

The Investigation and Management of Thyroid Nodules-A Retrospective Review of 183 Cases

W Y Chiu,*^{MBBS, FRCS, FCSHK}, N H Chia,*^{MBBS, FRCS, FCSHK}, S K Wan,**^{MBBS, FRCPA, FHKAM},
C H Yuen,*^{MBBS, FRCS, FCSHK}, M T Cheung,***^{MBBS, FRCS, FHKAM}

Abstract

The management of the patient with a thyroid nodule remains a clinical challenge because of its risk of malignancy. This is a retrospective audit of 183 patients undergoing thyroidectomy for thyroid nodules at the Queen Elizabeth Hospital, Hong Kong, in 1994. The history, physical examination and investigations done were charted and analysed against the final histopathology of the specimens. Age, sex, symptom duration and nodularity were not associated with malignancy statistically, whereas a nodule hard in consistency was shown to be associated with malignancy ($P < 0.05$). The sensitivity and specificity of ultrasonography, radionuclide scan and fine-needle aspiration cytology (FNAC) were 71% and 57%, 50% and 43%, and 93% and 60%, respectively. Hence, history and physical examination are unreliable for detecting malignant thyroid nodules and FNAC is mandatory. FNAC is superior to ultrasonography or radionuclide scan for evaluating thyroid nodules and should be used as the initial investigation.

Ann Acad Med Singapore 1998; 27:196-9

Key words: Fine-needle aspiration cytology, Radionuclide scan, Thyroid nodule, Ultrasonography

Introduction

Thyroid nodule is a common problem in surgical practice. In 1994, more than 350 thyroid operations were performed in our department, of which 183 were for thyroid nodules. Conventional preoperative assessment of a patient with a thyroid nodule, including history and physical examination, radionuclide scan and ultrasonography, has been shown to be relatively non-specific for diagnosing thyroid cancer.¹

In the last decade, with the introduction of fine-needle aspiration cytology (FNAC), the investigation and surgical treatment have changed dramatically. This study is a retrospective audit of thyroidectomies done for thyroid nodules in our hospital in 1994. The aims of the study were to detect if there is any association between malignancy, history and physical findings, as well as evaluating the usefulness of FNAC, ultrasonography and radionuclide scan for detecting thyroid malignancy.

Materials and Methods

The study population consisted of all patients undergoing thyroidectomy for thyroid nodules at the Queen Elizabeth Hospital, Hong Kong in 1994. A total of 183

patients were identified and their medical records were evaluated retrospectively.

The following parameters were recorded: age, sex, symptom duration and presenting symptoms, if any including mass, dyspnoea, hoarseness and hyperthyroid symptoms. Physical findings including the number and consistency of the nodule and cervical lymphadenopathy were noted for each patient.

Charts were also reviewed for the following diagnostic studies: ultrasonography, radionuclide scan and FNAC.

The age and sex of the patients, symptom duration, nodularity and consistency of the nodules of the malignant and benign disease groups were tested for any difference statistically. Student t-test was used for parametric data and chi-square test was used for non-parametric data. $P < 0.05$ was regarded as statistically significant.

The results of FNAC were compared to the histological diagnoses of the final specimens. Each FNAC was then classified as being either true-positive, true-negative, false-positive or false-negative for malignancy. If the FNAC diagnosis was "follicular lesion, indetermi-

* Medical Officer

*** Consultant

Department of Surgery

** Senior Medical Officer

Department of Pathology

Queen Elizabeth Hospital, Hong Kong

Address for Reprints: Dr W Y Chiu, Department of Surgery, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong.

nate" (where differentiation between colloid nodules and follicular neoplasm cannot be made with confidence), "neoplasm", "suspicious of malignancy" or "malignancy", it was regarded as true-positive if the final histopathology was malignancy. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of FNAC for detecting malignancy were then determined.

Similarly, ultrasonographic and radionuclide scan diagnoses were compared to the final histopathology in order to determine the above values. Ultrasonographic finding of a solid nodule or a cold nodule on radionuclide scan was regarded as positive test result for malignancy for each modality of imaging.

Results

A total of 183 patients underwent thyroidectomy for thyroid nodules at the Queen Elizabeth Hospital, Hong Kong in 1994. The age of patients ranged from 16 to 86 years, with a median of 44.9 years. One hundred and forty-two were female and 41 were male patients (F:M = 3.5:1).

Most (164 or 90%) patients presented with a neck mass, the rest were: 5 (3%) with cervical lymph nodes, 3 (2%) with hyperthyroidism symptoms, 1 (1%) with dyspnoea, and 8 (4%) asymptomatic.

On physical examination, the majority of the patients had a solitary firm nodule. One hundred and forty-three

(78%) had a single nodule, 20 (11%) was multinodular, 6 (3%) was diffusely enlarged whereas 14 (8%) had no mass palpable. Of the palpable thyroid nodules, 91 (56%) felt firm, 39 (24%) soft and 33 (20%) hard. Age, sex, symptom duration and nodularity were not associated with malignancy statistically (Table I). Only a hard consistency was found to be associated with malignancy statistically ($P < 0.05$).

All patients had FNAC done before surgery whereas ultrasonography and radionuclide scan were employed much less often: 44 (24%) and 30 (16%), respectively. The most common ultrasonographic finding was a solitary solid nodule (48%). When the ultrasonographic findings were compared to final histological diagnoses, 5 of the malignant lesions appeared as solitary solid nodules and were regarded as true-positive (Table II). One malignancy occurred in an ultrasonographic cyst and it turned out to be a large colloid nodule coexisting with a small focus of papillary microcarcinoma adjacent to it. Another malignancy occurred in a multinodular goitre. Both were regarded as false-negative. The sensitivity and specificity of ultrasonography were 71% and 57%, respectively. The overall accuracy was 59%.

The majority of the radionuclide scans showed cold nodules (57%). The radionuclide scan findings were compared to the final histological diagnoses (Table III). Only 1 out of the 17 cold nodules turned out to be malignant and was regarded as true-positive. One false-negative was a case of Graves' disease on radionuclide scan but found to be papillary carcinoma on histology. Overall, radionuclide scan gave sensitivity, specificity and accuracy of 50%, 43% and 43%, respectively.

One hundred and thirty-one patients had one FNAC done, 43 had two and 9 had three done preoperatively. Definitive FNAC diagnoses were made in 26/52 (50%) and 6/9 (67%) of the second and third repeat aspirates respectively. A total of 177 (97%) patients had definitive FNAC diagnoses made preoperatively.

A comparison of the cytological diagnoses and the histological diagnoses is listed in Table IV. The only two false-negative cases of FNAC were the two incidentally

TABLE I: A COMPARISON OF AGE, SEX, SYMPTOM DURATION, NODULARITY AND CONSISTENCY OF 183 PATIENTS WITH THYROID NODULES

	Thyroid nodules		
	Malignant (n = 36)	Benign (n = 147)	Statistical significance
Median age (year)	49.8	45.3	NS
Sex (F:M)	28:8	114:33	NS
Median symptom duration (months)	24.6	29.8	NS
Nodularity (solitary:others)	26:10	117:29	NS
Consistency (hard:others)	18:22	15:108	$P < 0.05$

NS indicates not significant

TABLE II: A COMPARISON OF ULTRASONOGRAPHIC DIAGNOSES AND HISTOLOGICAL DIAGNOSES IN 44 PATIENTS WITH ULTRASONOGRAPHY OF THE THYROID GLAND DONE

Ultrasonographic diagnoses	Histological diagnoses			
	Inflammatory	Colloid nodule	Adenoma	Malignancy
Cyst	1	6	2	1
Solitary solid nodule	0	11	5	5
Multinodular goitre	0	10	1	1*
Diffuse	0	1	0	0
Total	1 (2%)	28 (64%)	8 (18%)	7 (16%)
				44 (100%)

*incidental papillary thyroid carcinoma (microcarcinoma)

TABLE III: A COMPARISON OF RADIONUCLIDE SCAN DIAGNOSES AND HISTOLOGICAL DIAGNOSES IN 30 PATIENTS WITH RADIONUCLIDE SCAN OF THE THYROID GLAND DONE

Radionuclide scan diagnoses	Histological diagnoses				Total
	Inflammatory	Colloid nodule	Adenoma	Malignancy	
Cold nodule	1	11	4	1	17 (57%)
Warm nodule	0	0	1	0	1 (3%)
Hot nodule	0	3	0	0	3 (10%)
Multinodular goitre	0	8	0	0	8 (27%)
Graves' disease	0	0	0	1	1 (3%)
Total	1 (3%)	22 (73%)	5 (17%)	2 (7%)	30 (100%)

TABLE IV: A COMPARISON OF FNAC DIAGNOSES AND HISTOLOGICAL DIAGNOSES IN 183 PATIENTS

FNAC diagnoses	Histological diagnoses				Total
	Inflammatory	Colloid nodule	Adenoma	Malignancy	
Inadequate	0	6	0	0	6 (3%)
Inflammatory	1	1	0	0	2 (1%)
Colloid nodule	1	84	2	2*	89 (49%)
Follicular lesion, indeterminate	0	30	24	6	60 (33%)
Neoplasm	0	2	4	6	12 (7%)
Suspicious of malignancy	0	0	0	4	4 (2%)
Malignant	0	0	0	10	10 (5%)
Total	2 (1%)	123 (67%)	30 (16%)	28 (15%)	183 (100%)

*2 incidental papillary thyroid carcinomas (microcarcinomas) occurring next to large colloid nodules

FNAC: fine-needle aspiration cytology

detected microcarcinomas found adjacent to colloid nodules in the resected specimens. No false-positive for malignancy was noted if the FNAC diagnosis of "suspicious of malignancy" or "malignancy" was regarded as positive test. FNAC had sensitivity, specificity and accuracy of 93%, 60% and 65%, respectively.

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ultrasonography, radionuclide scan and FNAC were calculated (Table V).

Discussion

Although most thyroid nodules are benign, a significant proportion of them are malignant, approaching 15% in our series. The diagnosis of these malignant nodules remains a challenge for clinicians. History and physical examination are notoriously unreliable in distinguishing malignant from benign lesions.¹ Contrary to textbook descriptions, age, sex, symptom duration and nodularity were not associated with malignancy statistically, except the physical finding of a hard nodule ($P < 0.05$).

A test for thyroid malignancy must have a high negative predictive value. It must, however, also be specific enough so that not too many benign cases are subjected to unnecessary surgery.

TABLE V: A COMPARISON OF ULTRASONOGRAPHY, RADIONUCLIDE SCAN AND FNAC FOR DIAGNOSING MALIGNANCY IN THYROID NODULES

	Ultrasonography (n = 44)	Radionuclide scan (n = 30)	FNAC (n = 183)
True-positive (TP)	5	1	26
True-negative (TN)	21	12	89
False-positive (FP)	16	16	60
False-negative (FN)	2	1	2
Sensitivity	71%	50%	93%
Specificity	57%	43%	60%
Positive predictive value	24%	6%	30%
Negative predictive value	91%	92%	98%
Accuracy	59%	43%	65%

FNAC: fine-needle aspiration cytology

It has been claimed that ultrasonography can give a sensitivity of 74% and a specificity of 83% in diagnosing malignancy, and that malignant lesions tend to be solid and hypoechoic without a halo.² In our series using ultrasonographic finding of solid nodules as a criterion for diagnosing malignancy, ultrasonography gave a sensitivity of 71% and a specificity of 57% only. The negative predictive value was high (91%) but it was not specific enough. The 5 malignant lesions diagnosed by ultrasonography were, however, all picked up by FNAC already: 2 as malignancy, 1 follicular neoplasm and 2

follicular lesions. Two false-negative malignant lesions occurred. The ultrasonographic finding of the first lesion was multinodular goitre, but the FNAC finding was follicular lesion and the resected specimen turned out to be follicular carcinoma (minimal invasive type). The other case was a cyst on ultrasonography, colloid nodule on FNAC, but found to be a large colloid nodule next to a small focus of papillary microcarcinoma on histology. Ultrasonography therefore missed 2 out of 7 malignant lesions and offered no additional information to FNAC.

Although 10% to 20% of the cold nodules in radionuclide scans are malignant and the reported sensitivity was as high as 100%, it was disappointingly non-specific, with specificity as low as 3.6%.^{3,4} The sensitivity and specificity in our series were 50% and 43% respectively. Only 1 of the 17 cold nodules (6%) turned out to be a papillary carcinoma. This patient presented with a cervical lymph node and FNAC was already highly suspicious of malignancy. The false-negative case had a radionuclide scan showing Graves' disease. This patient too presented with a cervical lymph node with FNAC showing metastatic papillary carcinoma. Both malignant lesions had been picked up by FNAC, and radionuclide scan again offered no additional information to FNAC. The number of malignant cases in this group, however, was too small to be representative and must be interpreted with caution.

Because of its simplicity, low morbidity and low cost, FNAC has virtually replaced ultrasonography and radionuclide scan as our primary diagnostic tool in the evaluation of the euthyroid patient with a thyroid nodule. The reported sensitivity and specificity of FNAC for thyroid malignancy ranged from 85% to 94% and 75% to 85%, respectively.^{2,5} In our series, sensitivity, specificity and negative predictive value of FNAC were 93%, 60% and 98% respectively, far superior to those of ultrasonography and radionuclide scan. This can probably be accounted for by including "follicular lesions" as diagnostic of malignancy for FNAC. There was no false-positive if the FNAC diagnosis was suspicious of malignancy or malignant. The only two false-negative malignant lesions were microcarcinomas detected incidentally next to colloid nodules, which were the actual presenting symptoms. Although regarded by pathologists as incidental finding of latent papillary carcinoma, they were still calculated as malignancy. The vast majority of these small latent tumours, however, remain dormant and do not grow to clinically apparent disease; and

hence, no further treatment is required if it represents an incidental finding in a lobectomy or thyroidectomy specimen.⁶ They carry excellent prognosis. Hence, FNAC successfully detected all cancerous nodules that were detected by radionuclide scan or ultrasonography, except for the microcarcinoma adjacent to a colloid nodule. Ultrasonography or radionuclide scan offered no additional information to FNAC. FNAC is therefore mandatory.

The combination of FNAC with clinical examination is essential in the detection of cancerous thyroid nodules and can result in significant savings in costs. It is useful both in the initial triage and in the selection of patients for surgery. It is sometimes even therapeutic for simple cysts. After taking history and a careful physical examination, FNAC of the thyroid nodule is performed. If the FNAC result is "follicular lesion", "neoplasm", "suspicious of malignancy" or "malignant", the patient should undergo surgery. If the FNAC diagnosis is benign and there is no clinical suspicion, or the nodule disappears after aspiration, we can safely observe and follow up the patient. Only 2% (2/97) of these nodules turned out to be malignant and they were both latent papillary microcarcinomas. Any non-diagnostic FNAC should undergo re-aspiration. Patients with repeated non-diagnostic FNAC should undergo surgery as the morbidity and mortality of hemithyroidectomy for benign lesion are low; both being 0% in our series. Ultrasonography and radionuclide scan can only give very little additional information.

REFERENCES

1. Ashcraft M W, Van Herle A J. Management of thyroid nodules I: history and physical examination, blood tests, X-ray tests, and ultrasonography. *Head Neck Surg* 1981; 3:216-30.
2. Watters D A K, Ahuja A T, Evans R M, Chick W, King W W K, Metreweli C, et al. Role of ultrasound in the management of thyroid nodules. *Am J Surg* 1992; 164:654-7.
3. Ashcraft M W, Van Herle A J. Management of thyroid nodules II: scanning techniques, thyroid suppressive therapy, and fine-needle aspiration. *Head Neck Surg* 1981; 3:297-322.
4. Loy T J, Sundram F X. Diagnostic management of solitary thyroid nodule. *Ann Acad Med Singapore* 1989; 18:658-64.
5. Bouvet M, Feldman J I, Gill G N, Dillmann W H, Nahum A M, Russack V, et al. Surgical management of the thyroid nodule: patient selection based on the results of fine-needle aspiration cytology. *Laryngoscope* 1992; 102:1353-6.
6. Chan J. Papillary carcinoma of thyroid. *Histol Histopathol* 1990; 5:241-57.