

Usefulness of Ultrasonography in the Management of Nodular Thyroid Disease

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Background: Fine-needle aspiration biopsy is the standard diagnostic test for evaluating possible malignancy in a thyroid nodule.

Objective: To evaluate the role of routine ultrasonography in the management of nodular thyroid disease.

Design: Retrospective chart review.

Setting: Multidisciplinary thyroid nodule clinic (endocrinology and radiology).

Patients: Patients with suspected nodular thyroid disease or suspected recurrent thyroid cancer referred between October 1995 and March 1997. All patients had thyroid ultrasonography and ultrasonography-guided fine-needle aspiration biopsy of nodules at least 1 cm in maximum diameter.

Measurements: Medical records, ultrasonography findings, cytology reports, and histologic reports were reviewed. Ultrasonog-

raphy findings were compared with the referring physician's findings on physical examination.

Results: 223 patients were seen in the clinic. A total of 209 fine-needle aspiration biopsies were performed on 156 patients. Among 50 of 114 patients referred for a solitary nodule, ultrasonography detected additional nonpalpable nodules at least 1 cm in diameter in 27 and determined that no nodules required aspiration in 23. Of 59 patients referred for a diffuse goiter or a multinodular gland, ultrasonography detected discrete nodules at least 1 cm in diameter that required aspiration in 39 and determined that aspiration was unnecessary in 20.

Conclusions: Ultrasonography altered the clinical management for 63% of the patients (109 of 173) referred to the thyroid nodule clinic after abnormal results on thyroid physical examination.

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Thyroid nodules are a common diagnostic challenge encountered in clinical medicine. Approximately 4% to 7% of adults have palpable thyroid nodules, and up to 70% have thyroid nodules visible on ultrasonography, many of which are less than 1 cm in diameter (1–5). Fine-needle aspiration biopsy is the standard diagnostic test for evaluating a palpable thyroid nodule in euthyroid patients.

Previous studies have shown that the diagnostic accuracy of fine-needle aspiration biopsy is improved with ultrasonography guidance compared with palpation alone (6–9). In addition, ultrasonography guidance is required for aspiration of nonpalpable thyroid nodules (10–12). The objective of our study was to determine whether the routine use of ultrasonography in all patients with suspected thyroid nodules changed clinical management compared with palpation alone.

METHODS

Patients

The study sample consisted of all patients referred to the Brigham and Women's Hospital dual-discipline (endocrinology and radiology) Thyroid Nodule Clinic (Boston,

Massachusetts) for suspected nodular thyroid disease or suspected recurrent thyroid cancer between October 1995 and March 1997. Clinicians were instructed to refer patients with suspected or diagnosed nodular thyroid disease and a normal serum thyrotropin level to the Thyroid Nodule Clinic. If patients had a suppressed thyrotropin level and were not taking thyroid hormone, a radionuclide scan was suggested. The clinic visit included thyroid ultrasonography performed by a radiologist, an evaluation by an endocrinologist, and ultrasonography-guided fine-needle aspiration biopsy of all nodules measuring at least 1 cm in maximum diameter (up to a maximum of four nodules). A cutoff of 1 cm was selected on the basis of recommendations in the literature (13). For patients seen more than once, only the initial visit was analyzed.

Measurements

Medical records were reviewed for the specialty of the referring clinician, the referring clinician's examination of the thyroid before referral, and the indication for referral. Sonography was performed by using 5- to 10-MHz transducers. Nodules were measured in three dimensions. Fine-

needle aspiration was performed with a 25-gauge needle. Ultrasonography guidance was used to confirm placement of the needle in the nodule or to direct sampling into solid portions of partially cystic nodules. Four to six passes were made per nodule. The needles were rinsed and pooled in a single vial containing CytoLyt solution (CytoLyt Corp., Boxborough, Massachusetts).

Two ThinPrep slides (Cytoc Corp., Marlborough, Massachusetts) were stained by using a modified Papanicolaou method and were read by a cytopathologist at the Brigham and Women's Hospital as benign, atypical, suspicious for a follicular or Hürthle cell neoplasm, suspicious or positive for papillary cancer, or nondiagnostic. Aspirates were considered nondiagnostic if they contained fewer than six groups of benign follicular cells. The atypical category was applied to cases in which a mild degree of cellular or architectural atypia precluded a benign diagnosis but was insufficient for a suspicious or positive diagnosis. Cytology reports were reviewed for all patients who had fine-needle aspiration biopsy, and histologic reports were reviewed for all patients who had surgery.

Two endocrinologists reviewed the charts to compare the referring physician's findings on thyroid physical examination with the ultrasonography findings. If a discrepancy existed between the referring physician's clinical thyroid examination and the number of nodules requiring fine-needle aspiration biopsy based on ultrasonography (≥ 1 cm), ultrasonography was considered to have altered the clinical management.

Role of the Funding Sources

The funding sources had no role in the collection, analysis, and interpretation of the data or in the decision to submit the paper for publication.

RESULTS

Characteristics of the Study Group

A total of 223 patients (203 women and 20 men [mean age, 46.3 ± 15.3 years]) were evaluated at the Thyroid Nodule Clinic between October 1995 and March 1997. Sixty-one percent were referred by primary care physicians, 37% were referred by endocrinologists, and 2% were referred by surgeons. The indication for referral was abnormal findings on thyroid physical examination in 173 of 223 patients (78%); 114 were referred for a suspected solitary nodule, 33 were referred for diffuse or asymmetric

Table 1. Indication for Referral to the Thyroid Nodule Clinic in 223 Patients

Indication	Patients, n (%)
Abnormal results on physical examination	173 (78)
Solitary nodule	114 (51)
Diffuse or asymmetric goiter	33 (15)
Multinodular goiter	26 (12)
Other	
Follow-up for a benign nodule	23 (10)
Incidental radiologic finding of a thyroid nodule	10 (4)
Follow-up for thyroid cancer	7 (3)
Nondiagnostic palpation-guided fine-needle aspiration	6 (3)
Previous exposure to radiation	2 (1)
Unknown	2 (1)

goiter, and 26 were referred for multinodular goiter (Table 1). Ultrasonography-guided fine-needle aspiration biopsy was performed on 209 nodules in 156 patients. Sixty-seven patients had no aspirations, 112 had one aspiration, and 44 had two or more aspirations.

Sonographic Findings

Ultrasonography revealed solitary nodules in 33% of patients, a multinodular goiter (>1 nodule on ultrasonography) in 50%, and no nodules in 17% (excluding those with a history of thyroid cancer). Ultrasonography findings in the 173 patients referred for abnormal findings on thyroid physical examination are given in Table 2.

Management of Nodular Thyroid Disease

Ultrasonography changed management in 44% (50 of 114) of the patients referred for a solitary nodule on physical examination. In 27 patients, an additional nonpalpable nodule at least 1 cm in diameter was found on ultrasonography and more than one nodule required aspiration. Eighteen patients had no nodules, and 5 patients had only small nodules (<1 cm); therefore, despite the results of the physical examination, no aspiration was required. For the remaining 64 patients referred for a solitary nodule (46 with a solitary nodule ≥ 1 cm and 18 with multiple nodules but only one nodule ≥ 1 cm), clinical management was not affected because the palpated nodule was the only nodule that was at least 1 cm in diameter on ultrasonography.

Among the 33 patients referred for a diffuse or asymmetric goiter, 55% (18 of 33) had one or more nodules at least 1 cm in diameter on ultrasonography, which suggests that the examining physician recognized an abnormality

but could not detect a discrete nodule. Among the 26 patients referred for a multinodular goiter, 5 did not require an aspiration based on the ultrasonography findings and 21 required one or more aspirations for discrete nodules at least 1 cm in diameter. In summary, ultrasonography altered clinical management in 109 of the 173 patients (63%) referred for abnormal findings on physical examination. It was needed for guidance of nonpalpable nodules that were at least 1 cm in diameter in 66 patients (27 referred for a solitary nodule with additional nodules \geq 1 cm on ultrasonography, 21 referred for a multinodular goiter, and 18 referred for a diffuse or asymmetric goiter with discrete nodules \geq 1 cm on ultrasonography) and documented no nodules that were at least 1 cm in diameter in 43 patients.

In the 48 patients referred for other indications, ultrasonography helped 1) evaluate growth in patients with previous benign cytologic findings, 2) direct sampling of lymph nodes in patients with thyroid cancer, 3) direct sampling of nonpalpable nodules found incidentally on other radiology studies, and 4) screen for nodules in patients with previous exposure to radiation.

Cytologic Findings after Fine-Needle Aspiration

In the 153 patients with no history of thyroid cancer who had fine-needle aspiration, 130 of the 205 nodules aspirated (63%) were benign. Seven nodules (3%), all confirmed histologically, were positive for papillary cancer. Nine (4%) were suspicious for papillary cancer. Five of these (56%) were histologically confirmed as papillary cancer, and 2 were benign. One patient with 2 suspicious nodules sought a second opinion and was lost to follow-up. Seventeen nodules (8%) were suspicious for follicular or

Hürthle cell neoplasm, of which 9 were excised; 1 was a follicular carcinoma and the others were benign. Nine nodules (4%) were characterized as atypical. Of these, 2 were found to be benign after surgery. Thirty-three nodules (16%), of which 13 were more than 50% cystic, had nondiagnostic cytologic characteristics. In 1 patient, surgery for papillary carcinoma in 1 nodule revealed papillary carcinoma in a second nodule whose cytologic characteristics were nondiagnostic.

The occurrence of malignancy was similar in patients with solitary nodules and those with multiple nodules. Cancer was found in 4 of 60 patients with solitary nodules (6.7%) and 8 of 90 patients with multiple nodules (8.9%). In 4 of the 12 patients who received a diagnosis of thyroid cancer, the malignant nodule was not palpated by the referring physician. One patient was referred for a solitary palpable nodule, which was benign, but a nonpalpable malignant nodule in the contralateral lobe was detected on ultrasonography. In another patient, who was referred for follow-up of a benign nodule, a second nonpalpable nodule was found to be malignant. The malignant nodule was also nonpalpable in the other 2 patients who had either a multinodular or diffuse goiter on the referring clinician’s examination. Fine-needle aspiration biopsies of 4 nonpalpable lymph nodes in the 3 patients with a history of thyroid cancer were all positive for recurrent papillary cancer.

DISCUSSION

We routinely use ultrasonography and ultrasonography-guided fine-needle aspiration in patients referred to our Thyroid Nodule Clinic for suspected thyroid nodules. Almost half of the patients referred for a solitary nodule on

Table 2. Sonographic Findings in 173 Patients Referred to the Thyroid Nodule Clinic for Abnormal Results on Physical Examination

Results of Physical Examination	Patients with a Solitary Nodule on Ultrasonography		Patients with Multiple Nodules on Ultrasonography			Patients with No Nodules on Ultrasonography	Total Patients
	\geq 1 cm	<1 cm	At Least 2 Nodules \geq 1 cm	1 Nodule \geq 1 cm	0 Nodules \geq 1 cm		
	n (%)						
Solitary nodule	46 (40)	2 (2)	27 (24)	18 (16)	3 (3)	18 (16)	114 (100)
Diffuse or asymmetric goiter	7 (21)	2 (6)	6 (18)	5 (15)	4 (12)	9 (27)	33 (100)
Multinodular goiter	2 (8)	0	14 (54)	5 (19)	2 (8)	3 (12)	26 (100)
Total	55 (100)	4 (100)	47 (100)	28 (100)	9 (100)	30 (100)*	173 (100)

* Nineteen patients with no nodules had a heterogeneous echotexture on ultrasonography.

physical examination (a group previously not thought to benefit from ultrasonography) were found to have multiple nodules, and many (27 of 48) required additional aspiration of a nonpalpable nodule. More than 50% of patients (18 of 33) with suspected diffuse or asymmetric goiter had discrete nodules requiring fine-needle aspiration. In addition, 25% of patients (43 of 173) had no nodules greater than or equal to 1 cm on ultrasonography despite abnormal findings on physical examination. The occurrence of malignancy was similar in patients with solitary and multiple nodules.

Our study confirms previous findings that nonpalpable nodules are often at least 1 cm in diameter (14, 15). Previous studies have also suggested that fine-needle aspiration biopsy has better diagnostic accuracy and lower false-negative rates when guided by ultrasonography than when guided by palpation (6–12). However, published recommendations for the use of ultrasonography guidance have been limited to patients with nonpalpable nodules found incidentally on radiology studies, those with nodules that are difficult to palpate, and those with previous nondiagnostic results on cytology. Our results suggest that it is difficult to predict which patients will benefit from ultrasonography on the basis of the physical examination.

A recent study reported that risk for thyroid cancer is lower in patients with multiple nodules than in those with solitary nodules; however, nodularity was defined only by palpation (16). Our findings agree with those of other reports, which state that the prevalence of cancer in thyroid nodules is independent of the number of nodules (17–20). In 4 of the 12 patients with thyroid cancer, the malignant nodules were not palpated by the referring physician and therefore would not have been detected at the time of referral without ultrasonography. It is uncertain whether the long-term outcome of the affected patients would have changed if the malignancy was detected at a later time. Since the prognosis of thyroid cancer is partially dependent on its size at surgery, earlier detection is probably beneficial.

In summary, at our thyroid nodule clinic, endocrinology and sonographic consultation and, if needed, ultrasonography-guided fine-needle aspiration biopsy provided an accurate assessment of patients with suspected nodular thyroid disease at a single visit. Ultrasonography detected clinically significant nodules that were not found on physical examination. Our results suggest that routine thyroid ultrasonography should be seriously considered for all patients with suspected thyroid nodules.

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"Besides," growled Tock, who decided that he didn't much like Dr. Dischord, "there is no such illness as lack of noise."

"Of course not," replied the doctor, pouring himself a small glass of the liquid; "that's what makes it so difficult to cure. I only treat illnesses that don't exist: that way, if I can't cure them, there's no harm done—just one of the precautions of the trade," he concluded, and, seeing that no one was about to take his medicine, he again reached toward the shelf, removed a dark-amber bottle, dusted it carefully, and placed it on the table in front of him.

Norton Juster
The Phantom Tollbooth
New York: Random House; 1988:138

Submitted by:
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