ORIGINAL ARTICLE

Ultrasonographic guideline for thyroid nodules cytology: single institute experience

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Purpose: The main issue with the current ultrasonography (US) guidelines is the overestimation of malignant and indeterminate nodules as they do not aid in making decisions to treat patients. To overcome this, new US guidelines for thyroid nodules that have been shown to be better correlated with cytologic results have been proposed. We also suggested specific indications for US-guided fine needle aspiration (FNA) using the new US guidelines. **Methods:** Clinical and pathologic data from 925 patients and 1,419 thyroid nodules were retrospectively collected. All subjects underwent US- and US-guided FNA at Department of Surgery, Wonju Christian Hospital, between March 2010 and July 2011. Sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were calculated for both the current guidelines and the new guidelines. **Results:** The accuracy, sensitivity, specificity, PPV, and NPV for the current guidelines in predicting malignancy were 24.1%, 99.3%, 62.2%, 25.0%, and 99.8%, respectively. The accuracy, sensitivity, specificity, PPV, and NPV for the new guidelines in predicting malignancy were 66.0%, 96.0%, 86.7%, 47.7%, and 99.4%, respectively. **Conclusion:** The use of the new US guidelines allow for a more accurate and specific diagnosis and a better treatment plan than the current guidelines. Additionally, the use of the new FNA guidelines may help prevent unnecessary FNAs and promote cost-effective follow-up for patients.

Key Words: Ultrasonography, Guideline, Fine needle biopsy, Thyroid neoplasms

INTRODUCTION

Approximately 4% to 7% of all adults have thyroid nodules. Current epidemiologic data have shown that only 5% to 6.5% of the reported cases of thyroid nodules found by ultrasonography (US) are malignant and require further workup [1-3]. As the increasing prevalence of thyroid cancer increases, there is a need for a method that can identify malignant lesions that warrant further surgical treatment [4,5].

To date, fine needle aspiration (FNA) is not only the traditional diagnostic test for identifying malignant thyroid nodules [6], but also represents the "gold standard" preoperative test for diagnosing thyroid cancer. However, the sensitivity of FNA ranges from 65% to 98%, and the specificity from 72% to 98% [7]. The Bethesda classification system is typically used for indeterminate cytological results (atypical cells of undetermined significance, follicular ne-

oplasm or suspicion of follicular neoplasm, suspicion of malignancy), which can further complicate the situation. Consequently, surgical resection is often required in indeterminate cases for a definitive diagnosis. Therefore, a comprehensive diagnostic algorithm using US findings is of interest to ensure accurate diagnosis and therapeutic planning, and to decrease diagnostic operative resections.

Neck US has long been used to evaluate the size, character and location of thyroid nodules, monitor nodule growth, and identify locoregional lymphadenopathy [6,8-10]. Many studies have classified specific US characteristics predictive of malignant thyroid nodules. For instance, current US characteristics are that strongly correlated with malignancy include increased intranodular vascularity, the presence of micro- of macrocalcifications, a taller-than-wide pattern, hypoechogenecity, and speculated margins [11,12]. Although controversial, the current guidelines state that if any one of the above findings is observed, with the exception of increased intranodular vascularity, the nodule should be defined as suspicious for malignancy. In contrast, simple cysts defined as nodules that are predominantly cystic, cystic with comet tail artifacts, or nodules with a spongiform appearance are all likely to be benign. Indeterminate nodules are those that are not characteristic of either malignant or benign [11,13]. As the main issue with the current guidelines is the overestimation of malignant and indeterminate nodules, they are not useful in the decision-making process of a treatment plan as they result in unnecessary invasive procedures, including FNA and diagnostic thyroidectomy.

The purpose of this study is to address the disadvantages of the current guidelines by suggesting a new US-based guideline system for thyroid nodules. As well, with the use of these new guidelines, we discuss specific indications for US-guided FNA.

METHODS

Clinical and pathologic data were retrospectively collected from 925 patients with a total of 1,419 thyroid nodules, having undergone US- and US-guided FNA at Department of Surgery, Wonju Christian Hospital, between March 2010 and July 2011. All neck ultrasounds were performed by surgeons using high-frequency linear array transducers 7.5-13 MHz (Aloka Prosound α5, Hitachi Aloka Medical Ltd., Tokyo, Japan). US and FNA were performed by a surgeon under the supervision of three experienced endocrine surgeons.

Each patient was placed in the supine position with the neck extended. Examinations began with a transverse view of the neck from the supraclavicular to the submental area bilaterally, in order to evaluate the thyroid gland. Longitudinal views were also obtained with a color doppler to assess the vascularity of any nodules. After taking an image of the thyroid gland, the central and lateral compartment lymph nodes were assessed for any abnormality. FNA was performed by the same single surgeon following US evaluation.

The new US guidelines were established via discussions among experienced physicians who participated in this study. Each nodule was classified by standard US characteristics: suspicious for malignancy, indeterminate, probably benign. In total, 1,419 nodules were classified using both guidelines. From both guidelines, all classifications were correlated with the cytological results obtained by FNA. Benign cytological results were defined by the Bethesda classification system, including histopathology consistent with benign follicular nodule, Hashimoto thyroiditis, and subacute thyroiditis. The indeterminate category included results consistent with atypical cells of undetermined significance, follicular neoplasms, suspicion of follicular neoplasms, and suspicion of malignancies. Lastly, the malignant category was defined as all histopathology positive for malignancy. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for US characteristics that suspicious for malignant nodules of both current and new guideline. Sensitivity, specificity, accuracy, PPV, and NPV were calculated for both current and new guidelines, with PASW ver. 18.0 (IBM Co., Armonk, NY, USA) used for statistical analysis.

RESULTS

The mean age of the 925 subjects was 51.87 years (range, 14 to 85 years), with 104 male and 821 female patients enrolled. The new guidelines divided nodules into three groups: suspicious for malignancy, indeterminate, and probably benign. Nodules suspicious for malignancy were defined using the following ultrasound patterns: nodules characterized by speculated margins that were markedly hypoechoic, taller-than-wide and markedly hypoechoic nodules, nodules with micro- or macrocalcifications that were markedly hypoechoic, and taller-than-wide nodules with micro- or macrocalcifications. Indeter-

minate lesions were defined as nodules exhibiting any one of the following patterns: markedly hypoechoic, a taller-than-wide pattern, a spiculated margin, and micro- or macrocalcifications. Nodules were classified as probably benign if the US characteristics were not consistent with either malignant or indeterminate features (Table 1).

Sensitivity of US characteristics that suggested malignancy by current guidelines generally was higher than that of the new guidelines. Specificity, PPV of US characteristics that suggested malignancy by new guidelines generally was higher than that of the current guidelines (Tables 2, 3).

After cytologic classification, 1,035 cases were found to be benign, 139 indeterminate, and 148 cases malignant. Using the current US-guidelines, 132 cases were defined as benign, 600 cases as indeterminate, and 590 cases suspicious for malignancy, with such results clearly indicating a large discrepancy. Based on the data presented here, the accuracy of this cross table is 24.1% (Table 4). After comparing the new US guidelines with cytological results, 726 cases were found to be benign, 298 cases indeterminate, and 298 cases malignant. The accuracy of this cross table was 66.0% (Table 5).

The relative sensitivity, specificity, PPV, and NPV for the current guidelines in predicting malignancy were 99.3%, 62.2%, 25.0%, and 99.8%, respectively. In comparison, the relative sensitivity, specificity, PPV, and NPV for the new

Table 1. New ultrasonography (US) guidelines for thyroid nodules

US diagnosis	US characteristic
Suspicious for malignancy	Spiculated margin and markedly hypoechoic
	Taller-than-wide pattern and markedly hypoechoic
	Micro- or macrocalcification and markedly hypoechoic
	Taller-than-wide pattern and micro or macro-calcifications
Indeterminate	Taller-than-wide pattern
	Markedly hypoechoic
	Spiculated margin
	Micro- or macrocalcification
Probably benign	Neither malignant nor indeterminate US findings

Table 2. Ultrasonography (US) characteristics associated with thyroid cancer (current guideline)

US characteristic	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Taller-than-wide pattern	48.6	89.9	37.4	93.4
Markedly hypoechoic	93.8	82.0	39.4	99.1
Spiculated margin	48.6	92.5	44.7	93.5
Micro- or macrocalcification	52.1	84.7	29.8	93.4

PPV, positive predictive value; NPV, negative predictive value.

Table 3. Ultrasonography (US) characteristics associated with thyroid cancer (new guideline)

US characteristic	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Spiculated margin and markedly hypoechoic	45.9	86.6	62.6	93.5
Taller-than-wide pattern and markedly hypoechoic	44.5	95.8	57.0	93.3
Micro- or macrocalcification and markedly hypoechoic	47.9	96.1	60.3	93.7
Taller-than-wide pattern and micro- or macrocalcifications	20.1	97.3	43.9	90.4

PPV, positive predictive value; NPV, negative predictive value.

Table 4. Cross-table of the current guidelines and the cytologic results

Current guidelines	Cytologic diagnosis			
	Benign	Indeterminate	Malignancy	Total
Benign	127	5	0	132
Indeterminate	554	45	1	600
Malignancy	354	89	147	590
Total	1,035	139	148	1,322

Table 5. Cross-table of the current guidelines and the cytologic results

New guidelines	Cytologic diagnosis			
	Benign	Indeterminate	Malignancy	Total
Benign	676	50	0	726
Indeterminate	238	54	6	298
Malignancy	121	35	142	298
Total	1,035	139	148	1,322

Table 6. Sensitivity, specificity, PPV, NPV for the current guidelines and the new guidelines

	Current guidelines (%)	New guidelines (%)
Sensitivity	99.3	96.0
Specificity	62.2	86.7
PPV	25.0	47.7
NPV	99.8	99.4

PPV, positive predictive value; NPV, negative predictive value.

guidelines in predicting malignancy were 96.0%, 86.7%, 47.7%, and 99.4%, respectively (Table 6).

DISCUSSION

To date, there have been several studies that examined specific US characteristics that accurately distinguished malignant from benign thyroid nodules. However, most of this data merely confirms US characteristics associated with malignancy [10,14-16]. Thus, studies have suggested developing new US guidelines using data from many cases to resolve this problem. Among the established guidelines; the most widely accepted definition of a lesion causing concern for malignancy if any of the aforementioned characteristics are present. In contrast, a simple cyst, which is predominantly a cystic lesion or a cystic nodule with comet tail artifacts, or a nodule with a spongiform appearance are characterized as probably benign. Indeterminate nodules include lesions with US findings that are known to be neither malignant nor benign. However, these particular guidelines are controversial as they tend to overestimate malignant and indeterminate nodules. Cooper et al. [17] reported that with the exception of suspicious cervical lymphadenopathy, a specific but insensitive

finding, a combination of features made it possible to identify all malignant nodules, whereas a single US feature was unable to detect this. Therefore, studies proposed to use a combination of US characteristics with the purpose of resolving this problem by establishing a more precise US guideline. For instance, Horvath et al. [18] suggested a novel US reporting system for thyroid nodules, which the authors termed the Thyroid Imaging Reporting and Data System (TIRAD), and modeled after Breast Imaging-Reporting and Data System (BI-RADS). TIRAD stratifies lesions into six separate categories, each of which have a different risk of malignancy and specific treatment plan. However, this classification system is difficult to apply clinically due to its marked complexity [19]. Therefore, the intention to develop a more accurate, and simple guideline for thyroid nodules was explored.

Frates et al. [14] reported a range of sensitivity, specificity, PPV, and NPV of US characteristics suggested for malignancy by current guideline.

Sensitivity, specificity, PPV, and NPV of US characteristics suggesting malignancy by the current guidelines in this study was similar to that. Especially, sensitivity of marked hypoechogenecity is the highest. Generally, the new guidelines had better specificity and PPV than the current guidelines. Even though the current guidelines were more sensitive than the new guidelines. It seems to be the cause of lower sensitivity of the new guidelines than the current guidelines.

The results showed that the new guidelines had better accuracy, specificity, and PPV than the current guidelines, although the NPV was not significantly different between the two. Even though the current guideline system was more sensitive than the new guidelines, the new guidelines allowed for better diagnostic accuracy and proper

treatment planning. Also, the new guidelines were easily acquired easily when compared to TIRAD due to the complexity level. The principal issue associated with the new guidelines was the relatively low sensitivity. This may be explained by the three cases where the lesions were well-defined, taller-than-wide, and isoechoic with peripheral hypoechoic halos (Fig. 1), and three cases where the lesions were well-defined, oval-shaped, and markedly hypoechoic (Fig. 2). Together, these six nodules were diagnosed as "indeterminate" by the new guidelines and "suspicious for malignancy" by the current guidelines. To address this, nodules that were suspicious for malignancy, however categorized by the new guidelines as "indeterminate," should be referred for FNA, particularly if they are taller-than-wide or markedly hypoechoic.

Recommendations regarding the indications for US-guided FNA are variable. Cause of absence single recommendation for FNA was concerned absence of single treatment guideline for thyroid cancer. Recently, many studies have recommended various treatment plans for thyroid cancer, although the issue of subcentimeter cancer remains controversial. Among the subcentimeter cancers, carcinomas smaller than 5 mm are associated with better survival rates and better recurrence rates at five years [20]. Ito et al. [21] reported similar results from an observational study involving such patients. Generally, the most recent studies recommended against the biopsy of nodules smaller than 5 mm in size as the evidence suggested that these lesions are often associated with a high rate of false
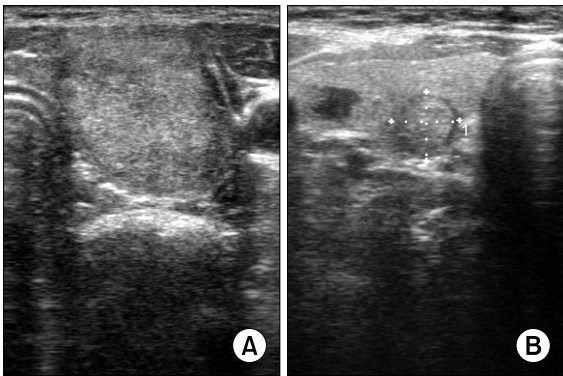

Fig. 1. (A, B) Well-defined taller-than-wide and isoechoic nodules with peripheral hypoechoic halo. These nodules resulted in the relatively low sensitivity of the new guidelines.

Fig. 2. Well-defined oval-shaped markedly hypoechoic nodules. These nodules resulted in the low sensitivity of the new guidelines.
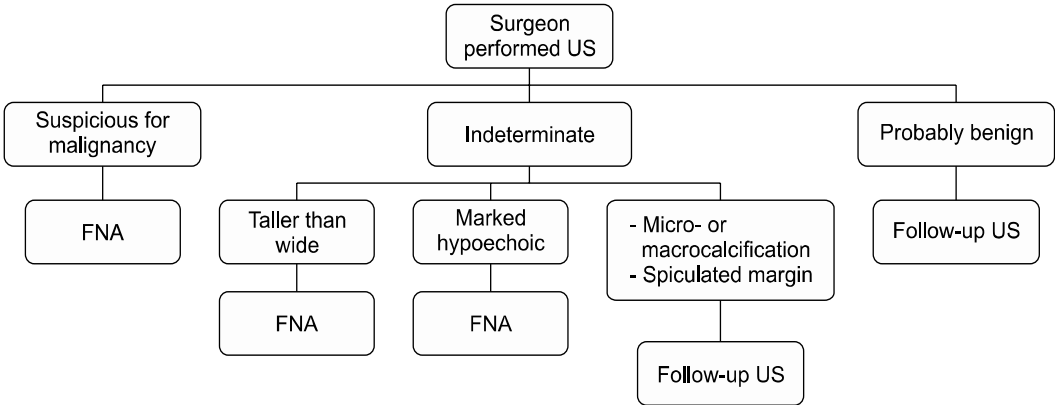

Fig. 3. Algorithm for follow-up ultrasonography (US) and US-guided fine needle aspiration (FNA) according to US findings.

positive US characteristics yielding inadequate cytology [22,23]. Aggressive behavior has been reported in some subcentimeter thyroid carcinomas. When prophylactic central compartment node dissection was later performed, the node metastasis rate ranged from 30% to 80%, even though metastatic lymph nodes were not seen on preoperative imaging [24-26]. Based on this evidence, thyroidectomy and prophylactic central compartment node dissection is performed by most endocrine surgeons in Korea, regardless of lesion size. Given the current practice in Korea, we recommend performing FNA for all nodules varying in size that have US findings that are suspicious for malignancy as defined by the new guidelines, as well as lesions that are markedly hypoechoic, or have a taller-than-wide pattern. For nodules that are classified as indeterminate, especially micro- or macrocalcifications and speculated margins, FNA is recommended if the lesion diameter is larger than 1 cm. For benign appearing nodules, we recommend the lesion be followed by US (Fig. 3). These new FNA guidelines help avoid unnecessary FNAs and promote a cost-effective follow-up for patients.

In conclusion, the use of the new US guidelines allow for greater accuracy with higher specificity for diagnosis and treatment planning than the current guidelines. Additionally, the use of the new FNA guidelines based on the new US guidelines help avoid unnecessary FNAs and promotes cost-effective follow-up for patients.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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