Original Investigation

# Sonographic Criteria Predictive of Malignant Thyroid Nodules: Which Lesions Should be Biopsied?

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**Rationale and Objectives:** The objective of this study was to evaluate the ultrasound features of thyroid nodules and their association with malignancy, focusing on establishing feature-oriented ultrasound criteria to determine proper management of a thyroid nodule.

**Materials and Methods:** A sample of 379 thyroid nodules were biopsied (from a total of 357 patients aged 59.8 ± 14.8 years) and 300 were included in the final study (271 benign nodules and 29 malignant ones). Ultrasound features were recorded for each nodule: size, echogenicity, homogeneity, contours, shape, texture, peripheral halo, calcifications, and the presence of adenopathy. Statistical analysis of the data was performed using the Mann-Whitney *U* test and chi-square test. The sensitivity and the specificity of variables seen to have a statistically significant association with the malignancy of nodules were assessed and a logistic regression was performed.

**Results:** A taller-than-wide shape, an ill-defined contour, the presence of a halo, microcalcifications, and adenopathy were found to have a statistically significant relationship ($P < 0.05$) with malignancy, although with a low sensitivity and a high specificity. The presence of at least one suspicious feature yields great sensitivity (89.7%) in detecting malignant disease.

**Conclusions:** The ultrasound features of thyroid nodules alone do not allow the radiologist to make a confident diagnosis regarding the malignancy of a nodule without performing a biopsy. However, a nodule showing a taller-than-wide shape, microcalcifications, a peripheral halo, an ill-defined contour, or associated adenopathy should be considered for cytology.

**Key Words:** Thyroid gland; ultrasound; thyroid nodule; thyroid neoplasms.



## INTRODUCTION

There is an increasing rate of diagnosis of thyroid nodules in the general population, much due to the widespread availability of ultrasound equipment and better health care worldwide (1). Up to two-thirds of the general population has thyroid nodules at an ultrasound examination. Although only a small percentage of nodules are malignant, prognosis for patients with thyroid cancer is good, attaining a 5-year survival rate of 98.1% in the United States, mainly related to the early diagnosis of small lesions (1–3).

Ultrasound examination, although very sensitive in identifying thyroid nodules, lacks the accuracy to differentiate between benign and malignant nodules (2,4,5). Fine-needle aspiration cytology (FNAC) technique under ultrasound guidance is the most used method to obtain biologic material from a thyroid nodule, leading to a definite benign or malignant result in about 90% of cases (6).

However, performing FNAC on every thyroid nodule detected with ultrasound is not cost-effective due to the high prevalence of nodules (7). More so, there has been rising concerns in the literature about the issue of overdiagnosis of thyroid cancer, furthering the need to better stratify the risk of patients (3,8,9).

Ultrasound features like microcalcifications, hypoechogenicity, ill-defined contours, lack of a peripheral halo, or intranodular vascularization have previously been associated with malignancy (1,2,10–13). On the other hand, some features like cystic changes in a nodule or a spongiform appearance are associated with benignity (14).

Although the sonographic features of malignant and benign thyroid nodules have been established, they have variable specificity and sensitivity (1,2,6,11,13,15) and no single sonographic feature can be used to identify or exclude nodules that should be subjected to FNAC (1,7,16). A combination of ultrasound features that can distinguish between nodules that require biopsy and "leave alone" nodules is crucial in the workup of the patients with thyroid nodules (17).

The aim of the present study was to establish feature-oriented ultrasound criteria to predict the presence of malignancy of thyroid nodules.

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We also determined the diagnostic accuracy of the ultrasound features of the thyroid nodules, using the pathologic results as the reference.

## MATERIALS AND METHODS

### Patients

Among the records of 379 consecutive FNAC studies in the radiology department at a single institution from January 2013 to December 2013, the cases of 357 patients (311 women and 46 men; average age, 59.8 years; range, 23–92 years) were identified, in which both pathology reports and ultrasound images were available.

The inclusion criteria were the following: (1) adult patients and (2) patients who underwent surgery or remained at least 12 months in follow-up if the first cytologic analysis revealed a benign nodule.

The present study was approved by our institutional review board with a waiver of informed consent.

### Ultrasound Technique

All punctures for the cytologic analysis were performed under ultrasound guidance by one of five radiologists, with 23-gauge needles, with at least three slides being air-dried and the other three being alcohol fixed (96% ethanol). There was no cytotechnologist or pathologist present during the procedure. All ultrasound studies and FNACs were performed using a General Electric LOGIQ L9 equipment, with a 9-MHz linear probe.

### Ultrasound Interpretation

Images were reviewed by an experienced radiologist (with 10 years of ultrasound experience) using our Picture Archiving and Communication System as a data source. Moreover, for each puncture, a report was made by the performing radiologist and was taken on account by the radiologist who reviewed the images.

For each nodule that was punctured, several variables were measured or observed: dimensions (in millimeter), echogenicity (hypo-, iso-, and hyperechoic), homogeneity (homogeneous or heterogeneous), contours (well defined or ill defined), shape (parallel to gland plane, spherical or taller-than-wide shape), texture (solid, cystic, or mixed type), presence of a peripheral halo, presence of calcifications (distinguishing between microcalcifications and gross ones), and the presence of adenopathy.

### Histologic Analysis

All cytologic analysis results were recorded ($n = 379$), as well as the histologic analysis of the surgical specimen when a thyroidectomy was performed ($n = 41$). In the case of discrepancy, the latter would prevail. For the cytologic analysis, the Bethesda system was used (18–20).

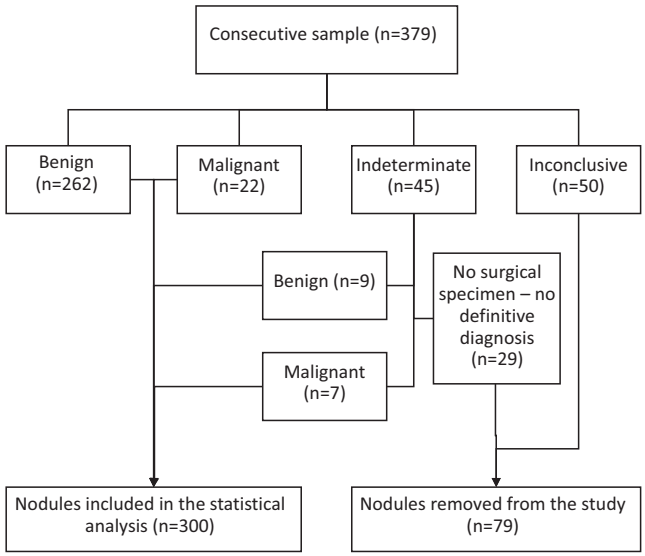


**Figure 1.** Flowchart depicting the sample selection.

We excluded the nodules that did not achieve a final diagnosis (mainly the Bethesda grade III and IV nodules that did not perform surgery) or if the cytologic analysis was inconclusive (grade I of the Bethesda classification).

A flowchart is presented to better visualize the sample selection (Fig 1).

### Statistical Analysis

The statistical analysis of the data was performed using R statistical software, version 3.0.2 and IBM-SPSS version 23 for Windows. A significance level of 0.05 was adopted. The Shapiro-Wilk test was used to assess the normality of quantitative variables. The Mann-Whitney $U$ test was used to assess differences between malignant and benign nodules. The association with categorical variables was assessed using chi-square tests. A multiple logistic regression analysis was performed to determine the predictive role of meaningful variables. The predictors were those that were significant in the univariate analysis or otherwise clinically meaningful variables. The Hosmer-Lemeshow goodness-of-fit test was performed to check model adequacy.

## RESULTS

The demographic features of our sample are presented in Table 1. Patients with malignant nodules differ significantly in age from patients with benign nodules (54.1 vs 60.4 years, $P = 0.034$). We found no significant gender differences.

Regarding the 29 nodules that were classified as malignant, 27 were papillary carcinomas, in which 7 were diagnosed as follicular variant. There was one case of follicular carcinoma and one case of medullary carcinoma.