

Ultrasound-Guided Fine-Needle Aspiration Biopsy in Nonpalpable Thyroid Nodules: Is It Useful in Infracentimetric Nodules?

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The purpose of this study was to evaluate the usefulness of an ultrasound-guided fine-needle aspiration biopsy (US-FNAB) for the evaluation and treatment planning of nonpalpable thyroid lesions, including infracentimetric nodules. One hundred and twenty one patients underwent US-FNAB for 149 non-palpable solid nodules. Sixty-five patients underwent surgery, and 84 were followed up for at least 36 months. The results of the US-FNAB correlated with the pathological findings and clinical follow-up results. The nodules ranged from 0.3 to 2 cm in diameter, with a mean of 0.8cm. Among the 149 nodules, 115 were infracentimetric and 34 were centimetric or supracentimetric in size. Of the 149 thyroid nodules, US-FNAB was true positive in 43, true negative in 90, false positive in 7 and false negative in 1. In 8 cases, the lesion was inadequately sampled. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of the US-FNAB for the infracentimetric nodules were 96.9, 93.4, 86.1, 98.6 and 94.4%, and for the centimetric or supracentimetric nodules, were 100, 90.5, 85.7, 100 and 93.9%, respectively. There were no significant differences in the results between the infracentimetric and centimetric or supracentimetric nodules. In conclusion, an US-FNAB is a useful tool for determining the treatment plan of non-palpable solid thyroid nodules, even when less than 1 cm in diameter, and shows high sensitivity, specificity and accuracy.

Key Words: Thyroid biopsy, thyroid neoplasms, ultrasound guidance

INTRODUCTION

The use of high-resolution ultrasonography (US) has made the detection of nonpalpable nodules in the thyroid gland possible.^{1,2} Most of these lesions are benign, however, the discovery of a nodule within an otherwise clinically normal thyroid gland raises concern about malignancy, and creates a difficult situation regarding treatment for the clinician and the patient. For palpable nodules, a FNAB is usually obtained, however, how to deal with nonpalpable nodules has not been clearly defined.³ On US, a solid hypoechoic nodule of the thyroid is generally suspected for malignancy, but its specificity is low.⁴⁻⁹

Recently, US has been increasingly used as a guide to the interventional procedures. A US-guided FNAB (US-FNAB) of the thyroid has numerous advantages over a biopsy by palpation only.¹⁰⁻¹⁴ Real time US examination permits confirmation of the needle within the lesion, so facilitating an accurate biopsy of a small nonpalpable lesion, although only a limited number of reports are available. Some authors have reported the possible usefulness of an US-FNAB in nonpalpable thyroid lesions;^{12,13} and others that US-FNAB of infracentimetric nodules has low accuracy and efficacy.¹⁴

For these reasons, we retrospectively reviewed our experiences of US-FNAB in the management of nonpalpable thyroid nodules, including infracentimetric nodules.

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MATERIALS AND METHODS

Subjects

Our study included 121 consecutive patients who underwent US-FNAB for 149 nonpalpable thyroid nodules, which showed solid (isoechoic or hypoechoic) on US examination, between July 1997 and December 1997. There were 117 women and 4 men, with a mean age of 48.5 years, ranging from 26 to 77 years. No patient had had a previous thyroid disease or a history of radiation. The nonpalpable thyroid nodules were incidentally detected by thyroid screening US during breast (n=85) and neck US examinations of patients with dysphasia, hoarseness or neck discomfort (n=36).

Methods

Ultrasound was performed using ATL (HDI 3000; Bothell, Wash, USA) or Diasonics Spectra (Milpitas, Calif, USA) with a 7.5-12 MHz linear-array probe. One board certified radiologist performed the initial and follow-up US studies, as well as the US-FNAB, in all patients. In patients with more than one nodule, aspiration was performed for each nodule.

During the US-guided FNAB, patients were placed in a supine position, with the neck slightly extended. After localizing the lesion, the patient's neck was sterilely prepared and draped. The transducer was placed over the lesion, and a small

amount of 1% lidocaine solution injected into the skin at the point of the intended insertion of the biopsy needle. A 23-gauge needle, attached to the 20 ml syringe, was placed just above the transducer. By watching the tip of the needle on a monitor, it was inserted almost perpendicular to the neck. The tip of the needle was clearly visible as a bright spot on the monitor (Fig. 1). When the needle reached the target, the aspiration biopsy was performed with a to-and -fro movement. Suction was released before the needle was removed from the lesion. During the procedure, all the needle movements could be continuously visualized in real time. At least two aspirates (2-4 times) were taken from each lesion, to obtain sufficient material for cytological examination. After samples were obtained, they were mounted onto a glass slide. The slides were fixed and stained with Papanicolaou stain. The cytology was interpreted by the cytopathologist, and the cytological diagnoses classified into one of four categories: malignant, suspicious, benign or inadequate material.

Sixty-five nodules were removed by surgery, and the remaining 84 nodules followed up, clinically, for at least 36 months, with a mean follow up duration of 48.8 month. The indication for surgery included: malignant (n=36) and suspicious (n=12) cytology, and cases showing sonographic findings of malignancy (irregular hypoechoic mass contained microcalcification), regardless of the cytological results (n=13). Four patients with a benign cytology and US findings had

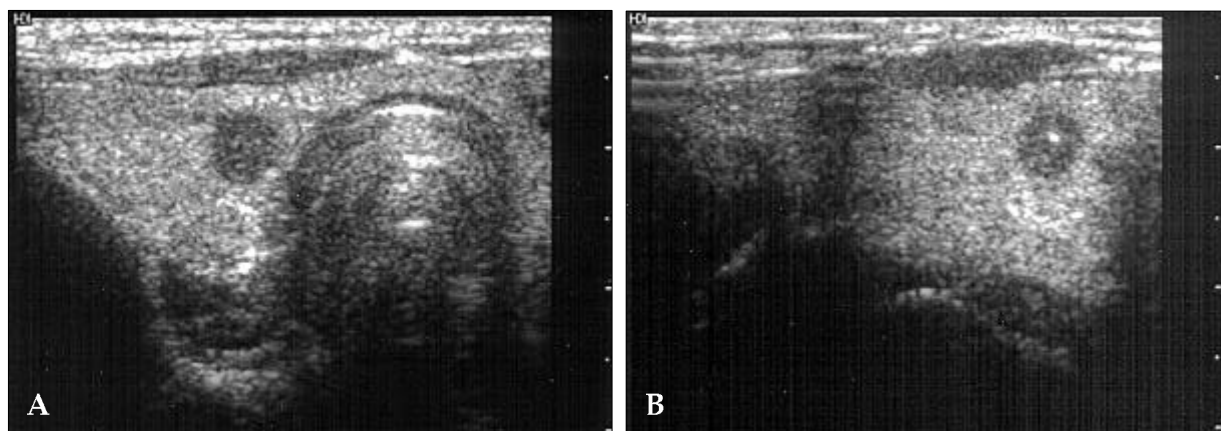


Fig. 1. Papillary carcinoma in a 39-year-old woman. (A) Relatively well-defined 8mm sized hypoechoic nodule was noted in the right lobe of the thyroid. (B) Bright echogenicity was noted at the same nodule demonstrated in figure 1A from the needle tip, as visualized during a procedure.

surgery at their own request.

The results of the US-FNAB were compared with the surgical pathology and clinical follow-up results. The overall sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of US-FNAB were obtained for the centimetric or supracentimetric (1 cm or more than 1 cm in diameter) and the infracentimetric nodules (less than 1 cm in diameter).

The statistical analyses were performed using the SPSS (SPSS, Inc, Chicago, IL, USA) software, and the values mentioned above for the infracentimetric and supracentimetric nodules compared. Nodules with inadequate cytological results were excluded, and suspicious cytological results were handled as a malignant diagnosis.

RESULTS

The nodules ranged from 0.3 to 2 cm in diameter, with a mean of 0.8 cm. Of the individual

nodules, 115 were smaller than 1 cm and 34 were 1 cm or larger. The cytology was benign in 91, malignant in 36 and suspicious in 14, and there were 8 inadequate specimens, comprising 5.4% of all the NAB specimens. Of the 115 infracentimetric nodules, 7 (6.1%) had inadequate specimens and of the 34 centimetric or supracentimetric nodules, 1 (2.9%) resulted in an inadequate specimen. Three nodules out of the 8 inadequate specimen were repeat NAB due to suspicious sonographic characteristics, but all were benign at cytology. The remaining 5 nodules of the 8 inadequate specimens were followed up, and showed no interval changes.

Table 1 shows the cytological and histological diagnoses, according to the nodule size. Of a total 149 nodules in 121 patients, 65 nodules were removed at surgery from 59 patients. Of the 65 operated nodules, 44 (66.7%) carcinomas were found at the final histology, corresponding to 43 papillary carcinomas and 1 medullary carcinoma.

Table 1. Cytological and Histological Diagnoses According to the Nodule Size

Cytology	Total	Operated	Carcinomas
Infracentimetric nodules			
Benign	72	11	1
Suspicious	11	9	6
Malignant	25	25	25
Inadequate	7	2	0
Total	115	47	32
Centimetric of supracentimetric nodules			
Benign	19	3	0
Suspicious	3	3	1
Malignant	11	11	11
Inadequate	1	1	0
Total	34	18	12
All nodules			
Benign	91	14	1
Suspicious	14	12	7
Malignant	36	36	36
Inadequate	8	3	0
Total	149	65	44

Twenty-five of the carcinomas were infracentimetric in size. There were 11 nodules showing a malignant cytology; all were malignant on surgical pathology (Fig. 2). There were 14 nodules with a suspicious cytology; 12 were removed by surgery, of which 7 turned out to be cancerous. There were 91 nodules with a benign cytology; 14 of these were surgically excised, but only one showed malignancy. Two nodules with a suspicious cytology, 77 with a benign cytology and 5 with an inadequate specimen were not surgically removed, however, they showed no change in size and morphology on the follow-up sonography after at least 2 years (Fig. 3).

Table 2 summarizes the diagnostic index of the US-FNAB. There were no significant differences in any of the diagnostic indices for the infracentimetric and the centimetric or supracentimetric nodules ($p > 0.05$, Chi-square test).

DISCUSSION

Thyroid malignancy is well known for its relatively lower invasiveness and benign course compared to other malignancies. Occult thyroid cancer, which cannot be detected on a clinical basis, and is only detectable by US, is not common. However, an occult papillary carcinoma is not always silent, and can be associated with local, or even distant, metastasis.¹⁵⁻¹⁷ Thus, a more careful evaluation is necessary in patients with nonpalpable nodules.

The technical advances in US, and its use to guide FNAB, have allowed the incidental detection of small carcinomas of the thyroid, as small as 2 or 3 mm. To our knowledge, there are only two reports on the clinical role of US-FNAB for non-palpable thyroid nodules: one, a small number of cases of nonpalpable nodules¹¹ and the other dealing with non-palpable nodules larger than 1 cm.¹² Leenhardt, et al.¹³ reported that during an US-FNAB adequate cytological material was obtained in 85% of the centimetric or supracentimetric nodules, and in 69% of the infracentimetric nodules. Therefore, they concluded that only supracentimetric nodules benefit from an US-FNAB.¹⁴ However, our results revealed similar sensitivities, specificities, PPV, NPV and accu-

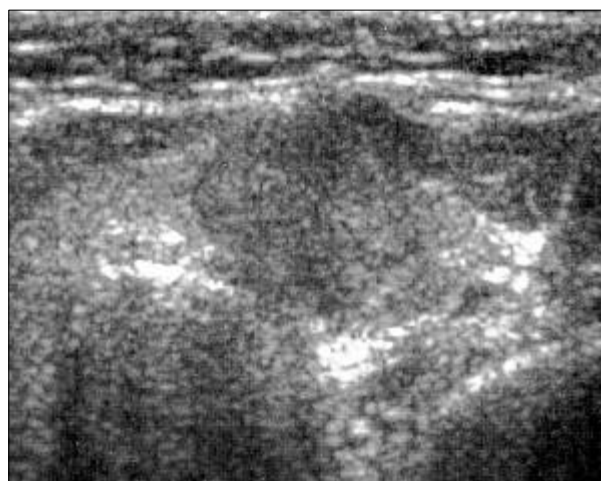


Fig. 2. Papillary carcinoma in a 60-year-old woman. A 13mm sized hypoechoic mass, with an indistinct margin, was noted in the left lobe of the thyroid. The result of FNAB was malignant, and subsequent surgery revealed a papillary carcinoma with extracapsular invasion.

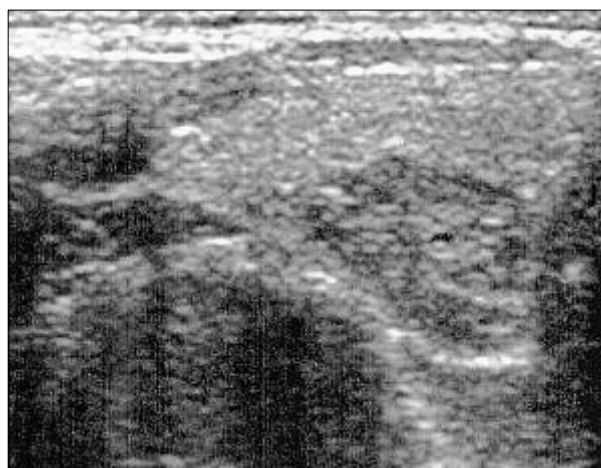


Fig. 3. Adenomatous hyperplasia in a 58-year-old woman. A 15 mm sized hypoechoic mass was noted in the right lobe of the thyroid. The result of FNAB was benign (adenomatous hyperplasia). Follow-up sonography, after 26 months, showed no interval change.

cies for the infracentimetric and the supracentimetric nodules (Table 2), which led us to conclude that an US-FNAB is also beneficial for the infracentimetric nodules. Moreover, the inadequacy rate of an US-FNAB was relatively low. Seven (6.1%) of the infracentimetric and one (2.9%) of the supracentimetric nodules showed inadequate cytological reports. This proportion of inadequate specimens was lower than that previ-

Table 2. Diagnostic Index of US-FNAB According to the Size

	Infracentrimetric	Centrimetric or supracentrimetric
Sensitivity	31/32 (96.9)	12/12 (100)
Specificity	31/36 (86.1)	19/21 (90.5)
PPV	71/76 (93.4)	12/14 (85.7)
NPV	71/72 (98.6)	19/19 (100)
Accuracy	102/108 (94.4)	31/33 (93.9)

^a(), percentage.

^bNodules with inadequate cytological results were excluded, and suspicious cytological results were handled as a malignant diagnosis.

^cAll diagnostic values: $p > 0.05$.

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

ously reported, especially for infracentrimetric nodules, which was about 31%.¹⁴ Our favorable results are certainly due to the accurate targeting of the nodules with the ultrasound guidance. For reducing the frequency of inadequate specimens, accurate targeting and smears are necessary. For this reason, the acquisition and maintenance of aspiration skills are important.

In a series of 132 thyroid nodules having undergone US-FNAB, Cochand-priollet, et al.¹⁸ reported a very high rate of adequate material (96.2%), but the nodules were all palpable. Yokozawa, et al.¹⁹ described a similar US-FNAB technique and reported good results (sensitivity: 94.3%, specificity: 89.7%, accuracy: 93.5%), but the nodule sizes were not reported. Moreover, when they inserted the needle perpendicular to the neck, with US-guidance, the probe was removed, and suction applied by the right hand, without US-guidance. In contrast, with our study, all the needle movements could be continuously visualized, in real time, during the procedure.

Although an US- FNAB is a simple and low-cost procedure, if it is to serve as a reliable guide for treatment, its predictive value for a definitely benign cytology, that is a true negative result, should approach 100%. There was only one false negative specimen in our study. The NPV for the infracentrimetric (98.6%) and the centrimetric or supracentrimetric nodules (100%) were similar, which enhances the benefit of an US-FNAB for infracentrimetric nodules.

Although our report suggests that an US-FNAB is very useful in diagnosing in nonpalpable solid

thyroid nodules, it has several limitations.

First, we considered the nodules, without ultrasonographic changes for a minimum of 36 months, as benign lesions. A thyroid malignancy is usually a slow growing tumor, thus 36 months may have been too short to rule out a malignancy. Kuma, et al.²⁰ showed that most of the untreated palpable thyroid nodules, with a cytologically benign diagnosis, remained benign during a follow-up of 9 to 11 years. Therefore, it may be reasonable to assume that the long-term course of nonpalpable thyroid nodules would be similar if they were left untreated, although there has been no longitudinal study on the long-term course of non-palpable thyroid nodules. In our series, clinical follow-ups were made on 84 nodules. Cytologically, 77 nodules were benign, 2 were suspicious and 5 had inadequate specimens. However, 5 nodules with an inadequate specimen, and 2 with a suspicious cytology, showed benign features on US examination. Therefore, these clinical follow-up results were considered as a benign outcome.

Second, the prevalence rate of 29.5% (44/149) in our study was high. Leenhardt and colleagues reported a prevalence of 4% in all nonpalpable nodules (cystic, mixed and solid), and 16% in solid and hypoechoic nodules.¹⁴ The high rate of malignancy in our study may have been related to the fact that all the nodules were solid, and most had suspicious malignant sonographic findings.⁹

In conclusion, the US-FNAB in our study showed good sensitivity, specificity and accuracy, with a relatively low rate of inadequate speci-

mens, allowing it to be a useful method for determining the treatment plan of non-palpable thyroid nodules, even when less than 1 cm in diameter.

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