Value of Sonography in Determining the Nature of Thyroid Nodules: Evaluation of the Sonographic Characteristics

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The purpose of this study was to evaluate all the sonographic characteristics in determining the nature of thyroid nodules. High-frequency sonograms of the thyroid were performed in 134 patients who were referred by three endocrinologists because of abnormal results on a thyroid physical examination. Sensitivity, specificity, positive and negative predictive value, and accuracy for individual sonographic characteristics were determined by comparing the results of the sonographic examination and fine needle aspiration biopsy (FNAB). Of 95 patients, 81 had benign FNAB reports that included nodular goiter, Hashimoto thyroiditis, and acute thyroiditis. Fourteen patients had cells that were malignant or suspicious of malignancy. The most accurate diameter for differentiating malignant from benign nodules was 3.9 cm. Considering the high level of negative predictive value of all the sonographic criteria, it is better to observe the patients rather than to apply FNAB when there is no suspicious finding of malignancy in the sonographic examination of a nodule.

Key words: thyroid nodule, sonography, malignancy

Thyroid nodules are common and may be caused by a variety of thyroid disorders. The prevalence of palpable thyroid nodules in members of the general population who are screened by palpation is 1% to 7%.[1] Although most are benign, about 5% to 10% of all palpable nodules are malignant.[2-5] Many tests and procedures are available for evaluating thyroid nodules, and appropriate selection of tests is important for accurate diagnosis.

Fine needle aspiration biopsy (FNAB) is now the "gold standard" in the evaluation of thyroid nodules.[6]

FNAB has some potential complications, such as pain, hematoma, entry into the trachea, transient

thyroid swelling, cystic degeneration, transient bradycardia, transient vocal cord paralysis, formation of calcification necrosis of the nodule, capsular pseudoinvasion, fibrosis, transient thyrotoxicosis, and elevation of thyroglobulin level.[6]

Because of the complications of FNAB and the difficulty in clinical decision making when it reports a "suspicious" or "unsatisfactory" specimen, there is a general tendency to evaluate thyroid nodules through other modalities.

Now, the diagnosis of thyroid cancers on the basis of sonography alone is nearly impossible. Many sonographic criteria have thus been developed to allow an early and more accurate diagnosis. Of course, the use of sonographic characteristics has limitations concerning sensitivity and specificity.

To approach this problem, we reviewed the literature to find as many sonographic characteristics as possible.

We undertook this work to assess all the sonographic criteria together and their potential role in differentiating benign from malignant thyroid nodules and to compare them with each other.

Methods and Materials

PATIENTS

This is a cross-sectional study on 134 consecutive patients. At first, we prepared the checklist shown in Figure 1. The first box of the checklist includes identification data of the patients, and the second box includes thyroid cancer risk factors and demographic data. The third box includes all the sonographic criteria we have gathered based on previous reports.[7-9]

The study sample consisted of patients with clinically suspected thyroid nodules who met the indications of undertaking FNAB, based on the American Association of Clinical Endocrinology (AACE) guidelines[10] between January and September 2003.

Three endocrinologists performed the physical examination of the thyroid for all their patients in their offices. They completed the first box of the checklist in Figure 1 and referred the patients with suspected thyroid nodules for sonographic examination.

SONOGRAPHY

Sonography was performed by one of two radiologists at Khorshid Hospital, Esfahan, on 134 patients with suspected thyroid nodules. Thyroid nodules were found in 100 of 134 patients by sonography; the remaining 34 were excluded from the study group.

A real-time scanner equipped with a 7.5-MHz linear transducer (EUB 40, Hitachi) was used in all sonographic examinations. The second box of the checklist in Figure 1 was completed by the sonographers.

In patients with more than one nodule, sonographic characteristics were evaluated on the dominant (palpable) and/or suspected malignant nodule.

FINE NEEDLE ASPIRATION BIOPSY

After the sonographic examination, we performed FNABs. There was no apparent indication for sonographic-guided fine needle aspiration biopsy because all of the nodules were palpable, but we preferred performing standard FNABs. In the patients with more than one nodule, FNAB was performed on the dominant (palpable) and/or suspected malignant nodule; thus, only one nodule in each patient was biopsied.

FNAB samples were evaluated by one pathologist. Suspicious FNAB reports were handled as a malignant diagnosis because they had to be referred to a thyroid surgeon. Five patients with unsatisfactory reports of FNAB were excluded from the study group, so the resulting study group consisted of 95 patients—12 men (12.6%) and 83 women (87.3%). Their ages ranged from 18 to 84 years (mean age, 42 ± 14).

STATISTICS

Sample size was calculated based on the estimation of a proportion formula. Type II error was considered to be 10%. Significance level was .05. Comparisons between groups concerning the sonographic criteria were performed by the Fisher exact test. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for individual sonographic characteristics were determined by comparing the results of sonography and FNAB. Data were evaluated by SPSS (Statisti-

Name: Tel:
Address:

1. Age: . . . 2. Sex: Male ☐ Female ☐
2. Past history of : Thyroid cancer ☐ Graves ☐ Hashimoto ☐
Hypothyroidism ☐ Hyperthyroidism ☐ Multinodular goiter ☐
Other: . . .
3. Physical examination: Single nodule ☐ Multinodules ☐ Lobular thyroid ☐
4. Past history of radiation to head & neck: Yes: Above 20 y ☐ Below 20 y ☐ No:
5. Other: . . .

1. Size of nodule: …		
2. Nodule count: …		
3. Cystic Solid Mixed		
4. Solitary Multiple		
5. Microcalcification:	Yes	No
6. Hypoechogenicity:	Yes	No
7. More tall than wide:	Yes	No
8. Associated lymphadenopathy:	Yes	No
9. Incomplete peripheral halo:	Yes	No
10. Irregular margin:	Yes	No
11. Microlobulated margin:	Yes	No
12. Extension of tumor out of thyroid:	Yes	No
13. Other:		

Fine needle aspiration report:

FIG. 1. Checklist of thyroid nodules.

cal Package for the Social Sciences), version 10.0. Risk factors and demographic data were reported by descriptive methods (mean, standard deviation, frequency, and percentage). We evaluated the greatest diameter of the thyroid nodules versus malignancy by the receiver operating characteristic (ROC) curve of SPSS 10.0 software.

Results

FINDINGS OF DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Past medical histories of the patients are summarized in Table 1. Three patients (3%) had previous histories of radiation to the head and neck, and two

TABLE 1.
Distribution of Past Medical History in Patients

Past Medical History	Frequency	%
Thyroid cancer	1	1.1
Grave disease	2	2.1
Hashimoto thyroiditis	0	0
Multinodular goiter	24	25.3
Hyperthyroidism	6	6.3
Hypothyroidism	4	4.2
Single nodule	25	26.3

patients (2%) had positive family histories of thyroid cancer. Others had nothing important in their past medical histories concerning thyroid disorders.

The physical examination revealed that of the patients, 51 (53.7%) had single nodules, 24 (25.3%) had multiple nodules, 2 (2.1%) had lobular thyroids, and the remaining 18 (18.9%) had no definite diagnoses concerning the thyroid.

SONOGRAPHIC FINDINGS

The sonographic examinations revealed that of the patients, 70 (73.7%) had one nodule, 15 (15.8%) had two nodules, 6 (6.3%) had three nodules, and 4 (4.2%) had more than three nodules.

There were no sonographic reports concerning lymphadenopathy or extension of the tumor out of the thyroid.

The largest diameter of the thyroid nodules averaged 3.38 ± 1.83 cm. We found significant statistical differences with the average of the largest diameter of the thyroid nodule. We evaluated the largest diameter of the thyroid nodules by the ROC curve graph of SPSS, as it was a quantitative variable.

Four pure cysts were found in the sonographic examinations of the patients. There were no suspicious sonographic findings, as shown in Table 2.

FNAB REPORTS

Fine needle aspiration biopsy was performed in 100 patients. Five patients who had an FNAB report of an unsatisfactory specimen were excluded from the study group, as mentioned previously. In the remaining 95 patients, 81 (85%) had benign FNAB reports that included nodular goiter, Hashimoto thyroiditis, and acute thyroiditis. Fourteen patients (14%) had FNAB reports that indicated malignant cells or cells suspicious of malignancy.

Discussion

Palpable thyroid nodules are considered clinically significant and warrant further evaluation. The discovery of one or more nodules in the thyroid gland raises concern about malignancy.

Many reports have discussed sonographic findings of the thyroid mass; however, a considerable overlap of characteristics in benign and malignant lesions was found. Endocrinologists themselves

TABLE 2.
Diagnostic Index for Individual Sonographic Criteria of Malignant Thyroid Nodules (n = 95)

Sonographic Characteristics	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Accuracy (%)
1. Solitary versus multiple	78	29	16	88	36
2. Solid versus mixed	42	40	11	81	40
3. Microcalcification	28	77	18	86	70
4. Hypoechogenicity	57	61	20	89	61
5. Incomplete peripheral halo	50	74	25	89	70
6. Irregular margin	42	71	20	87	67
7. Largest diameter > 3.9 cm	64	69	26	91	68
8. More tall than wide	7	96	25	85	83
9. Microlobulated margin	14	92	25	86	81

Most malignant nodules had multiple sonographic findings suggestive of malignancy. The mean number of suspicious findings per malignant nodule was 1.65, but if we select the first seven criteria, the mean number of suspicious findings per malignant nodule changes to 5.6.

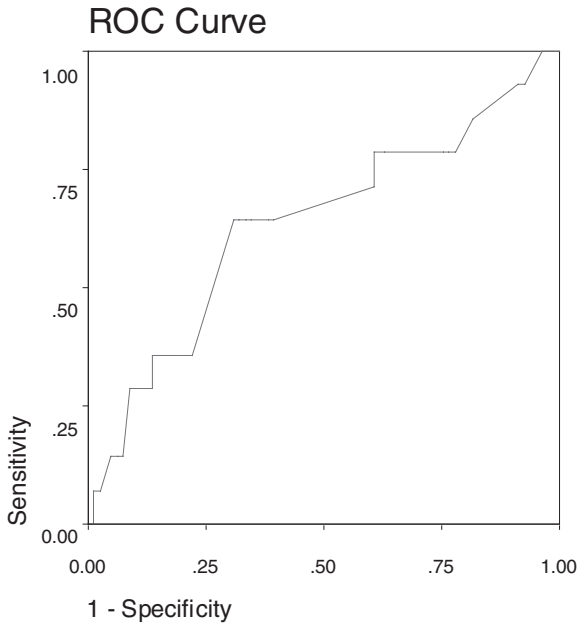

FIG. 2. The largest diameter of the nodules versus malignancy.

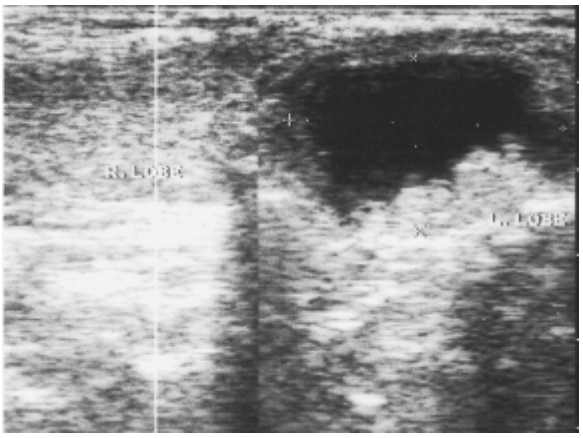

FIG. 3. A middle-age woman with a solitary left-lobe thyroid nodule. The nodule is mixed and has an irregular margin, a microlobulated margin, an incomplete peripheral halo, and hypoechogenicity. The largest diameter of the nodule is 3.2 cm.

are using sonography more frequently. A recent study suggested that sonography would alter the clinical management of nodular thyroid disease in 63% of patients.[11]

We tried to identify the characteristic sonographic findings of benign and malignant nodules because, to our knowledge, no study has evaluated all the sonographic characteristics together.

We evaluated the nine criteria together and found that the mean number of suspicious findings per malignant nodule was 1.65, but if we select only the first seven criteria in Table 2, the mean number of suspicious findings per malignant nodule changes to 5.6.

This indicates that the first seven criteria in Table 2 are more valuable in this regard.

In a prospective study by Kim et al.,[12] no statistically significant difference between benign and malignant nodules was found with regard to size in 155 patients with nonpalpable thyroid nodules who later underwent FNAB. Sidawy et al.,[13] however, reported a higher frequency of thyroid cancer in nodules larger than 4 cm. In our study, the largest diameter of the nodules was evaluated by the ROC of SPSS (Fig. 2). The most accurate diameter for differentiating malignant from benign nodules was 3.9 cm (sensitivity = 64%, specificity = 68%, P = .16).

Solbiati et al.[14] and Propper et al.[15] showed that a peripheral sonolucent halo that completely or incompletely surrounds a thyroid nodule may be present in 60% to 80% of benign nodules and 15% of thyroid cancers. In our study, evaluation of the incomplete peripheral halo as a finding suggestive of malignancy showed 70% accuracy and an 89% negative predictive value (Fig. 3).

Kim et al.[12] also regarded a nodule that is more tall than wide as suggestive of malignancy (Fig. 4). They applied this criterion, which had been documented in breast nodules, to thyroid nodules. In their study, the findings were not sensitive but very specific (sensitivity = 32%, specificity = 92%). In our study, evaluation of this criterion on palpable nodules showed the same result in specificity but less sensitivity. Our study is apparently too small to validate this hypothesis ($P > .05$). Additional and extensive studies are required in this regard.

Other sonographic characteristics were not statistically significant but were compatible with other studies,[11-15] as all of the criteria are more specific than sensitive and have more negative predictive value than positive predictive value. Figures 1 through 6 show some of the sonographic characteristics in this regard.

Kuma et al.[16] examined the long-term outcome of benign thyroid nodules that were untreated.

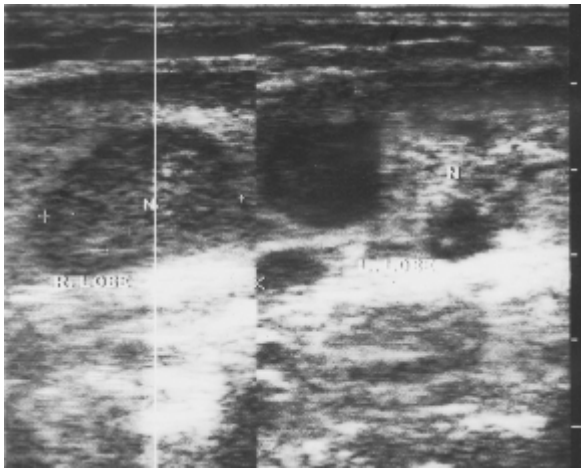

FIG. 4. A middle-age woman with a multinodular goiter. The right-lobe nodule is solid and has hypoechogenicity. The largest diameter of this nodule is 2.3 cm. The left-lobe nodule is mixed and has an irregular margin that is more tall than wide.

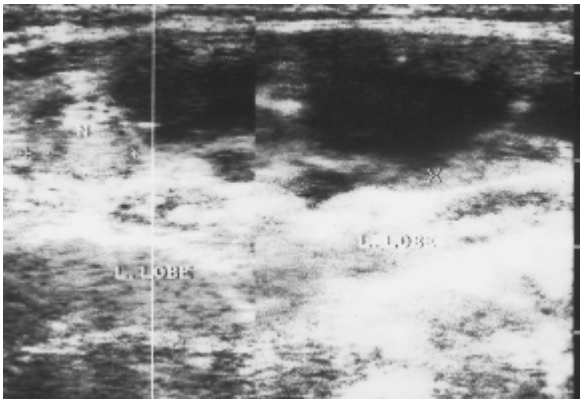

FIG. 5. A middle-age woman with a multinodular goiter. A small solid nodule (N) in the left side of the figure and two cystic nodules in the right. The largest diameter of the left-lobe nodule is 3 cm. It has an irregular margin and hypoechogenicity.

Among 134 patients with cytologically benign thyroid nodules who were followed for 9 to 11 years, most nodules (133/134, 99.3%) remained benign. This finding clearly shows that benign thyroid nodules remain benign for a long time. In our study, the negative predictive value of all the criteria ranges from 81% to 91% (Table 2), which means that the probability of malignancy is very low when there is not a single suspicious sonographic finding.

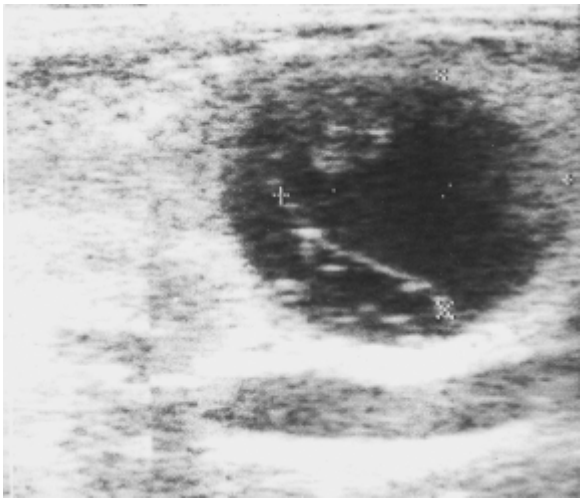

FIG. 6. A middle-age woman with a solitary thyroid nodule with septation. It is solid and has hypoechogenicity. The largest diameter is 2 cm.

Contrary to this, the positive predictive value of all the criteria ranges from 11% to 25% (Table 2). Therefore, when we encounter suspicious sonographic criteria, the patient should be referred for FNAB.

Finally, many different results obtained from different sonographic criteria that have substantial imperfections must be integrated into a diagnostic conclusion about the probability of disease in a given patient. To approach this problem in a critical manner, we must estimate the pretest likelihood of disease (defined by age, sex, signs, and symptoms) and the sensitivity and specificity of each sonographic criterion. With this information, test results can be analyzed by using the Bayes theorem of conditional probability.[17] We introduce this method for future studies with a larger sample size.

This approach has several advantages. It pools the diagnostic experience of many physicians and integrates fundamental pretest clinical descriptors with many varying sonographic results, which can reproducibly summarize the probability of thyroid cancer. This approach also aids but does not replace the physician's judgment and may assist in making decisions on the cost-effectiveness of tests.

Conclusion

Considering the high level of negative predictive value of all the sonographic criteria, when

there is not a single suspicious finding of malignancy in the sonographic examination of a nodule, we can observe the patients and follow up on them with clinical and sonographic evaluation.

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