the thyroid gland.

Keywords:
fine-needle aspiration cytology, solitary thyroid nodule, ultrasonography

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Introduction

The American Thyroid Association described the thyroid nodule as a discrete lesion within the thyroid gland. It is radiologically obvious from the surrounding thyroid parenchyma [1].

Thyroid gland is a usual site for benign and malignant diseases, so early diagnosis is necessary for greater management and survival of the patient. Solitary thyroid nodule (STN) is a common finding mostly in females and in the elderly people. They are found in 5% of the people with the use of palpation [2], but ultrasonography (US) allows their identifications in up to 67% of cases [3].

US is noninvasive, widely accessible, less expensive, and does not use any ionizing radiation. The main restriction of thyroid US is that it cannot detect thyroid function [4,5].

Thyroid fine-needle aspiration cytology (FNAC) under US guidance is a well-established approach for preoperative diagnosis of thyroid diseases [6]. The principal function of thyroid FNAC is to triage cases for either surgery or conservative management. Cases with FNAC results that favor malignancy and/or neoplasia are managed surgically, whereas cases with

FNAC results that suggest a benign lesion can be followed clinically [7].

Patients and methods

This prospective study was conducted in patients who presented with STN at the Radiology Department, Assiut University Hospital, from May 2017 to May 2019. It included 20 females and 10 males. Their ages ranged from 19 to 74 years old. The study protocol was approved by Ethics Committee of Faculty of Medicine Assiut University (IRB: 17101086). Consent for publication has been obtained.

Preprocedural assessment

(1) Complete history taking included the following:
   (a) Present illness such as neck pain, dysphagia, or neck swelling.
   (b) Past history of irradiation exposure.
   (c) Family history of hyperparathyroidism or pheochromocytoma.
(2) Routine neck US was done carefully for all patients included in the study to record the sonomorphological features of the STN as well as presence of cervical lymph nodes enlargement or not with their criteria.
(3) Complete examination by surgeons included consistency of the nodule, its relations to the surrounding structures, and presence of secondary lymph nodes enlargement or not.
(4) Other investigations:
   (a) Prothrombin time and concentration.
   (b) Thyroid function tests.
   (c) Complete blood count.

Patient instructions and preparation

(1) The patients were informed of the procedure steps and were reassured.
(2) The patients were asked to keep in supine position with hyperextension of neck.

The procedure

FNAC was performed with the freehand technique under US guidance. The transducer was covered with a sterile plastic cover. To prevent image degradation, US gel was placed inside the sterile cover to provide acoustic coupling. In addition, sterile gel was placed on the skin's surface after sterilization of the skin by betadine and alcohol. Hand sterilization was done carefully by hand washing with water and medical soap followed by hand rubbing with alcohol. Then sterile gloves were used.

Fine-needle aspiration cytology technique

(1) Needle used was a 20-G needle attached to a 10-ml plastic syringe.
(2) No anesthetic was required.
(3) The number of needle passes was 3–4.
(4) The used approach was parallel or perpendicular approach according to accessibility of the thyroid nodule.
(5) The number of slides obtained was 4–8 clean dry slides.
(6) Before the needle entered the thyroid nodule, the plunger was retracted to create a negative pressure in the syringe.
(7) The needle was further pushed into the nodule and moved back and forth several times maintaining the negative pressure to suck the material.
(8) When any material or blood was seen in the hub of the needle, the syringe was removed from the patient and the needle was detached and air was sucked into the syringe, the needle was reattached, and the material was ejected forcefully onto 4–8 clean dry slides.
(9) Gently, the smear was waved in the air for a few seconds for quick drying and then the smear was immersed in 99% ethyl alcohol for subsequent stain.
(10) For cytological evaluation, wet preparations were stained by H and E stain. The slides of all cases were examined by conventional cytology to determine the cytomorphological features.
(11) The cytologic evaluation included six main items regarding Bethesda system for thyroid cytology.
(12) All our patients underwent FNAC before surgery as it helped us to decide the type of surgery.
(13) Then the cytologic diagnoses were compared with the surgical histopathological results of the same nodules as the gold standard.

Statistical analysis

Data were collected and analyzed using Statistical Package for the Social Science (version 20; IBM, Armonk, New York, USA). Continuous data were expressed in the form of mean ± SD or median (range), whereas nominal data were expressed in the form of frequency (percentage).

Results

The current study was performed at Radiology Department of Assiut University Hospitals. It was conducted in period between May 2017 and May 2019.

Table 1 shows the baseline data of studied patients. Mean age of studied group was 41.50 ± 15.16 years,

with range between 19 and 74 years. Of the studied patients, 20 (66.7%) patients were females and 10 (33.3%) patients were males.

The main presentation in the current study was neck swelling, which presented in 17 (56.7%) patients, whereas nine (30%) patients were complaining of dysphagia. Thyroid nodule was accidently discovered in four (13.3%) patients.

Table 2 shows US findings in the studied patients. Most patients [19 (63.3%) cases] had the STN at the right thyroid lobe. Regarding echogenicity of thyroid nodules, it was noticed that 16 (53.3%) patients, five (16.7%) patients, four (13.3%) patients, four (16.7%) patients, and one (3.3%) patient had hyperechoic, hypoechoic, heterogeneous, anechoic, and isoechoic thyroid nodules, respectively.

Content of the thyroid nodules was mixed (solid and cystic) in 17 (56.7%) patients, whereas it was solid in nine (30%) patients and cystic in four (13.3%) patients. Halo sign and calcification presented in 15 (50%) and seven (23.3%) patients, respectively. Based on US findings, benign nodules presented in 21 (70%) patients, whereas nine (30%) patients had malignant nodules. Majority of the nodules [25 (83.3%) cases] were well defined.

The result of FNAC of thyroid nodules is shown in Table 3 and Fig. 1. Based on the results of cytology, 20 (66.7%) patients had benign nodules based on FNAC [colloid (50%) and adenoma (16.7%)]. Moreover, eight (26.7%) patients had malignant nodules [medullary carcinoma (3.3%), papillary carcinoma (13.3%), and Hurthle cell lesion (10%)]. There were only two patients in whom samples were taken by FNAC were unsatisfactory.

The result of histopathological evaluation of thyroid nodules is shown in Table 4 and Fig. 2. A total of 25 (83.3%) patients had benign nodules based on histopathological evaluation [colloid (56.7%), follicular adenoma (16.7%), Hurthle cell adenoma (10%)]. Only five (16.7%) patients had malignant nodules [medullary carcinoma (3.3%) and papillary carcinoma (13.3%)].

Regarding the two unsatisfactory cases, they underwent surgery (hemithyroidectomy), as one of them showed suspicious US criteria and was diagnosed as having Hurthle cell adenoma by histopathology. The other one had pressure symptoms and diagnosed as having colloid nodule by histopathology.

Table 5 shows the diagnostic performance of US and FNAC in diagnosing thyroid nodules. Halo

Table 1 Baseline data of studied patients

	n=30 [*n* (%)]
Age (year) (mean±SD)	41.50±15.16
Range	19-74
Sex	
Female	20 (66.7)
Male	10 (33.3)
Presentation	
Neck swelling	17 (56.7)
Dysphagia	9 (30)
Accidently discovered	4 (13.3)

Table 2 Ultrasonographic findings in studied patients

	n=30 [*n* (%)]	Benign [*n* (%)]	Malignant [*n* (%)]
Site of nodule			
Right lobe	19 (63.3)	17 (56.7)	2 (6.7)
Left lobe	8 (26.7)	6 (20)	2 (6.7)
Isthmus	3 (10)	2 (6.7)	1 (3.3)
Echogenicity			
Hyperechoic	16 (53.3)	16 (53.3)	-
Hypoechoic	5 (16.7)	1 (3.3)	4 (13.3)
Heterogeneous	4 (13.3)	3 (10)	1 (3.3)
Anechoic	4 (13.3)	4 (13.3)	-
Isoechoic	1 (3.3)	1 (3.3)	-
Internal content			
Mixed	17 (56.7)	16 (53.3)	1 (3.3)
Solid	9 (30)	5 (16.7)	4 (13.3)
Cystic	4 (13.3)	4 (13.3)	-
Halo sign	15 (50)	15 (50)	-
Calcification	7 (23.3)	3 (10)	4 (13.3)
Nodule definition			
Well defined	25 (83.3)	25 (83.3)	-
Ill-defined	5 (16.7)	-	5 (16.6)
US diagnosis			
Benign nodules	21 (70)		
Malignant nodules	9 (30)		

US, Ultrasongraphy.

Table 3 Result of fine-needle aspiration cytology of thyroid nodules

	n=30 [*n* (%)]
Benign nodules	20 (66.7)
Colloid	15 (50)
Adenoma	5 (16.7)
Malignant nodules	8 (26.7)
Medullary carcinoma	1 (3.3)
Papillary carcinoma	4 (13.3)
Hurthle cell lesion	3 (10)
Unsatisfactory	2 (6.7)

Table 4 Result of histopathological evaluation of thyroid nodules

	n=30 [*n* (%)]
Benign nodules	25 (83.3)
Colloid	17 (56.7)
Adenoma	5 (16.7)
Hurthle cell adenoma	3 (10)
Malignant nodules	5 (16.7)
Medullary carcinoma	1 (3.3)
Papillary carcinoma	4 (13.3)

sign had 100% sensitivity and 60% specificity, calcification had 80% sensitivity and 88% specificity, hyperechogenicity had 100% sensitivity and 52% specificity, and nodular definition had 100% sensitivity and 100% specificity for prediction of malignant nodules. US findings had 100% sensitivity and 84% specificity and FNAC had 100% sensitivity and 87.5% specificity for prediction of malignant thyroid nodules (Figs. 3 and 4).

Discussion

STN is a usual clinical problem. It is also a common finding mostly in females and in the elderly people [2].

The role in evaluating a thyroid nodule is to detect if it is benign or malignant, so that cases with malignant thyroid nodule can undergo surgical treatment at an earlier stage to reduce possible morbidity and mortality, whereas cases with benign nodules can undergo conservative treatment in most cases or surgical treatment in the following conditions: if the benign nodule is precancerous lesion like Hurthle cell adenoma, if the lesion increases in the size and causes pressure symptoms, and for cosmetic effects.

During our study period, there were 20 (66.7%) females and 10 (33.3%) males with STN. Final histopathological examination showed malignancy in two (20%) cases of 10 male patients and in three (15%) cases of 20 female patients. Hence, the incidence of thyroid nodules increased in female and the incidence of malignant thyroid nodules increased in male in our study. The study by Jena *et al.* [8] reported similar results.

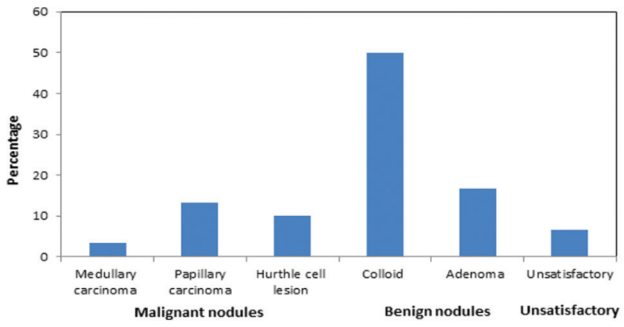
Our study recorded that age and sex incidence are not necessary criteria in identifying benign and malignant thyroid nodules, which is in consensus with other studies [9–11].

US has become the first-line imaging technique for assessment of the thyroid gland owing to perfect visualization of its parenchyma. It is very sensitive in identification of small nodules, calcification, septations, and cysts as well as in guiding FNA biopsies [12].

In the present study, the right lobe of the thyroid gland was involved in maximum number of cases (63.3%) followed by the left lobe in 26.7% and the isthmus in 10%. The study of Bhuyar *et al.* [13] recorded that the right lobe of the thyroid gland was involved in maximum number of cases (78%) followed by the left lobe in 22%. However, in literature no significance has been attached to the side of involvement.

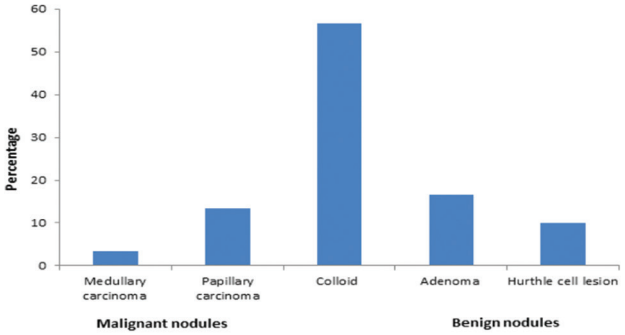
Our study did not show connection between size of the thyroid nodule and final pathological results, and this agreed with the study by Titton *et al.* [14].

Figure 1



A graph showing result of FNAC. FNAC, fine-needle aspiration cytology.

Figure 2



A graph showing final diagnosis of thyroid nodules based on histopathology.

Table 5 Diagnostic performance of ultrasonography and fine-needle aspiration cytology in diagnosing thyroid nodules

Indices	Halo sign (%)	Calcification (%)	Hyperechogenicity (%)	Nodular definition (%)	US (%)	FNAC (%)
Sensitivity	100	80	100	100	100	100
Specificity	60	88	52	100	84	87.5
PPV	33	57	29.4	100	56	63
NPV	100	96	100	100	100	100
Accuracy	66.7	86.7	60	100	86.7	90
AUC	0.80	0.84	0.76	1	0.92	0.94
P	0.01	0.01	0.01	0.01	0.01	0.01

AUC, Area under curve; FNAC, Fine-needle aspiration cytology; NPV, Negative predictive value; PPV, Positive predictive value; US, Ultrasonography. $P<0.05$.

The present study showed 53.3% of cases had hyperechoic nodule, and all were benign. We found the sensitivity and specificity of hyperechogenicity of 100 and 52%, respectively. Moreover, 16.7% of cases had hypoechoic nodules. Of these, 13.3% of cases had malignant lesions and 3.3% of cases had benign lesions. This is in agreement with other literature studies, where most of the malignant nodules are hypoechoic, whereas most hyperechoic nodules are benign [15].

In the present work, there are four (13.3%) cases with totally cystic thyroid nodule and all were benign. These results were in accordance with the study of Yoon *et al.* [16].

In our work, benign nodules that presented in 83.3% tended to have well-defined margins, whereas malignant thyroid nodules that presented in 16.7% tended to have ill-defined margins. On the contrary, the study by Moon *et al.* [17] proved that an ill-defined margin can be present in benign and malignant nodules.

Our work showed that a halo sign presented in 15 cases from 25 benign ones. We found the sensitivity and specificity ratios of the halo sign of 100 and 60%, respectively. The study by Lu *et al.* [18] recorded that it is a finding usually suggestive of benign lesion, whereas the study by Chan *et al.* [19] revealed that some papillary carcinomas may have a halo sign.

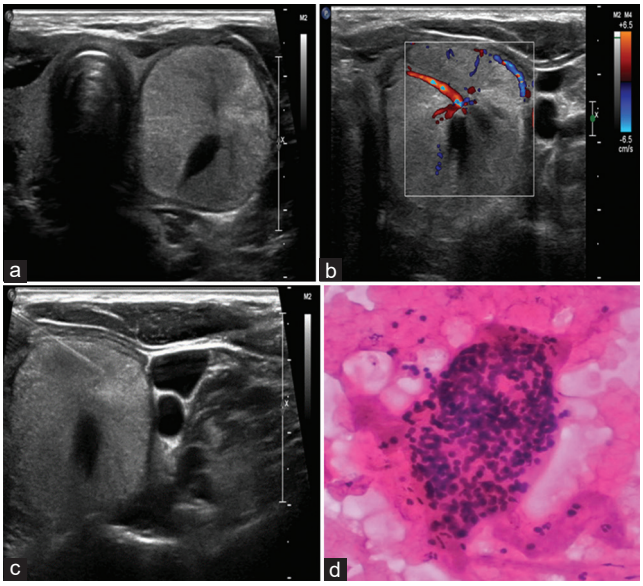
In this study, of 30 cases, nine cases were found suspicious for malignancy on US. Among these nine suspicious cases, five cases were found to be malignant on gold standard histopathological examination and four cases were benign, giving an overall sensitivity and specificity of 100 and 84%, respectively, for US to differentiate between benign and malignant nodules. However, the study of Sharma [20] found that the sensitivity and specificity of US in suggesting a malignant disease were 74 and 83%, respectively. However, a study by Kim *et al.* [9] recorded that the US sensitivity was 93% with a specificity of 81%.

We found that the diagnostic accuracy of US in the assessment of STN was 86.7% which in comparable to study of Paarthipan *et al.* [21], who recorded that the US diagnostic accuracy was 85%.

The result of our study showed that the incidence of malignancy in STN is indeed high. The chance of malignancy is more in those nodules where US shows solid hypoechogenicity nodule with ill-defined margins.

FNAC is easy to apply, has a little complication rates, and has high diagnostic value in the diagnosis of thyroid problems [22]. The use of FNAC resulted in a reduction in the proportion of cases that underwent surgical management by 25–50% [23].

Figure 3



(a) A well-defined hyperechoic focal lesion seen at left thyroid lobe. (b) The nodule had a small area of cystic degeneration and surrounded by a halo sign with perinodular and intranodular blood flow (TIRADS score 3) (mildly suspicious). (c) FNA from the nodule. (d) Photomicrograph showing features of adenomatoid nodule.

Figure 4

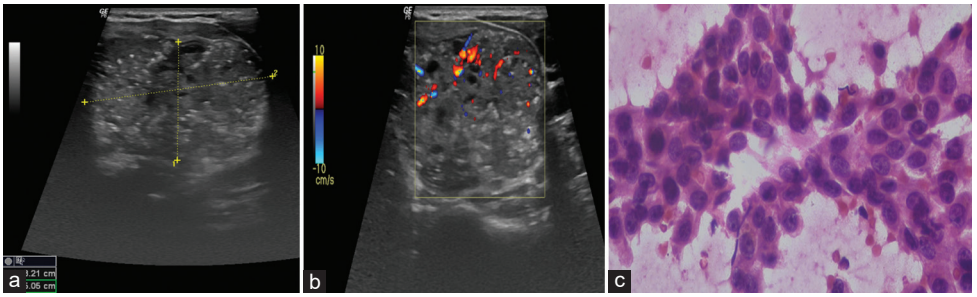


Figure 4 (a) A well-defined hypoechoic focal lesion seen at the left thyroid lobe. (b) The nodule had multiple scattered foci of microcalcifications with internal vascularity and small area of cystic degeneration (TIRADS score) five (highly suspicious). (c) Photomicrograph showing features of papillary carcinoma.

The solitary colloid goiter is the most common benign lesion and was ~56.7%, and the papillary carcinoma was the most common malignant lesion and was ~13.3% identified by FNAC in our study. The study by Bhuyar *et al*. [13] recorded that the solitary colloid goiter is the most common benign lesion and was approximately 56%, and the papillary carcinoma was the most common malignant lesion and was ~8% identified by FNAC.

In our study, five cases were found to be malignant on histopathological examination (four papillary carcinoma and one medullary carcinoma). All cases of papillary carcinoma diagnosed by FNAC were papillary carcinoma on histopathological examination also. This is in accordance with the study of Kessler [24].

We found the sensitivity and specificity of FNAC of 100 and 87.5%, respectively. The study by Muratli *et al*. [25] demonstrated that the sensitivity and specificity of FNAC were 64.6 and 87.1%, respectively. However, the study by Sharma [20] recorded that the sensitivity and specificity were 89.5 and 98%, respectively.

We found that the diagnostic accuracy of FNAC in the assessment of solitary nodule was 90%, whereas the study of Sharma [20] recorded that the FNAC diagnostic accuracy was 97%.

In our study, we found the rate of nondiagnostic FNAC tests was 6.7%. These results were in agreement with study of Ali [26] who suggested that the rate of nondiagnostic tests should be kept below 10%.

Conclusion

Thyroid US is the main diagnostic technique for assessment of thyroid diseases. In our study, the US criteria of hypoechogenicity and ill-defined margins were found to have high diagnostic accuracy for identifying malignant thyroid nodules. Although many US features were found to be associated with malignant lesion, none of these features can be used as separate predictors to screen cases for malignancy.

FNAC is considered the gold standard diagnostic technique and has a main role in differentiating between benign and malignant thyroid nodules. It is a fast outpatient minimally invasive technique with low complications rates. It significantly guides the treatment decision.

No investigation was found to be 100% accurate in diagnosing malignant thyroid nodule, but a combination of US and FNAC rather than any single technique will give accurate findings and avoid unnecessary operations in a large number of cases without missing any malignancy.

Finally, we found that FNAC is superior than US in the diagnosis of STN.

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Conflicts of interest
There are no conflicts of interest.

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