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Diagnosis of Occult Thyroid Carcinoma by Ultrasonography

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The increased sensitivity of many imaging devices has increased the identification of asymptomatic nodules in the thyroid gland. In this study we investigated the actual incidence of nonpalpable thyroid nodules and occult carcinoma in women. Between January and June 2003, among the women who were scheduled to undergo breast ultrasonography, 697 without palpable thyroid nodules were screened for thyroid nodules. They were classified into four categories according to ultrasonographic findings: negative, benign, indeterminate and malignant. Ultrasound-guided fine-needle aspiration biopsy (FNAB) was carried out for all malignant lesions and for some of the benign and indeterminate ones. The nodule detection and malignancy rates were determined and the effectiveness of ultrasonography as a diagnostic tool was also investigated. Out of the 697 subjects, 246 (35.3%) were found to have thyroid nodules. The malignancy detection rate based on the FNAB results, including both suspicious and malignant groups, was 3.6% (25/697) for all subjects. In addition, 3.0% (21/697) of all the women were confirmed to have thyroid cancer by surgery. The sensitivity of sonographic classification was increased from 80% to 100% when the indeterminate class was added to the malignant one, although this decreased the specificity from 91.7% to 33.3%. In conclusion, high-resolution ultrasonography detected a high percentage of malignant nodules. Ultrasonography can augment its value by guiding FNAB, in addition to providing diagnostic images.

Key Words: Nonpalpable thyroid nodules, ultrasonography, occult thyroid carcinoma

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INTRODUCTION

Thyroid carcinoma accounts for 4.2% of all newly diagnosed malignant disease in Korea. It also accounts for 8.3% of all cancers among women in Korea, according to the annual report of the Korea Central Cancer Registry in 2001. Recent studies have shown that the incidence rate of thyroid cancer is steadily increasing in several countries, including the United States, Canada, Sweden, Norway, and Britain.[1-6]

The increased sensitivity of many imaging devices has increased the identification of asymptomatic nodules in the thyroid gland. Thyroid incidentaloma can be discovered in several ways. Autopsy and surgical data suggest that less than 5% of nodules, whether palpable or nonpalpable, are malignant.[7,8] Ultrasonographic data also presented similar data.[9-11]

In this study we investigated the actual incidence of nonpalpable thyroid nodules and occult carcinoma in women revealed by ultrasound. The effectiveness of ultrasound as a diagnostic tool and its special use for fine-needle aspiration biopsy (FNAB) are also evaluated.

MATERIALS AND METHODS

Between January and June 2003, 697 women who were scheduled to undergo either breast cancer screening or a follow-up examination for breast cancer (48), and who had no palpable thyroid nodules were screened for thyroid cancer. They included 13 patients with newly diagnosed breast cancer. The palpation and ultrasonographic

examinations were performed by one surgeon with an HDI 5000 scanner, using electronically focused near-field probes of 12-5MHz bandwidth, following the completion of a breast ultrasound examination. Patients were classified into four different categories according to the ultrasonographic findings: negative, benign, indeterminate, and malignant. Malignant sonographic features were defined as hypoechogenicity relative to the adjacent normal tissue, poorly defined margins, internal microcalcification, irregular shapes, and large height to width ratio. Benign sonographic characteristics were defined as mixed or hyperechogenicity, significant cystic component, egg-shell-like calcification, sonolucent rim around a nodule, and well-defined margins. If at least one malignant characteristic was identified, the nodule was classified as malignant category. The benign category was defined if the nodule had only benign characteristics. The indeterminate category consisted of borderline sonographic features, which made the classification difficult; for example, in the case of excessively small sized nodules. Ultrasound-guided FNAB was carried out for all malignant lesions, and for some benign and indeterminate lesions, at the patient's request. The FNAB results were divided into four different groups: benign, suspicious, malignant, and insufficient. Patients in the suspicious and malignant groups were advised to undergo surgical treatment, those in the benign group to maintain close observation, and those in the insufficient group to complete short-term follow-up. The nodule detection and malignancy rates were determined, as was the effectiveness of ultrasonography as a diagnostic tool. The clinical and pathological characteristics of those who underwent surgical treatment were also analyzed. The association between age group and frequency of thyroid nodules was assessed using Chi-square test. The significance was determined using linear-by-linear association. A p value of < 0.05 was considered significant. Unless otherwise specified, data are presented as mean ± SD. Data analysis was done using the Statistical Package for the Social Sciences (SPSS Inc, Chicago, Chicago, Ill, USA).

RESULTS

Out of the 697 subjects, 246 (35.3%) were found to have thyroid nodules based on the ultrasound examination. Following division of the women into 10-year age intervals, the nodules were more frequently found in older women (p=0.000) (Table 1). Ultrasound-guided FNAB was conducted in 42 patients, in whom 24 had malignant lesions, 14 indeterminate lesions, and 4 benign lesions, according to the ultrasonographic features. Twenty-five patients (3.6%) were preliminarily diagnosed with malignancy from FNAB results, including 5 suspicious and 20 malignant lesions. Diagnosis was uncertain in 5 cases (11.9%) after FNAB. Four patients refused surgery, and the remaining 21 underwent surgery and were confirmed to have papillary thyroid carcinoma (Fig. 1). The malig-

Table 1. Frequency of Thyroid Nodules and Carcinomas According to Age Group

Age group	Nodules (%)	p value	Carcinoma (%)	p value
10-19	0/3(0)		0/3(0)	
20-29	22/87(25.3)		6/87(6.9)	
30-39	59/200(29.5)		6/200(3)	
40-49	90/248(36.3)	0.000*	4/248(1.6)	0.870*
50-59	55/126(43.7)		6/126(4.8)	
60-69	20/33(60.6)		3/33(9.1)	
Total	246/697(35.3)		25/697(3.6)	

*chi-square test: linear-by-linear association.

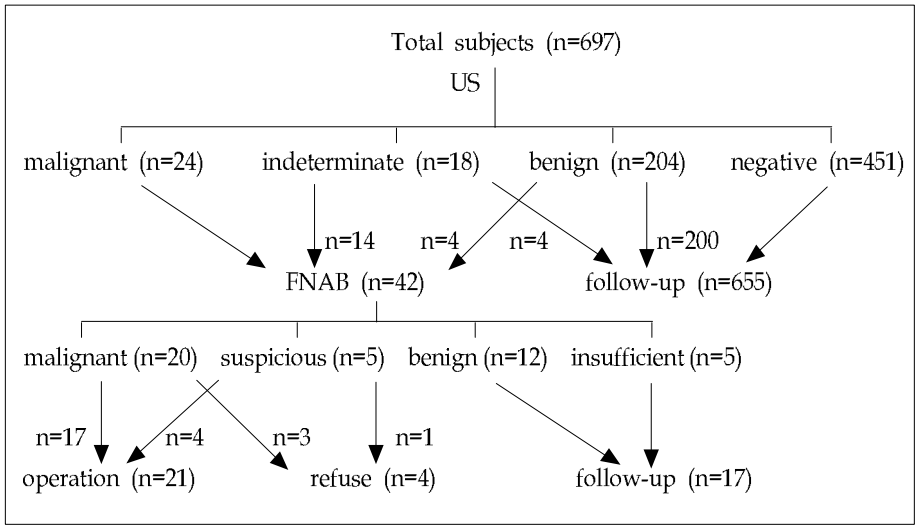

Fig. 1. Flow chart of study design. (US, ultrasonography; FNAB, fine needle aspiration biopsy; n= number of patients)

nancy detection rate based on the FNAB results including both the suspicious and malignant groups, was 3.6% (25/697). In addition, 3.0% (21/697) of all patients were diagnosed with thyroid cancer after surgery. The malignancy detection rate in the patients with a diagnosis of breast cancer was 3.3% (2/61), which demonstrated no statistical difference compared with the 3.6% (23/636) of the patients with no diagnosis of breast cancer ($p>0.05$).

A unilateral lobectomy was performed in 11 patients (52.4%) and total thyroidectomy in 10 (47.6%). A central compartment neck dissection was performed in all cases and 7 (33.3%) had nodal involvement. The mean tumor size was 0.8 cm (0.3-1.8 cm) and 15 cases were confined to microcarcinoma. Extrathyroidal extension was seen in 9 cases (42.9%) and bilaterality was noted in 3 (14.3%) (Table 2).

The sensitivity of sonographic classification was increased from 80% to 100% when the indeterminate class was added to the malignant one. However, this decreased the specificity from 91.7% to 33.3%. The positive predictive value of malignant and indeterminate sonographic features was 83.8% and 38.5%, respectively (Table 3).

Table 2. Demographic Characteristics (n=21)

Age (range) (years)	42.7 (25-64)
Tumor size (range) (cm)	0.8 (0.3-1.8)
Histology	
papillary carcinoma	21 (100%)
Multifocality	4 (19%)
Bilaterality	3 (14.3%)
Extrathyroidal extension	9 (42.9%)
LN metastasis (central)	7 (33.3%)
Operation	
Lobectomy	11 (52.3%)
Total	10 (47.6%)

DISCUSSION

Thyroid nodules are common in the general population, but the prevalence of nodular thyroid disease depends on the degree of scrutiny and the population studied. The diagnostic methods to determine the prevalence of thyroid nodules are palpation, autopsy studies, and ultrasonographic studies.[7-11] The most recent prevalence data from ultrasonographic studies have reported a prevalence ranging from 19% to 46% in the general population.[12,13] The high prevalence of 35.3% reported in our study falls within this range. As expected, the thyroid nodules were more frequently found among older women (p=0.000).

The management of thyroid incidentaloma is influenced by the data on the risk of malignancy. Autopsy and surgical data suggest that less than 5% of nodules, whether palpable or nonpalpable,

Table 3. FNAB Results According to Ultrasonographic (US) Classification

US classifications	FNAB classifications				
	Benign	Suspicious	Malignant	Insufficient	Total
Benign	4	0	0	1	5
Indeterminate	7	2	3	1	13
Malignant	1	3	17	3	24
Total	12	5	20	5	42

US sensitivity: 80% (for malignant only), 100% (for both indeterminate and malignant).
US specificity: 33.3% (for benign only), 91.7% (for both indeterminate and benign).
Positive predictive value (PPV) for malignant: 83.3%, PPV for indeterminate: 38.5%.

are malignant.[7,8] Our result showed that 10.6% of nonpalpable thyroid nodules were malignant. It is likely that the actual malignancy rate would increase if the false negative cases of ultrasound, in which FNAB was not preformed, were considered, along with those in which FNAB results were insufficient.

The relatively stable prevalence of occult carcinoma throughout life is documented in autopsy series.[14] Our data also indicated that young age is not a predictive factor for a benign lesion (p= 0.087).

Many reports have discussed sonographic findings of thyroid nodules with overlapping characteristics in benign and malignant lesions.[15,16] Recently, Kim, et al. suggested a new sonographic criteria for malignant, nonpalpable thyroid nodules, which includes tiny and punctuate microcalcifications, large height to width ratio, irregular or microlobulated margins, and marked hypoechogenicity.[17] We also used exclusion criteria for benign sonographic characteristics: namely, mixed or hyperechogenicity, significant cystic component, a sonolucent rim around a nodule or well-defined margin. Our result showed a sensitivity of 100% when the indeterminate class was added to the malignant class; however, this decreased the specificity from 91.7% to 33.3%. This result confirms the importance of performing FNAB in cases of indeterminate class. The positive predictive value of the indeterminate class was 38.5%. In addition, the ultrasonographic guide is essential for performing FNAB for nonpalpable nodules as has been discussed in many studies.[10,11,18]

The term occult thyroid carcinoma has been used to describe thyroid carcinoma when the primary tumor is less than 1.5 cm in diameter. In our data, all malignant cases, except one which was 1.8 cm in pathologic size but 1.3 cm in sonographic measurement, were occult carcinomas, for which the optimal management strategy has not been clearly defined. In their report on the mortality associated with thyroid carcinoma, Wang and Crapo concluded that the mortality rate from thyroid cancer was low, despite the fact that the prevalence of occult thyroid cancer was high.[19] In addition, many reports recommended observation for nonpalpable thyroid nodules less than 1.5 cm.[12,20] In our study, 9 cases (42.9%) showed extrathyroidal extension, while the mean tumor size was 0.8 cm. These results were similar to those of Chung's report in which the AMES (Age-Metastasis-Extent-Size) and MACIS (Metastasis-Age-Completeness of resection-Invasion-Size) scores were not different between small cancers and clinically detectable cancers.[21] Many studies have reported the recurrence, metastasis, and mortality associated with small thyroid carcinoma.[22-25] However, none could identify the subsets of occult carcinoma with a potential for aggressive clinical course.[26]

In conclusion, high-resolution ultrasonography detected a high percentage of malignant nodules. Ultrasonography can augment its value in the diagnosis of occult thyroid cancer by guiding FNAB, in addition to providing diagnostic images.

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