Ultrasound Findings in Thyroid Nodules: A Radio–Cytopathologic Correlation

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Abstract

**Introduction:** Ultrasound (USG) can be a good screening tool to identify high-risk nodule requiring fine-needle aspiration cytology (FNAC). The study aimed to assess the association of USG characteristic of thyroid nodule with malignancy. **Methods:** A cross-sectional study was performed from August 2011 to July 2012 at Tribhuvan University Teaching Hospital. Patients referred for USG of the neck with thyroid nodule more than 10 mm were offered FNAC and included in the study after taking informed consent. USG characteristics were compared with histopathologic diagnosis of benign or malignant nodule. **Results:** USG characteristics significantly \( P < 0.05 \) associated with malignancy were as follows: size of thyroid nodule more than 30 mm, ill-defined margin, solid echotexture, hypoechoic lesion, microcalcification, and any form of increased vascularity. High sensitivity was seen in microcalcification, hypoechoic echogenicity, and ill-defined margin and high specificity was seen in ill-defined margin and solid echotexture. Relatively high sensitivity and specificity was found in ill-defined margin. Hypoechoegenicity, vascularity of any type, ill-defined margin, and microcalcification were independent predictors of malignancy. None of the characteristics were sensitive and specific to be used independently as screening tool to identify high risk of malignancy. **Conclusions:** Texture, size, margin, echogenicity, and vascularity are important factors for discriminating benign from malignant nodule.

Keywords: Malignant, thyroid nodule, ultrasound

**INTRODUCTION**

The first ultrasound (USG) for thyroid nodules was performed in 1967 by Fujimoto; since then, many advances have developed in the ultrasonography of thyroid including real-time gray-scale imaging and color Doppler study. However, no USG findings are diagnostic to differentiate benign from malignant lesions. Many findings such as ill-defined margins, hypoechoic lesions, and microcalcification have shown association with malignant nodules. Fine-needle aspiration cytology (FNAC) is a well-established technique for differentiation of benign from malignant lesion with high sensitivity and specificity. USG can also be used to guide FNAC, which increases the yield of FNAC.

This study aims to identify associations of USG characteristics of large nodules (more than 10 mm) with malignancy and to identify diagnostic accuracy of these characteristics to be used as a screening test to identify clients with a large nodule who require FNAC.

**METHODS**

The study was a cross-sectional study conducted at Department of Radiology and Imaging of Tribhuvan University Teaching Hospital (TUTH), Kathmandu, from August 2011 to July 2012. The study was conducted as a thesis research for the partial fulfillment of the requirements for the degree of MD in radiodiagnosis. Ethical approval was taken from the Institutional Review Board of Institute of Medicine, TUTH.

The study sample includes all patients referred to the Department of Radiology and Imaging for USG of the neck

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during the study period and who were found to have thyroid nodules larger than 1 cm in size. Patients were offered to participate in the study and subjected to USG-guided FNAC after taking informed consent. Patients, who refused to participate in the study, with thyroid nodules smaller than 1 cm in size and patients with inconclusive FNAC reports were excluded from the study.

Internal consistency of thyroid nodules was classified as solid when the entire nodule was solid without any cystic foci and cystic when the entire nodule was cystic without any solid areas. Predominantly solid nodules were nodules with more than 50% solid areas with scattered cystic areas, and predominantly cystic nodules were nodules that had more than 50% cystic areas with some solid areas. Similarly, echogenicity was defined as hypoechoic, isoechoic, or hyperechoic comparing the echogenicity of the thyroid nodule with the normal thyroid gland. Heterogeneous echogenicity was noted when the same nodule showed mixed echoes. Margins were classified as ill defined when more than 50% of its border is not clearly demarcated. Microcalcification was defined as fine calcification of size 1 mm or less, single or in groups. Macrocalcifications were larger calcific foci and were classified as eggshell calcification (peripheral calcification), coarse calcification, and nodular calcification. The presence of any vascularity was defined as any color Doppler signal pickup in the nodule or periphery of the nodule. Perinodular vascularity was defined as vascularity only surrounding the nodule, and intranodular vascularity was defined as vascularity within the nodule.

Data were collected in a predesigned proforma. Data were analyzed using SPSS Statistics for Windows, Version 17.0. (Chicago, SPSS Inc.). Qualitative data were compared using Chi-square test, and quantitative data were compared with independent sample t-tests. Data associations were considered statistically significant at \( P < 0.05 \).

**Results**

A total of 85 patients participated in the study. The age of the sample ranged from 14 to 70 years with a mean age of 42.35 ± 14.1. Out of the 85 participants, 70 (82.4%) were females and 15 (17.6%) were males.

On histopathology, 15 (17.6%) of the participants were found to have malignant nodule and 68 (80.0%) were found to have benign disease. Histopathology was indeterminate (follicular neoplasm) in 2 (2.4%) participants; these participants were then excluded from the study.

The size of nodules ranged from 11 to 117 mm with a mean of 30.2 ± 16.2 mm. Malignant nodules had a large mean diameter than benign nodules (\( P = 0.02 \)). Furthermore, nodules with size more than 30 mm were more likely to be malignant than benign nodules (\( P = 0.03 \), odds ratio [OR] = 1.8) [Table 1].

Solid lesions were more associated with malignant lesion than benign lesion (77.3% vs. 33.8%; \( P = 0.005 \); OR = 2.17). Other statistical significant morphological characteristics of malignant nodules were ill-defined margins and hypoechoic echotexture [Table 2].

Macrocalcification was more frequent with benign lesions; however, the association was not statistically significant. Microcalcification was seen in malignant lesion more frequently than benign lesion (20% vs. 1.5%, \( P = 0.002 \), OR = 13.6) [Table 3].

Increase in vascularity was seen in malignant nodules more frequently; however, no specific pattern of increase in vascularity was significantly associated with malignant nodule [Table 4].

| Table 1: Size distribution in benign versus malignant nodules |
|-------------------------------------------------------------|
| **USG characteristics** | **Benign** (\( n=68 \)) | **Malignant** (\( n=15 \)) | **\( P \) (OR)** |
| **Size** | | | |
| Mean±SD | 28.3±13.8 | 38.7±23.6 | 0.02 |
| Size >30 mm | 25 (36.8) | 10 (66.7) | 0.03 (1.8; CI-1.12-2.91) |

SD: Standard deviation, OR: Odds ratio, CI: Confidence interval

| Table 2: Morphologic characteristics of benign versus malignant nodules |
|---------------------------------------------------------------|
| **USG characteristics** | **Benign** (\( n=68 \)) | **Malignant** (\( n=15 \)) | **\( P \)** |
| **Margins** | | | |
| Well defined | 15 (22.1) | 14 (93.3) | <0.001 (49.5; CI-6.0-407.2) |
| Ill defined | 53 (77.9) | 1 (6.7) | |
| **Echotexture** | | | |
| Solid | 23 (33.8) | 11 (73.3) | 0.005 (2.17; CI-1.38-3.4) |
| Cystic | 4 (5.9) | 7 (46.7) | 0.005 (2.17; CI-1.38-3.4) |
| Predominantly solid | 31 (45.6) | 4 (26.7) | 0.17 |
| Predominantly cystic | 10 (14.7) | - | |
| **Echogenicity** | | | |
| Hypoechoic | 8 (11.8) | 6 (40.0) | 0.008 (3.4; CI-1.38-8.3) |
| Isoechoic | 5 (7.3) | 1 (6.7) | 0.98 |
| Hyperechoic | 11 (16.2) | - | |
| Heteroechoic | 45 (66.2) | 8 (53.3) | 0.35 |

USG: Ultrasonography, CI: Confidence interval

| Table 3: Calcifications in benign versus malignant nodules |
|----------------------------------------------------------|
| **USG characteristics** | **Benign** (\( n=68 \)) | **Malignant** (\( n=15 \)) | **\( P \)** |
| **Macrocalcification** | | | |
| Present | 44 (64.7) | 5 (33.3) | 0.72 |
| Coarse | 18 (26.9) | 3 (20.0) | 0.26 |
| Egg shell | 15 (22.1) | 1 (6.7) | 0.42 |
| Nodular | 2 (2.9) | - | |
| **Microcalcification** | | | |
| Present | 1 (1.5) | 3 (20.0) | 0.002 (13.6; CI-1.5-121.8) |
| Absent | 67 (98.5) | 12 (80.0) | |

USG: Ultrasonography, CI: Confidence interval
Multivariate regression analysis showed that hypoechoicity, vascularity of any type, ill-defined margin, and microcalcification were found to be significant independent predictors of malignancy.

The sensitivity for prediction of malignancy was highest for ill-defined margin (93.3%), and specificity was highest for microcalcification (98.5%) [Figure 1]. However, no single parameter had high sensitivity and specificity both to be used as a predictor of malignancy and screen patients for FNAC.

**DISCUSSION**

Thyroid ultrasonographic finding is frequently misperceived as being unable to differentiate benign and malignant nodules. None of the single USG findings have been able to accurately differentiate between benign and malignant nodules; however, combination of the suspicious findings can help differentiate nodules that are definitely benign and suspicious nodules that may require FNAC. USG findings such as microcalcification, irregular ill-defined margin, markedly hypoechoic echotexture, and solid internal consistency and internal vascularity are findings that are associated frequently with malignant lesions. The utility of these findings in a goiter-endemic area like Nepal has been explored in this study.

In our study, larger nodules were more likely to be associated with malignant lesion with size more than 30 mm being more frequently malignant. Some studies have also demonstrated that malignancy was associated with larger size, while others have demonstrated an opposite association with size. Size is not considered helpful for distinguishing malignant nodule from benign nodule.

This study showed solid lesions to be associated with malignancy, which is consistent with most studies done previously. Predominantly solid lesions are also considered to be associated with malignancy; however, in this study, the association was not seen. Because of this association, FNAC is recommended in solid or predominantly solid nodules.

Hypoechoic nodules and ill-defined margins were seen more frequently in malignant lesion in this study. These factors have been established as independent predictors of malignant nodules. However, another study has shown that echogenicity did not show any significant difference between benign and malignant nodules. Calcification, especially coarse and rim calcifications and microcalcification, have also been shown to be predictors of malignancy by some studies; however, other study has shown only microcalcification to be associated with malignancy, while the association of malignancy with coarse and rim calcification is debatable. This study shows significant associations of microcalcification with malignancy, while macrocalcification was not found to be significantly associated with malignancy.

Increased vascularity of any type was associated with malignant nodule; however, perinodular or intranodular increase in vascularity was not significantly associated with malignant lesions. Increased in vascularity of any type has been established by some other studies to be predictors of malignancy, while others consider vascularity as a nonspecific finding. Ill-defined margin, hypoechoic echogenicity, microcalcification, and increased vascularity were found to be independent predictors of malignancy with multivariate regression analysis in this study.

None of the USG findings have shown high sensitivity and specificity to be independent predictors that can be used for screening in various studies. Microcalcification, marked hypoechoogenicity, ill-defined margin, and intranodular vascularity have shown high specificity. Solid structure and marked hypoechoogenicity have shown high sensitivity in various studies. This study also demonstrated high sensitivity in ill-defined margin and solid echotexture and high sensitivity in microcalcification, hypoechoic echogenicity, and ill-defined margin.
margin. Relatively high sensitivity and specificity were found in ill-defined margin; similar results were also seen with other studies.\(^9\) The study also found that size more than 30 mm had a sensitivity and specificity of 66%–63%, respectively, and a high negative predictive value of 89%. This finding may be indicative that in a nodule, more than 1 cm larger size (>30 mm) may be useful to screen benign from malignant nodules; however, this finding needs to be established by a study of larger sample.

There were some limitations to the study. The small sample size in our study is the main limitation; only 15 participants had the malignant nodule. We did not evaluate the shape of the lesion, spongiform appearance of the lesion as predictor of its nature in our study, which are however considered predictors of malignancy from previous studies. We did not use modern advances in USG like elastography to evaluate the lesion.

**Conclusions**

Although many ultrasonologic characteristics were found to be associated with malignant lesion, none of these features can be used as single independent predictors to screen patients for malignancy. Size though considered indeterminate to identify malignant lesions, size larger than 30 mm has been shown to be predictor of malignant lesion in our study and may be useful independently or in combination with other ultrasound features to identify malignant lesions.

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**Conflicts of interest**

There are no conflicts of interest.

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