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Are scintigraphy and ultrasonography necessary before fine-needle aspiration cytology for thyroid nodules?

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هل المسح باشعة جاما والتصوير بالموجات فوق الصوتية ضرورى قبل أخذ عينة عن طريق الابر الرقيقة على مرضى عقد الغدة الدرقية؟

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الملخص: الهدف: تقويم فعالية المسح باشعة جاما والموجات فوق الصوتية وأخذ العينه عن طريق الأبر الرقيقة من عُقيدات الغدة الدرقية واستنباط الطريقة الأمثل لتشخيص سرطان الغدة الدرقية. **الطريقة:** تم فحص عُقيدات الغدة الدرقية لعدد ٢١٦ مريض بواسطة الموجات فوق الصوتية عالية التميز و بتكنشيوم برتكنيتيت- ٩٩م لمسح الغدة الدرقية باشعة جاما، وأخذ العينة عن طريق الإبرة الرقيقة بارشاد الموجات فوق الصوتية. تمت ازالة عُقيدات الغدة الدرقية جراحيا من ١١٣ مريضا اما الآخرين (١٠٣ مريض) فقد تمت متابعتهم لمدة سنتين ولم يتم اكتشاف أية اورام سرطانية. **النتائج**: اوضح التصنيف عن طريق فحص الخلايا أن ٧١% من العينات حميدة، ٣% منها إيجابية للاورام السرطانية، ٢١% يشتبه وجود سرطان و٥% غير مقنعة. إثبتت دراسة الخلايا التى أخذ ت بالابر الرقيقة نسبة حساسية مقدارها ٨٧'٥% ونسبة دقة ٨٠%. اوضحت الموجات الصوتية أن ٣٣% من العُقيدات السرطانية بها ضعف الصدى وبمسح اشعة جاما ١٦% من العُقيدات الوحيدة الباردة بها أورام سرطانية. كلا الاختبارين لم يكونا مقنعين لتشخيص سرطان الغدة الدرقية. **الخلاصة:** يجب أن يكون أخذ عينة بالابرة الرقيقة لفحص الخلايا بارشاد الموجات فوق الصوتية الاختبار الاول الذى يتم إجراؤه لمريض سوى الغدة الدرقية مع وجود العقيدات. يجب استخدام المسح باشعة جاما والتصوير بالموجات فوق الصوتية في المتابعة وللمرضى الذ ين لديهم مستوى منخفض من الهورمونات المحفزة للغدة الدرقية.

ABSTRACT. ***Objective:*** To evaluate the efficacy of scintigraphy, ultrasound and fine-needle aspiration in thyroid nodules and to establish the best diagnostic pathway in detecting thyroid cancer. ***Method:*** Two hundred and sixteen patients with thyroid nodules were examined using high-resolution ultrasonography, ^{99m}Tc thyroid scintigraphy and ultrasound-guided fine-needle aspiration. Of these, 113 patients subsequently underwent thyroidectomy. The remaining 103 were followed up for two years without any evidence of malignancy. ***Results:*** Cytopathology classified 71% of the aspirate as benign, 3% as positive for malignancy, 21% as suspected neoplasia and 5% as unsatisfactory. Fine-needle aspiration cytology had a sensitivity of 87.5% and specificity of 80%. On ultrasound 33% of malignant nodules were hypo-echoic and on scintigraphy 16% of solitary cold nodules were malignant. Neither test could reliably diagnose thyroid cancer. ***Conclusion:*** Ultrasound-guided fine-needle aspiration cytology should be the first test performed in euthyroid patients with a thyroid nodule. Scintigraphy and ultrasound imaging should be reserved for follow-up studies and patients who have suppressed levels of thyroid stimulating hormone.

Key words: thyroid nodule, ultrasonography, thyroid scintigraphy, fine-needle aspiration cytology.

The investigation and management of nodular thyroid disease remains a clinical problem. It is more common in women, in older patients, following exposure to ionising radiation and in areas of iodine deficiency.[1–5] Clinically detectable thyroid nodules occur in approximately 4–10% of the population, but only 5–30% of those nodules are malignant.[6,7] The apparent prevalence of thyroid nodules depends on the technique of detection, which ranges from 30–50% in different ultrasound series, to approximately 50% at autopsy.[8–10]

The most widely used screening procedure in the evaluation of thyroid nodules was scintigraphy, and the radionuclides used were technetium pertechnetate (^{99m}Tc) and Iodine-123 (^{123}I).[2,10,11] The value of thyroid scintigraphy is in the identification of cold nodules, because they are more likely to be malignant than functioning nodules. The incidence of malignancy in cold nodules is said to vary from 5 to 15% .[1,12,13]

High-resolution ultrasonography (US) categorises nodules as solid, cystic or mixed, with over 90% accuracy.

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Despite such accuracy, current ultrasonography is unable to reliably separate benign thyroid nodules from malignant ones.[2,12,14]

Fine-needle aspiration (FNA) is a well-established diagnostic procedure often used as one of the initial screening tests for patients with thyroid nodules. Several studies have shown that following the introduction of FNA, the number of thyroid surgical procedures has decreased by 50% while the percentage yield of cancer in operated patients has doubled.[2,12–19]

This paper presents an analysis of the results we obtained in Sultan Qaboos University Hospital using ^{99m}Tc-pertechnetate scintigraphy, US and ultrasound-guided FNA done at one sitting in patients with thyroid nodular disease. The analysis has been used to decide the best diagnostic approach to the management of thyroid nodules.

METHOD

A total of 216 patients seen in the thyroid clinic with nodular thyroid swelling were referred for investigation. All had high-resolution sonography, ^{99m}Tc-pertechnetate scintigraphy and fine-needle aspiration under ultrasound guidance on the same day. The ages of the patients ranged from 17 to 88 years (mean 38 years) and 187 (87%) were women.

THE INVESTIGATIONS

THYROID SCINTIGRAPHY was done after intra-venous injection of 80 MBq of ^{99m}Tc pertechnetate. Standard images were obtained after 20 minutes, anterior, both anterior oblique views, and one view with a marker over the abnormal area.

HIGH-RESOLUTION SONOGRAPHY was performed with a 7.5 MHz linear probe with the patient supine and the neck hyper-extended.

FINE NEEDLE ASPIRATION (FNA) was performed using ultrasound guidance to introduce a 23–25 gauge needle and a 10 ml disposable syringe. Aspiration was performed with short back and forth movements while suction was applied. Suction was released before the needle was removed from the lesion. The aspirate was expelled on to the glass slides and fixed with 95% alcohol immediately. The rest of the specimen was rinsed in saline balanced solution. The specimens were sent to the cytopathology laboratory for cytological evaluation.

Table 1. *Comparison between results of high resolution ultrasonography (US) and scintigraphy*

	US (%)	Scintigraphy		
		Solitary	Multiple	No Nodule
Solitary	118 (55)	93	13	12
Multiple	81 (38)	27	47	7
No Nodule	17 (7)	4	4	9
Total	216 (100%)	124 (57%)	64 (30%)	28 (13%)

RESULTS

SCINTIGRAPHY showed that 124/216 (57%) patients had solitary cold nodules, 64/216 (30%) had multiple cold lesions, and 28/216 (13%) had no nodule.

SONOGRAPHY showed 118/216 (55%) patients to have solitary lesions, 81/216 (38%) with multiple lesions and 17/216 (7%) without nodules [Table1].

FINE-NEEDLE ASPIRATION results of the 216 patients were grouped as benign (cyst, nodule, lymphocytic thyroiditis, sub-acute thyroiditis), malignant (papillary, medullary, anaplastic, lymphoma), suspicious neoplasia (follicular lesion, follicular neoplasm, hurthle cell neoplasm) and inconclusive (foam cell, cyst fluid, few follicular cells, too much blood). Fine needle aspirates were reported as showing benign cells in 154/216 (71%) patients, malignant in 6/216 (3%), 'suspicious' cells in 46/216 (21%) and were inconclusive in 10/216 (5%) [Table 2].

SURGERY was performed in 113 patients, because the cytology result was malignant, suspicious or inconclusive or the patient had a large thyroid mass. The remaining 103 patients were followed up clinically and with US to see any change in nodule size. No patient of this group showed any sign of malignancy during a two year follow up.

In the operated group, 16/113 (14%) had a malignant lesion (12 papillary, 2 follicular, 1 medullary, 1 lymphoma)

Table 2. *Results of fine-needle aspiration cytology (FNAC) of thyroid nodules*

Cytological Diagnosis	FNAC (%)	Histology in Operated Patients	
		Benign	Malignant (%)
Benign	154 (71)	53	2 (1.3)
Malignant	6 (3)	1	5 (83.3)
Suspicious	46 (21)	37	9 (20)
Inconclusive	10 (5)	6	0 (0)
Total	216	97	16 (14)

Table 3. *Correlation between ultrasonography (US) texture and histology*

Nodule Echotexture	No. Cases	Histology	
		Benign	Malignant
Hyperechoic	27	24	3 (11)
Hypoechoic	6	4	2 (33)
Cystic	8	7	1 (13)
Mixed	66	56	10 (15)
No Nodule	6	6	0 (0)
Total	113	97	16 (14)

and 97/113 (86%) were benign. Of the 64 patients who had a solitary nodule on US, 13/64 (20%) had malignant lesions on histology [Figure 1]. Out of the 71 solitary lesions detected on scintigraphy, 11/71 (16%) were malignant on histology [Figure 2]. Eleven percent of the hyper-echoic and 33% hypo-echoic nodules were malignant. Six patients who did not show a definite nodule on US examination had abnormal scintigraphy. On histology, 3 patients showed features of Hashimoto's thyroiditis and 3 had multi nodular goitre [Table 3].

For analysis the inconclusive cytology group (10 cases) were excluded in statistical calculations. The cytological diagnosis of 206 patients was true positive in 14/206 (6.8%), false negative in 2/206 cases (1%), true negative 152/206 (73.7%) and false positive in 38/206 cases (18%) with a sensitivity of 87.5% and specificity of 80%.

DISCUSSION

Historically, thyroid scintigraphy using ^{99m}Tc or ^{123}I has been the foundation for assessment of the thyroid nodule.[10,11] Nodules detected by thyroid scintigraphy are classified as cold (hypo functioning), hot (hyper functioning) or indeterminate. Generally, 85% of thyroid nodules are cold, 10% are indeterminate and 5% are hot. 85% of cold nodules, 90% of indeterminate nodules and 95% of hot nodules are benign.[1] The incidence of malignancy in cold nodules varies from 5% to 15%.[1,12,13] Therefore, although most thyroid nodules are cold, most cold lesions are benign.

We observed similar findings: 16% of solitary cold lesions and 11% multiple cold lesions were malignant. While we detected 118 solitary lesions on US, only 93 solitary cold lesions were demonstrated on scintigraphy. The remainder were multiple lesions (13 cases) with no nodule being shown in 12 cases. It has also been observed by Solbiati et al[20] that US is more sensitive than scintigraphy in detecting nodules. ^{99m}Tc-pertechnetate thyroid scintigraphy cannot truly differentiate benign or malignant nodules and cannot be used as the basis for recommending treatment of the nodule, including thyroid surgery. Certainly, not all patients with thyroid nodules require thyroid scintigraphy, but it is helpful in cases having suspicious or inconclusive cytology on FNA, and in cases with clinical evidence of thyrotoxicosis or having suppressed thyroid stimulating hormone (TSH).

Misken and Rosen[21] described the use of US to examine the thyroid in 1973. Originally, US was primarily used to distinguish between cystic and solid thyroid lesions. However, the development of high-resolution, real time, hand-held sonographic probes has allowed the collection of information that enhances clinical examination. US can confirm the presence of a lesion and define its characteristics better than manual palpation.[8] Sonography has demonstrated that non-palpable thyroid nodules are 4 times more common than those which are detected clinically.[8] Unfortunately, US characteristics such as size, echogenicity, and the presence of a halo sign cannot truly differentiate between benign and malignant. Hyper-echoic solid nodules are usually benign (96%), but sclerosing papillary neoplasms can also have this appearance. Mixed lesions represent solid lesions that have undergone variable degrees of cystic degeneration and are benign in 85% of cases. The rare cystic lesions with smooth wall and echo-free, are almost always benign. Hypo-echoic nodules are more likely to be malignant than benign, 63% of hypo-echoic lesions representing malignancy in one series.[20] In the present series, 33% of hypo-echoic nodules and 11% of hyper-echoic nodules were malignant. US is useful to guide the needle for FNAC of a thyroid nodule although it does not differentiate benign and malignant nodules. It improves the quality of diagnosis in preoperative assessment of thyroid nodules

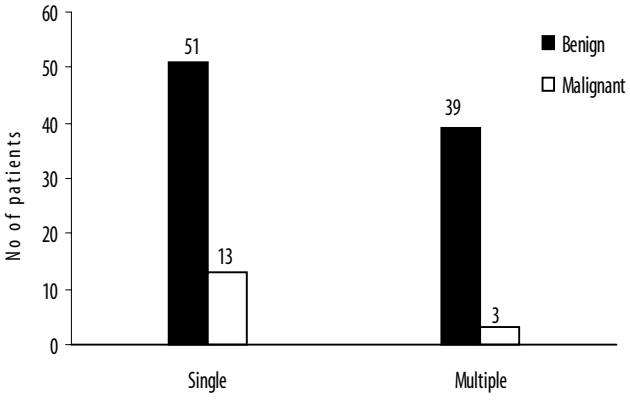

Figure 1. *Correlation between number of nodules on ultrasonography and histology*

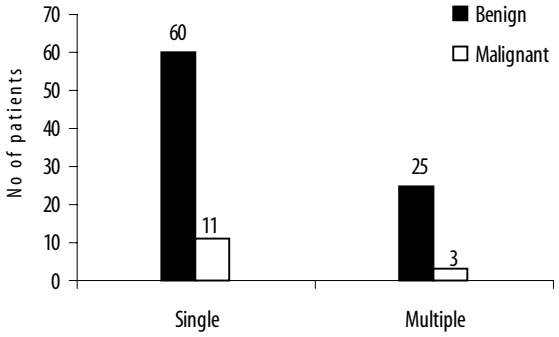

Figure 2. *Correlation of cold nodules with histology*

to select patients for surgery. It may have a more important role in the follow up of a nodule to assess its size and echo pattern once a decision is made not to operate. It can also be most useful in the long-term follow-up of patients with thyroid cancer by detecting small nodules that could represent recurrence of cancer.[3, 22, 23]

The present study shows that FNAC has a high sensitivity of 87.5% and specificity of 80%. On reviewing other large series of thyroid FNAC, the sensitivity of thyroid FNA ranges from 65% to 99% and its specificity from 72% to 100%.[15,17,24–29] Several FNAB series and reviews have been performed to establish the efficacy of this procedure. In Caruso's[24] report on ten series with 9,119 patients, results of needle biopsy were benign in 74%, suspicious and inadequate in 22%, and malignant in 4%. Gharib[25] evaluated seven series with a total of 18,183 FNA where 69% were benign, 27% were suspicious and inconclusive and only 4% were malignant. The suspicious or inconclusive groups were approximately equally divided. Of the suspicious group of nodules, 10–30% were ultimately malignant. Overall, 70% of patients had a definitive diagnosis of either benign or malignant disease by FNA. In the present series, 20% of nodules in the suspicious group were malignant on histology. In 216 patients (operated and non-operated), the false negative rate was 1% and the false positive rate 18%, considering both the malignant and suspicious categories as positive. However, it is difficult to know the true frequency of false negative results because only a small percentage of patients (approximately 10%) with benign cytological findings undergo surgery.[12] The reported false negative rate ranges from 1% to 11%.[24,25] Because FNA is considered a screening procedure, particular attention should be given to minimizing false-negative diagnosis, even at the expense of accepting false-positive diagnosis.[30] The FNA remains the first test in majority of cases for the evaluation of thyroid nodule.

We believe that ultrasound-guided fine-aspiration cytology is the most effective method available. Ultrasound-guidance allows continuous visualization of the needle during insertion and sampling which results in pin-point accuracy with a high level of safety. It also permits multiple sampling of the same lesion which reduces the risk of obtaining an inadequate sample.[22,23] The following thyroid malignancies can be diagnosed by FNA : papillary, follicular variant of papillary, medullary, anaplastic, thyroid lymphoma, and metastases to the thyroid. Follicular carcinoma, Hurthle cell carcinoma and some cases with cellular atypia cannot be diagnosed by FNAC.

Ultrasound-guided FNAC has reduced the cost for evaluation and treatment of thyroid nodules and has improved yield of cancer found at surgery. Due to the wide spread acceptance and low morbidity of FNA, it has virtually replaced large needle (16–18 gauge) or cutting needle (14 gauge) biopsy procedure for sampling the thyroid. Its use should reduce the number of imaging procedures needed.

CONCLUSION

Thyroid nodules are common and only a small percentage is malignant. The initial evaluation of thyroid nodules should effectively select patients for surgery who are likely to have malignancy. It appears from this study that Ultrasound-guided FNAC should be the first test performed in an euthyroid patient with a thyroid nodule as it is safe, inexpensive, and has a high sensitivity.

US is indicated in thyroid nodules with non-suspicious cytological findings for follow up and is also useful in follow-up cases of thyroid malignancies. Thyroid scintigraphy should be reserved for patients with indeterminate or inconclusive findings on cytology, those with thyrotoxicosis and patients with suppressed TSH.

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