Vascular pattern and spectral parameters of Doppler ultrasound in differentiation between malignant and benign thyroid nodules

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Received 11 June 2020
Revised 09 July 2020
Accepted 28 August 2020
Published 23 February 2021

Journal of Current Medical Research and Practice
2021, 6:82–86

Back ground
Thyroid nodules are common pathologies detected in thyroid gland. A thyroid nodule is the manifestation of a wide range of thyroid diseases, some benign and others malignant. Currently, the use of imaging methods has increased the diagnosis of asymptomatic nodules. Ultrasound studies of the population have reported a nodular thyroid disease rate of nearly 67% in elderly women. Most of these nodules are benign, and the incidence of malignancy is low (3–7%).

Purpose
To evaluate the role of vascular pattern and spectral wave forms and resistivity and pulsatility indices to differentiate between malignant and benign features.

Patients and methods
A total of 40 patients who were presented with thyroid nodules scheduled for surgery and preoperative fine-needle aspiration cytology were examined in a prospective way. Gray-scale and color Doppler patterns were used to rank each thyroid nodule on a scale from 0 to 4 as follows: none, solely perinodular, accompanied by per-nodular prominence, accompanied by intranodular prominence, and only intranodular, respectively. Final diagnosis (benign or malignant) was confirmed by pathological correlations.

Results
Value of malignancy in thyroid nodules with a mean resistivity index of 0.72±0.13 is found to be significantly higher than with benignity (0.60.0.08).

Conclusion
Duplex Doppler parameters are helpful in distinguishing malignant from benign thyroid nodules.

Keywords:
Vascular, Doppler, Ultrasound, Benign, Malignant, thyroid, nodules

J Curr Med Res Pract 6:82–86

2357-0121

Introduction

The accurate clinical diagnosis of the thyroid nodules is usually difficult. Thyroid nodules are reported to be malignant in 5% of the cases, and early diagnosis is mandatory, as early treatment may improve the survival rate [1,2].

The commonest pathology of the thyroid gland are thyroid nodules; some of them are benign and the others are malignant. The different imaging modalities have increased the diagnosis of asymptomatic nodules [3,4].

The thyroid gland is superficial and largest endocrine gland. It is easy and unique for clinical examination and palpation and ultrasonography (US)-guided biopsy [5].

The most common presentation of cancer thyroid is the thyroid mass or nodule. Thyroid cancer is relatively rare; the incidence of thyroid nodules is significantly higher, affecting ~ 4–7% of the population [6,7].

Many studies revealed the importance of gray-scale US and color Doppler US in the diagnosis of malignant thyroid nodules. In these studies, color Doppler US itself or with B-mode US features was useful more than suspicious B-mode US features alone for detection of thyroid malignancy [8].

New studies have concluded that spectral power Doppler US is helpful in detection of malignancy of thyroid nodules [1,5]. Other studies have reported that vascularity or RI values by power Doppler US are useless in differentiation between malignant and benign thyroid nodules [9].

US examination of the population has revealed the rate of the thyroid nodules was ~67% in elderly women. Most nodules are benign, and only 3–7% are malignant, and the incidence is low [6,7].

US is deemed the first selection in the evaluation of the shape of the gland. It displays the echotexture of enlarged gland, size, and number of nodules; distinguishes solid from cystic lesions; and picks the region areas of degeneration and calcification. Furthermore, it has the value of finding the relation between an enlarged gland and the surrounding structures [10].

Sonographic criteria that favor malignancy are punctate calcification, an irregular or microlobulated margin, marked hypoechogenicity, and morphology that was more tall than wide. US is especially helpful during follow-up, as it can differentiate nodular growth from intramodular bleed [11].

Fine-needle aspiration cytology (FNAC) is deemed the most amenable tool for the diagnosis of malignancy in solitary thyroid nodule. In nonpalpable thyroid nodules, US has become the chief method for FNAC guidance; furthermore, US is the most effective method to furnish information about number, size, echo structure, location, and echogenicity of thyroid nodules. [12].

The aim of our study is to determine the value of Doppler US in differentiation between benign and malignant thyroid nodules, in correlation with the preoperative or postoperative pathological data.

Patients and methods

This study was conducted over 40 patients presented with thyroid nodules admitted at Surgery Department, Assiut University Hospital. Duplex Doppler was done for all patients as part of their initial assessment.

After clinical history taking and clinical examination, all patients were subjected to Neck Ultrasound in Radiology Department, Assiut University Hospital, followed by Doppler US. The study protocol was approved by Ethics Committee of Faculty of Medicine, Assiut University and patients signed an informed consent.

FNAC was applied to exclude malignancy that confirmed or denied some clinical suspicions.

Institutional review board (IRB) of Assiut Faculty of Medicine approved the study (Institutional review. number: 17101045).

Inclusion criteria

Patients admitted to the Surgery Department who presented with thyroid nodules were included.

Exclusion criteria

The following were the exclusion criteria:

(1) Patients discharged from the hospital without undergoing Doppler US.
(2) Patients who had no preoperative or postoperative pathological data.
(3) Patients who underwent total thyroidectomy.

Ethical consideration

(1) All examinations were done confidentially.
(2) Written consent was obtained from every included patient in the study either from adults or from the parents of minors.
(3) Approval of Ethical Committee at Faculty of Medicine, Assiut University, was obtained.

Ultrasound examination

Examination of all detecting nodules was done by 7.5–15-MHz linear transducer array used in both US apparatus (GE LOGIQ_P5 and GE LOGIQ_P6 [General Electric Company (GEC) USA, New York city, Boston]). The patient was placed in dorsal decubitus position with slightly extending neck, with a pillow under shoulder region. The examination of the thyroid gland was done in two perpendicular planes (longitudinally and transversely). The whole of the neck region was studied, including whole thyroid gland, other salivary glands, upper and lower cervical regions, and major blood vessels of the neck.

Duplex Doppler include color Doppler and Doppler energy, although power Doppler US is more useful than Color Doppler US:

(1) It is more sensitive in detection of slow flow in small vessels.
(2) Direction of US beam is not related.
(3) The vessel signal could be affected by a random signal in color Doppler not likely the homogenous appearance of the noise in power Doppler.
(4) The vascular patterns of all nodules were evaluated by power Doppler US and classified to nonvascular, peripheral, central, or mixed vascular according to blood supply distribution. Nonvascular nodules have no prominent vasculature, whereas others have peripheral, central, or mixed vascular. Resistance index (RI) and pulsatile index (PI) were examined in the central and peripheral arteries of nodules by power Doppler US. The parameters of spectral Doppler depend on the based formulas:
(5) PI = peak systolic velocity – mean diastolic velocity/mean velocity, and RI = peak systolic velocity – mean diastolic velocity/peak systolic velocity.
(6) Two central and two peripheral arteries from each nodule at least were examined to detect RI and PI

values. For each nodule, the peripheral RI–PI and central RI–PI values were examined separately, and the averages of the calculations were recorded. Moreover, mean RI–PI values were calculated. Only single measurement could be considered, if there was no second artery to be measured at any region of the nodule.

Results

A total of 40 patients (35 women and 5 men) were examined in this study. Their age ranged from 16 to 70 years old, and the mean ± SD of the age was 37.63 ± 12.47 years.

The age was significant more than sex in differentiation between benign and malignant nodules. Other measurements were also helpful. It also revealed that larger nodules are more malignant than benign ones (P = 0.001). Demographic characteristics of the patients are summarized in Table 1.

Gray-scale US examination revealed that most of examined nodules were single nodules and 40% was multiple nodules (Fig. 1).

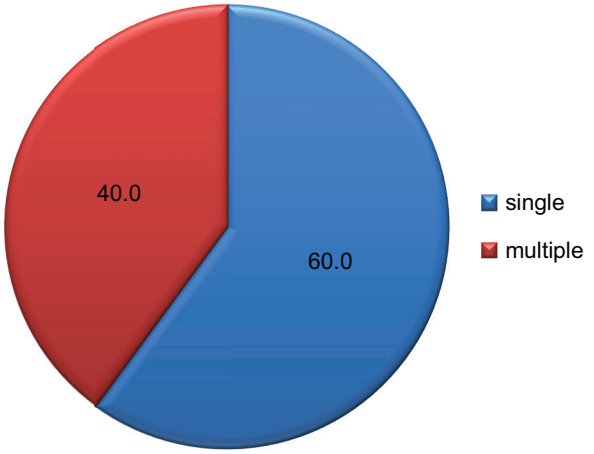
Grades 0, I, and IV were very difficult to be found. Although, both types of nodules mostly have vasculature central or peripheral (intranodular); all examined nodules vascularity were (70%) type II and (30%) type III with a significant correlation between malignancy and grade III (P = 0.001). These patterns of blood flow were detected in eight (69.9%) nodules of the malignant nodules (Fig. 2 and 3). According to pulsed Doppler, malignant nodules had mean ± SD PI of 1.15 ± 0.33 and mean ± SD RI of 0.72 ± 0.13, as shown in Fig. 4. These values were significantly higher than those associated with the benign groups (P = 0.005 for both) (Tables 2 and 3).

FNAC of all thyroid nodules was done, and the histopathology was as follows: 37.5% of nodules were clearly negative for malignancy either SNG or MNG, 20% were adenoma, 10% colloid nodules, 17.5% were papillary carcinoma, 7.5% micropapillary carcinoma, 5% capillary carcinoma, and 2.5% as papillary adenocarcinoma (Tables 4 and 5).

Table 1 Demographic criteria of the study

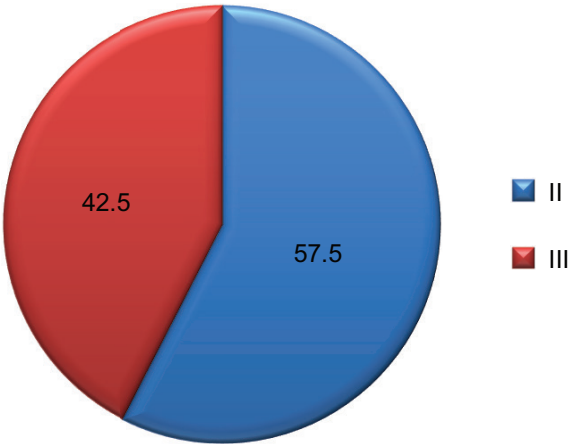
	n (%)
Sex	
Male	5 (12.5)
Female	35 (87.5)
Age	
Range	16-70
Mean±SD	37.63±12.47

Figure 1



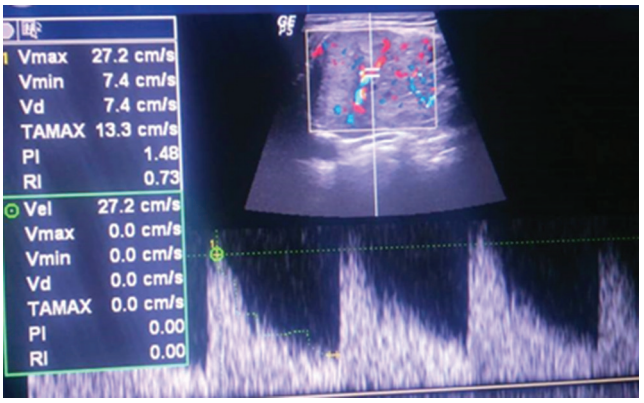
Multiplicity of the nodules.

Figure 2



Grades of color vascularity.

Figure 3



A single large nodule in right thyroid lobe measuring ± 4 × 4 cm shows hypoechogenic with cystic degeneration, no calcification, has central and peripheral blood supply. It was grade III and has PSV 27 cm/s, EDV 7 cm/s, and RI 0.7. It was histopathologically proved by FNAC as papillary adenocarcinoma. FNAC, fine-needle aspiration cytology; RI, resistance index.

Table 2 The relation between the different duplex Doppler parameters and different histopathological pattern of thyroid nodules

	Mean±SD							*P*
	Adenoma	Capillary carcinoma	Colloid nodule	Micropapillary carcinoma	Negative for malignancy	Papillary adenocarcinoma	Papillary carcinoma	
PSV (cm/s)	25.63±13.23	25.63±13.23	33.5±2.12	36.5±12.34	18.67±3.06	26±11.39	17±0	0.187
EDV (cm/s)	9±5.01	9±5.01	8±1.41	13±6.98	6±1.73	8.33±5.22	6±0	0.520
RI	0.66±0.07	0.75±0.07	0.63±0.11	0.67±0.06	0.6±0.1	0.73±0	0.86±0.05	<0.001**
PI	0.97±0.2	0.97±0.2	1.55±0.49	1.18±0.32	1.03±0.15	0.83±0.15	1.5±0	<0.001**

Anova *t* test. PI, pulsatility index; RI, resistance index. *Statistically significant difference (P<0.05). **Highly statistically significant difference (P<0.01).

Table 3 Mean values of resistance index in histopathologically proved nodules

RI	Positive	Negative	*P*
Mean±SD	0.85±0.053	0.68±0.05	0.002**
Median (IQ)	0.85 (0.8-0.9)	0.7 (0.65-0.71)	

Mann-Whitney Test. IQ, interquartile; RI, resistance index. *Statistically significant difference (P<0.05). **Highly statistically significant difference (P<0.01).

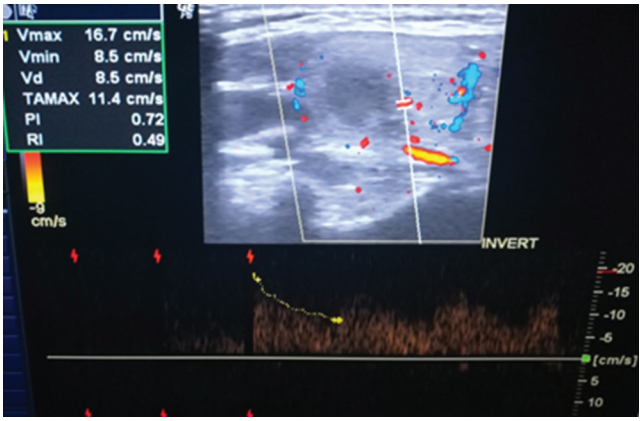
Table 4 Histopathology of the different thyroid nodules

Histopathology	*n* (%)
Adenoma	8 (20)
Capillary carcinoma	2 (5)
Colloid nodule	4 (10)
Micropapillary carcinoma	3 (7.5)
Negative for malignancy	15 (37.5)
Papillary adenocarcinoma	1 (2.5)
Papillary carcinoma	7 (17.5)

Table 5 Correlation between malignant histopathologically proved cases and their resistance index

	n (%)
Negative	5 (38.5)
Positive	8 (61.5)

Figure 4



Multiple nodules in right thyroid lobe. The largest measures ± 3 × 3 cm and appears hypoechogenic with cystic degeneration, no calcification, and has central and peripheral blood supply. It was grade III and has PSV 17 cm/s, EDV 9 cm/s, and RI 0.5. It was histopathologically proven as micropapillary carcinoma. RI, resistance index.

Discussion

Current US equipment are cheaper, more sensitive, and easy to be used in examination. Gray-scale US is the most accurate and cheapest examination for early evaluation of the thyroid nodules [13]. The accurate diagnosis is confirmed after being indicated by means of histopathology examination [14,15].

It is known that increased vascularization is directly correlated with the growing tumor. With development of technology and power Doppler US, it is now possible to detect vascularity distribution within superficial lesions. So, this recent method is potentially helpful for detecting thyroid nodules that should undergo FNAC or undergoing surgical intervention [16]. In our study, grades 0, I, and IV were very difficult to be found. Although, both types of nodules mostly have vasculature central or peripheral (intranodular); all examined nodules vascularity were (70%) type II and (30%) type III with a significant correlation between malignancy and grade III (P = 0.001).

New confirmed results of the consensus panel have defined the importance of the size and sonographic criteria for those thyroid nodules that should undergo FNAC. Color Doppler US examination has become very important technique for evaluation of nature the thyroid nodule [17,18]. In our study, thyroid nodules' size ranging between 10 and 50 mm is to be suspected: 60% (24 cases) of all thyroid nodules are single nodules, and only six cases of them are malignant nodules, which represents 15% of all thyroid nodules.

Marked hypoechogenicity is significant for malignant nodule, with a specificity of about 92–94% [19]. In our study, almost all of our malignant nodule cases were truly hypoechogenic, but also about 55% (22 cases) of examined thyroid nodules were benign and also hypoechogenic.

Assessment of thyroid nodules by RI and PI values measured by spectral Doppler US is not affected by course of artery, angle of insonation, or nodule size. Contrarily, blood velocity measurements may be altered by Doppler parameters chosen by radiologists. Many studies investigated blood velocity parameters in the diagnosis of thyroid cancer, and generally it is not considered useful [20], which agrees with our results

where we analyzed only RI and PI values instead of velocity measures, and we also found that malignant nodules have significantly higher RI and PI values according to benign nodules.

One of the better spectral Doppler parameters for evaluating thyroid nodules is RI, because it is not related to the angle of beam, with vascular resistance close observation. Holden[21] approved that mean RI values of 0.76 in carcinomas, 0.66 in adenomas, and 0.57 in colloid nodules. Cerbone *et al*.[22] stated similar results and found an RI greater than 0.75 in 18 of 21 carcinomas and in two of 232 benign nodules. In more recent studies, many authors reported similar findings to our study and concluded that RI values in malignant nodules were higher than in benign nodules [9]. In many of these studies, an RI cutoff point of 0.75 was found as a reliable criterion for predicting malignancy, and this correlated with our study, where 61.5% of malignant cases had positive higher RI and PI values in correlation with histopathological examination, or else had negative results [23].

Conclusion

US evaluation and power Doppler are good choice, with acceptable sensitivity and specificity, in the screening of thyroid nodules at high risks for malignancy, especially those with undetermined or suspicious FNAC result.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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