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Original Article

Role of ultrasound, color doppler, elastography and micropure imaging in differentiation between benign and malignant thyroid nodules

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ABSTRACT

Purpose: To evaluate the role of ultrasound elastography, Doppler and micropure imaging in the assessment of thyroid nodules, using the pathological analysis as the reference standard.
Patients and methods: A prospective study was carried on all patients referred to radio-diagnosis department at Tanta Cancer Centre between November 2015 and November 2016 for evaluation of undiagnosed thyroid nodules. All patients were examined by B-mode ultrasound, color Doppler, micropure imaging and ultrasound elastography. All thyroid nodules were subjected to fine-needle aspiration biopsy.
Results: 90 patients (78 women, 12 men) with 159 incompletely diagnosed thyroid nodules. 24 nodules were malignant and 135 nodules were benign, micro calcification was detected by micropure imaging in 40 nodules (29.6%) in the benign thyroid nodules and in 20 nodules (83.3%) in the malignant thyroid nodules (sensitivity 83.3%, specificity 70.4%, and accuracy 84.9%). Color flow Doppler (type III) with marked intranodular and absent or slight perinodular blood flow, was detected in 19 malignant nodules, with sensitivity 79.2%, specificity 95.6%, and the overall accuracy rate was 88.7%. The predictivity of ultrasound elastographic score measurement has high sensitivity 87.5%, and specificity 91.1%, Strain elastography cutoff value for malignant nodules was 2.7 (Sensitivity 83.3% and specificity 91.1%).
Conclusion: Elastography and micropure imaging technique are useful imaging modalities to detect the nature of thyroid nodules. In combination with Doppler and B-mode sonography, they could give a better assessment for undiagnosed thyroid nodules.

1. Introduction

One of the common finding in the general population is thyroid nodules, however, they are mostly unpalpable and usually firstly discovered either during neck ultrasound (US) examination or by pathological examination at autopsy. They are found in about 8% of adults. Most thyroid nodules "incidentalomas" are benign, however 7% may be malignant. Early detection of thyroid cancer helps in early treatment and better survival [1–3]. Therefore, Imaging modalities that can differentiate between benign and malignant thyroid nodules are very useful in the clinical practice.

US identifies the presence of nodules, and is an accurate method for the detection of thyroid nodules; however, US has a low accuracy in differentiating between benign from malignant thyroid nodules [4]. US could suggest a malignancy likelihood criteria of a thyroid nodule, such as hypoechogenicity, increased intranodular vascularity, irregular margins, microcalcifications, absent halo, and a taller-than-wide shape measured in the transverse dimension. Several benign and malignant ultrasound gray scale and Doppler features have emerged in TIRADS (Thyroid Imaging Reporting and Data System) and ATA (American Thyroid Association) guidelines to provide effective malignancy risk stratification for thyroid nodules [5].

US elastography used to detect the nature of thyroid nodules, by measuring the tissue stiffness noninvasively. It depends on tissue deformation or strain that is caused by external compression. Malignant nodules tend to be much harder than benign ones, however the ultrasound cannot predict the hardness of a nodule [6].

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Color Doppler US is an available imaging technique for assessing thyroid nodules vascularity, and considering nodules with central intranodular vascularity as suspicious nodule [7].

Currently, micropure imaging algorithm considered as a new adapted filter which can enhance bright echoes to demonstrate calcifications, particularly microcalcifications [1].

Fine-needle aspiration biopsy is the most reliable screening method of thyroid nodules; it can distinguish benign and malignant lesions with a high accuracy level. It is a simple, low cost investigation that has no major complications [1,8].

Contrast enhanced US delineates vascularity and tissue perfusion of the thyroid nodules in real time imaging with excellent spatial resolution [9]. Diffusion-weighted magnetic resonance imaging is considered a new promising noninvasive imaging approach used for differentiating malignant from benign solitary thyroid nodules [10]. Positron Emission Tomography Computed Tomography (PET CT) is another method to detect nature of the thyroid nodule but it is often used in staging of a known case of cancer thyroid. However, they are expensive imaging modalities and not easily available in the daily clinical practice.

The purpose of this study is to evaluate the role of non-expensive, non-invasive imaging modalities (US elastography, Doppler and micropure imaging) in differentiating benign and malignant thyroid nodules.

2. Patients and methods

2.1. Patients

A prospective study was carried on 90 patients, referred to radio-diagnosis department at Tanta Cancer Centre, from surgery and oncology departments between November 2015 to November 2016 for evaluation of incompletely diagnosed thyroid nodules detected by initial US examination. Thyroid nodules with cystic changes or predominantly cystic without solid component were excluded from the study, In patient with multiple nodules, we selected the solid nodule which have at least one of suspicious thyroid nodule criteria based on the Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules.

All nodules were subjected to fine-needle aspiration cytology within one week of the initial diagnosis by US, benign nodules were monitored by ultrasound for 6 months, and repeated FNAC were performed. However patients with malignant nodules underwent thyroid surgery and the pathologic diagnosis was confirmed.

Our study was approved by the Medical Research Ethics Committee, Tanta Cancer Center. A written consent was obtained from each patient included in our study.

2.2. Methods

All patients were examined by B-mode US, US elastography, color Doppler, and micropure imaging using a 10-MHz linear transducer (Aplio, Toshiba) by the same operator, during the same examination. All thyroid nodules were subjected to US guided fine-needle aspiration cytology aspiration(FNAC) within one week of the initial diagnosis by US.

2.2.1. Real time US

B-mode ultrasound was performed initially for all thyroid nodules, the following ultrasound parameters were evaluated: echogenicity of the nodule with respect to normal thyroid parenchyma (hyperechoic, isoechoic, or hypoechoic); anterior posterior/transverse diameter A/T ($\leq$1 or >1 cm); margins (well defined and smooth, blurred, or speculated); and calcifications which may be (microcalcification, microcalcifications, peripheral rim of calcifications, or absence of calcifications) and Halo sign (presence or absence), these criteria based on the Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules, it considered the following US features as suspicious criteria of malignancy: hypoechoic nodule; (A/T) is 1 cm or greater, blurred margins and microcalification, presence of one or more criteria is considered the thyroid nodule as suspicious or indeterminate [5].

2.2.2. Color Doppler

Using color Doppler imaging, the blood flow pattern in thyroid nodules was classified as follows: type 1, absence of blood flow; type 2, perinodular and absent or slight intranodular blood flow; and type 3, marked intranodular and absent or slight perinodular blood flow [11].

2.2.3. Micropure imaging

Micropure images appears as blue layer filter with microcalcifications displayed as “white spots” which improves localization of the calcifications of question in the B-mode images.

Micropure grades of analysis are: grade 1 cannot be visually identified; grade 2 can be clearly visually identified. Following Kurita, 2010 [12].

2.2.4. US elastography

Color coding US elastography is classified into 5 groups according to the Ueno classification, score one (softest component) and score five (hardest component) [13] (Table 1).

For real time US strain elastography, repeated compression in a longitudinal direction with fine pressure was done followed by decompression (repeated 4 times for each nodule), dividing the strain value of thyroid nodule to the nearby muscle was calculated and the average result was estimated using a special software within the ultrasound machine, measurements acquired at the same depth of the nodule and adjacent muscle or both are in the same plane.

Table 1
Color coding of elastographic image [13].

Score	Score characteristics
I	The whole nodule is shaded green, as well as the surrounding thyroid tissue; Denoting low stiffness over the whole nodule
II	The nodule is almost totally green but showing some blue spots; denoting low stiffness over most of the nodule
III	The central portion of the nodule is blue, associated with peripheral green part; denoting low stiffness at the periphery, high stiffness in the center of the nodule
IV	The nodule is almost totally blue mixed with some green spots; denoting high stiffness over most of the nodule
V	The whole nodule is evenly shaded blue; denoting high stiffness over the whole nodule

Table 2
Histopathological types of benign & malignant thyroid nodules.

		N	Percent
Benign	Follicular adenoma	120	75.5
135	Hyper plastic nodule	15	9.4
Malignant	Follicular carcinoma	3	1.9
	Papillary carcinoma	12	7.5
24	Poorly differentiated adenocarcinoma	3	1.9
	Medullary carcinoma	6	3.8
	Total	159	100.0