

Importance of Fine Needle Aspiration in Evaluation of Single Nodular Goiter

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Abstract:

Background: Improvements in the sensitivity and specificity of biochemical thyroid tests, as well as the development of fine needle aspiration biopsy (FNA) and improved cytological techniques, have dramatically impacted clinical strategies for detecting and treating thyroid disorders.

Fine needle aspiration is a safe and relatively painless procedure where a hypodermic needle passed into the lump and samples of tissue taken out. This procedure will provide us with more information about the nature of the lump, and especially differentiate between a benign and malignant mass.

Objectives: The current prospective study designed to evaluate the sensitivity, specificity and accuracy of FNA. The study was performed in the regional major hospital, Khartoum, Sudan.

Patients and methods: A thousand and three hundred thirty one patients who underwent thyroid surgery 'between' January 2004 to June 2007 were enrolled.

Results: 247 (18.3%) had single nodular goiter. The incidence of benign and malignant lesions in single nodular goiter were 204 (87.6%) and 29 (12.4%) respectively. The overall sensitivity, specificity and accuracy of FNA were 95.5%, 99.5% and 99.4% respectively.

Conclusion: Also there is correlation between the nodule size and the result of FNA, as the nodular size increase there is increase of the probability of malignant changes. So, solitary or dominant nodules ≥ 1 cm in diameter might be evaluated by FNA.

Keywords: Thyroid, Single nodule, Malignancy.

The thyroid gland is a butterfly-shaped organ and is composed of two cone-like lobes or wings - lobus dexter (right lobe) and lobus sinister (left lobe) - connected with the isthmus¹. It is an endocrine gland which produces thyroxin (T4), triiodothyronine (T3), and calcitonin².

A thyroid nodule is a palpable swelling in a thyroid gland with an otherwise normal appearance. In adults, the thyroid nodules are common and may be caused by a variety of thyroid disorders. While most are benign, about 5 to 10 percent of all palpable nodules are malignant³⁻⁷. In contrast, although rare (0.22% to 1.8%) patients with thyroid nodules who are under 21 years of age have a higher incidence of malignancy (33% versus 5%,

children versus adults, respectively)⁸⁻¹¹.

Palpable thyroid nodules occur in 4 to 7 percent of the population, but nodules found incidentally on ultrasonography suggest a prevalence of 19 to 67 percent^{3,12-15}.

In one study, 30 percent of subjects 19 to 50 years of age had an incidental nodule on ultrasonography. In addition, more than one-half of the thyroid glands studied contained one or more nodules, with only about one in 10 being palpable¹⁶.

Approximately 23 percent of solitary nodules are actually dominant nodules within a multinodular goiter¹⁷. Thyroid nodules are four times more common in women than in men and occur more often in people who live in geographic areas with iodine deficiency. New nodules develop at a rate of about 0.1% per year, beginning in early life, but they develop at a much higher rate (about 2% per year) after exposure to head and neck irradiation^{12,15,17-19}.

Nodules are often discovered by the patient as a visible lump, or they are discovered

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incidentally during a physical examination. Thyroid nodules may be smooth or nodular, diffuse or localized, soft or hard, mobile or fixed, and painful or non-tender. While palpation is the clinically relevant method of examining the thyroid gland, it can be insensitive and inaccurate depending on the skill of the examiner^{15,16}. Nodules that are less than 1 cm in diameter are not usually palpable

unless they are located in the anterior portion of the thyroid lobe. About one half of all nodules detected by ultrasonography escaped detection on clinical examination. In addition to palpation of the thyroid gland, a thorough examination of the lymph glands in the head and neck should be performed¹⁵. The various types of thyroid nodules are listed in Table 1.

TABLE 1: Types of Thyroid Nodules .

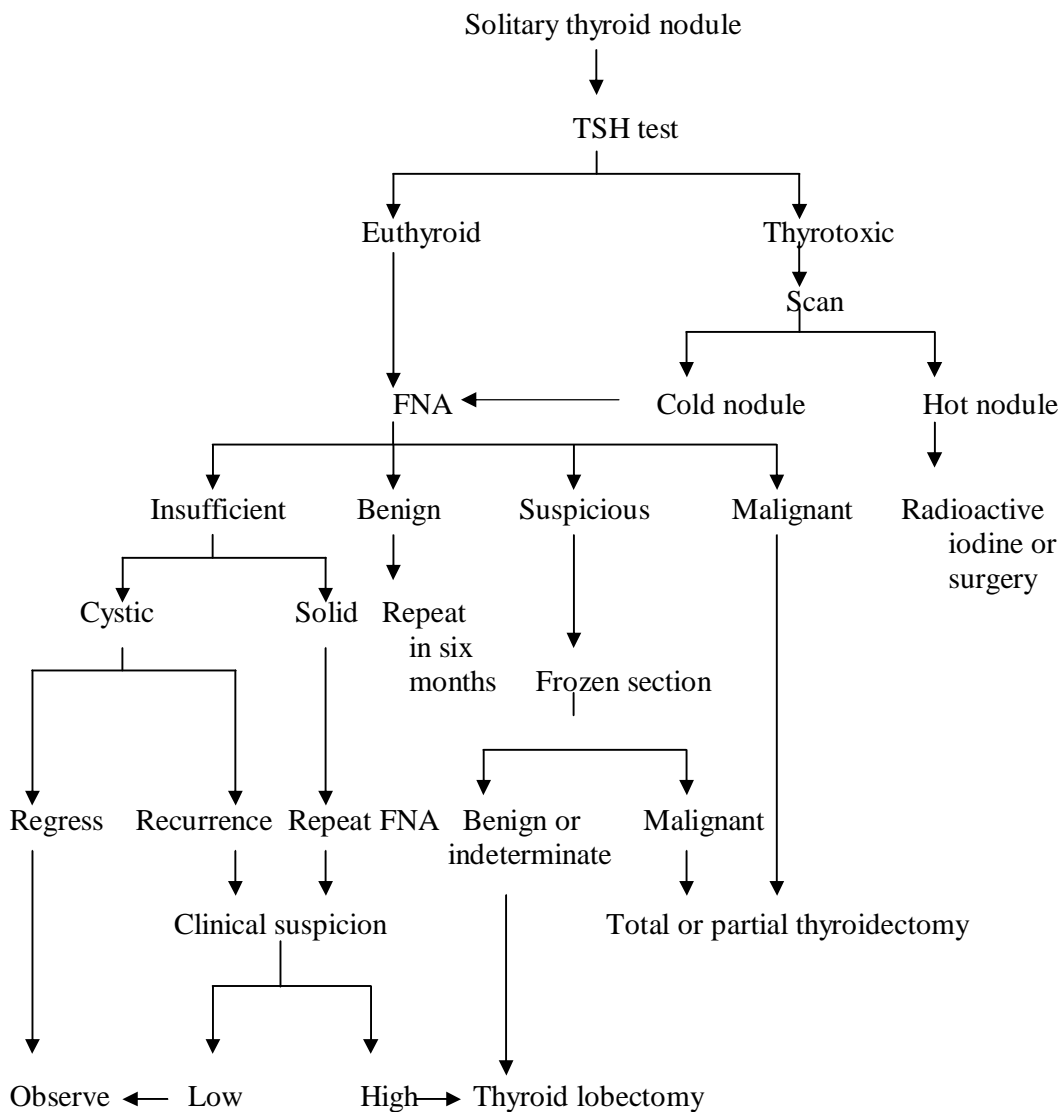
<p>Adenoma Macrofollicular adenoma (simple colloid) Microfollicular adenoma (fetal) Embryonal adenoma (trabecular) Hürthle cell adenoma (oxyphilic, oncocytic) Atypical adenoma Adenoma with papillae Signet-ring adenoma</p>	<p>Carcinoma Papillary (75 %) Follicular (10 %) Medullary (5 to 10 %) Anaplastic (5 %) Other Thyroid lymphoma (5 %)</p> <p>Cyst Simple cyst Cystic/solid tumors (hemorrhagic, necrotic)</p>	<p>Colloid nodule Dominant nodule in a multinodular goiter</p> <p>Other Inflammatory thyroid disorders Subacute thyroiditis Chronic lymphocytic thyroiditis Granulomatous disease Developmental abnormalities Dermoid Rare unilateral lobe agenesis</p>
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A practice guideline for patients with thyroid nodules was established to formulate a clear, concise and easy approach to the evaluation of thyroid nodules and “to increase the understanding of the diagnosis and treatment of thyroid nodules for physicians and patients²⁰. Figure 1 is a diagnostic algorithm for the evaluation of a thyroid nodule²¹.

The currently used methods for assessing thyroid nodules include, fine needle aspiration (FNA), ultrasound and thyroid scan. Practice guidelines suggest that an initial FNA is more diagnostically useful and cost effective than other forms of investigation²². In spite that, some studies reported that, FNA only was

used as the initial procedure in 53% of thyroid nodule cases²³. Studies showed that, as isotopically cold thyroid nodules usually considered suspicious for carcinoma, most benign thyroid nodules such as cysts, colloid nodules, benign follicular lesions, hyperplastic nodules and nodules of Hashimoto’s thyroiditis also present as cold nodules. In addition, warm or iso-functioning nodules that do not result in a completely suppressed TSH and thus surrounding normal thyroid tissue is not suppressed, can be malignant. Logistic regression analysis indicates that adequate cytological material significantly increases with the size of the nodule²⁴.

FIGURE 1: Algorithm for the evaluation of thyroid disorders²³.



TSH = thyroid-stimulating hormone; **FNA** = fine-needle aspiration.

Although, ultrasound can be used to detect non-palpable nodules, ultrasound cannot differentiate between benign and malignant lesions. Ultrasound typically used for evaluating complex cystic masses and nodules that are difficult to palpate²⁵. Ultrasound also used to determine the size of nodules and to monitor nodule growth, as well as to verify the presence of non-palpable nodules that were detected incidentally by other imaging procedures. Therefore, ultrasound-guided FNA should be performed for hypoechoic

nodules and when aspiration cytology fails to yield adequate cellular material^{26,27}. There are several “red flags” that may indicate possible thyroid cancer including Male gender, extremes in age (younger than 20 years and older than 65 years), rapid growth of nodule, symptoms of local invasion (dysphagia, neck pain, hoarseness), history of radiation to the head or neck, and family history of thyroid cancer or polyposis (Gardner’s syndrome)^{15,17}.

Patients and methods:

The study was conducted in the surgical and medical clinics of multicentre in Khartoum, capital city of the Sudan with more than six million inhabitants. All patients with thyroid disorder who attended the clinic for the first time were enrolled in our study after their informed consents. The study was performed in the period from January 2004 to June 2007. During this period, 1351 patient participated in the study. The participants completed a questionnaire based on British Medical Research Council recommendations. It included personal data, habits, family history of thyroid disease and subject disease history. Then participants had undergone general clinical examination, and were enrolled into appropriate investigations. Patients were treated appropriately. The collected data were analyzed.

Fine needle aspiration (FNA) was defined as the removal of a few clusters of individual thyroid cells by means of a small needle (smaller than the type used to draw blood). In case of more than one thyroid nodule, this technique used on each of them whenever practical, with special attention to nodules that have recently grown in size. The cells are then examined microscopically by a cytopathologist and the results of this test are usually available within a few days.

Results:

A total of 1351 patient were enrolled into this study, of which 69.95 % (945) were female patients. Female to male ratio was 2.3: 1. Diffuse goiter was detected in 617 (45.7%) patients, 487(36.04%) had multinodular goiter and 247 (18.3%) single lobe nodular goiter. Of those with single nodular goiter 162

(65.6%) patients were diagnosed clinically and 85 (34.4%) diagnosed incidentally by ultrasound. FNA was performed in 233 (94.3%) patients. In the remaining 14 (5.7%) patients lost follow up, therefore they were excluded from our study.

Ultrasound showed multinodular goiter with dominant nodule in 69(29.6%) and single nodule in 164(70.4%) cases with variable sizes.

Result of FNA showed benign cells in 168 patients, follicular cells in 57 patients, and eight patients with malignant cells. The study showed that there is an increase in the incidence of malignancy with the increase in size of the nodule. The correlation between the nodule size and the result of FNA, and the incidence of the size were shown in table 2.

Papillary malignant cells were found in six patients, and lymphoma in two patients.

Postoperatively the specimens of the removed thyroid tissue were sent for histopathology, which revealed; among those with follicular cells, 19 patients had follicular cell carcinoma and the reminder 38 patients had benign follicular adenoma, and among those who diagnosed as having papillary cell carcinoma by FNA five of them were confirmed to have the disease and one had a follicular cell carcinoma.

Table 3 compares the findings of FNA and histopathology.

The overall sensitivity, specificity and accuracy of FNA were 95.5%, 99.5% and 99.4% respectively (table 4). The incidence of benign versus malignant lesion in single nodular goiter were 204 (87.6%) and 29 (12.4%) respectively.

Table 2: Correlation between the nodular size and the outcome of FNA.

Nodule size /mm	Benign	Malignant	Follicular cells	Total	%
< 5	71	-	7	78	33.5
5-10	43	-	11	54	23.2
10-15	30	3	16	49	21
>15	24	5	23	52	22.31
Total	168	8	57	233	100%

Table 3: The results of FNA versus histopathology.

	Benign cells	Follicular cells Follicular adenoma	Follicular cell carcinoma	Papillary cell carcinoma	lymphoma	Total
FNA	168	57		6	2	233
Histopathology	166	38	22	5	2	233

Table 4: The sensitivity, specificity and accuracy of FNA in detection of different cell types

FNA	True (+ve)	False (+ve)	True (-ve)	False (-ve)	Sensitivity	Specificity	Accuracy
Benign	166	2	65	-	98.8%	100%	99.14%
Follicular cells	57	-	173	3	100%	98.3%	98.7%
Papillary cell carcinoma	5	1	227	-	83.3%	100%	99.6%
Lymphoma	2	-	-	-	100%	100%	100%
Total	-	1.3%	-	1.3%	95.5%	99.5%	99.4%

Discussion:

Fine-needle aspiration of the nodule or clinically suspicious lymph nodes is recommended as the first diagnostic test in a clinically euthyroid patient before any imaging studies are done²⁸.

FNA is preferred to thyroid scanning or ultrasonography as the initial diagnostic test for evaluating patients with thyroid nodules²⁹. According to guidelines from the American Association of Clinical Endocrinologists, it is "believed FNA to be the most effective method available for distinguishing between benign and malignant thyroid nodules,"²⁰. FNA has become popular in the 1970s. Since then the number of thyroid surgical procedures has decreased by 50% whereas the percent yield of cancers for patients undergoing surgery for thyroid nodules has increased from 10- 15% to 20-50%³⁰. Gharib H. et al. reported an accuracy of FNA approaching 95 percent,^[4]. In our study, the accuracy was found to be 99.4%.

Analysis of the data suggests a false-negative rate of 1 to 11 percent, a false-positive rate of

1 to 8 percent, a sensitivity of 68 to 98 percent, and a specificity of 72 to 100 percent^{4,20}. Going with that in this study, a false negative rate, a false-positive rate, sensitivity, and specificity was of 1.3%, 1.3%, 95.5%, and 99.5% respectively.

The frequency of false negative FNA reports is related to the skill of the operator and the experience of the cytopathologist³¹. Experience with aspiration cytology is essential. If the cytologist or ultrasonographer performs the FNA, there must be an exchange of appropriate information with the clinician³². A cytologic diagnosis of malignancy can be made from fewer cells, provided that the characteristic cytologic features of malignancy are present. Some cytopathologists believe that there must be at least six clusters of follicular cells of 10 to 20 cells each on two different slides in order to accurately report a thyroid lesion as benign³³⁻³⁵. A cytologic diagnosis cannot be reached if there is poor specimen handling and preparation or if inadequate cellular

material was obtained at the time of FNA. The principal reasons for insufficient material for diagnosis may be inexperience on the part of the physician performing the procedure, insufficient number of aspirations done during the procedure, the size of the mass, or the presence of a cystic lesion. When small nodules are of concern, the repeat FNA should be done with ultrasound guidance. FNA using ultrasound guidance reduces the incidence of inadequate specimens from 15-20% down to 3-4% in such patients^{26, 27, 36-38}. Ultrasound guided FNA is also indicated for nodules <1.5 cm, cystic (complex) nodules to assure sampling of the solid component, posterior or high substernal nodules or any nodule difficult to palpate, especially in the obese, muscular or large frame patient^{26, 27, 36,37}.

The study showed that there was an increase in the incidence of malignancy with the increase of nodule size. FNA results showed that 8 cases had malignant cells (nodule size of 10-15 mm in 3 cases and > 15 mm in 5 cases), and 57 had follicular cells. Moreover, of those with follicular cells, 22 cases proved histopathologically to have malignant cells the nodule size was < 10 mm in 2 cases 10-15 mm in 8 cases, and > 15 mm in 12 cases (P < 0.003). Some authors have recommended biopsy of nodules larger than 1.0 or 1.5 cm, whereas others have not shown a relationship between size and malignancy³⁹.

Conclusion:

FNA is a very sensitive test, particularly for papillary, medullary and anaplastic carcinomas. False-negative results were sometimes obtained; therefore, a reassuring FNA should not override concerns in the presence of worrisome clinical findings.

Study showed correlation between the nodule size and the result of FNA, as the nodular size increase there is increase of the probability of malignant changes, and vice versa. So, solitary or dominant nodules \geq 1cm in diameter might be evaluated by FNA.

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