

## The Diagnostic Value of Fine Needle Aspiration as Compared to Pathology Results in Diagnosis of Thyroid Nodules: A 22-Year Follow-up Study

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### ABSTRACT

**BACKGROUND AND OBJECTIVE:** Recently, the efficiency of thyroid fine needle aspiration (FNA) as a method of choice in evaluation and management of thyroid nodules has been questioned. The aim of this study was to determine the diagnostic value of FNA as compared to pathology results in diagnosis of thyroid nodules in Shahid Behashti Hospital of Babol, Iran, within 22 years.

**METHODS:** This cross-sectional study was performed on cytology samples of 225 patients who were undergoing thyroidectomy at Shahid Beheshti Hospital of Babol during 1990-2012. Patients' age and gender, physician's experience in performing FNA, type and location of surgery, FNA samples and pathology results were recorded. According to the pathology reports, FNA results were divided into four groups i.e. inadequate, benign, malignant and suspicious. The pathology results were divided into benign and malignant groups. The results of both methods were compared with each other.

**FINDINGS:** The sensitivity and specificity of FNA in diagnosis of thyroid nodules were 60% and 96%, respectively. Also, its positive and negative predictive values and diagnostic accuracy were 65%, 95% and 81.8%, respectively. Among the 225 cytology samples, 127 (56.7%), 47 (20.9%), 27 (12%) and 24 (10.7%) were benign, suspicious, malignant, and inadequate, respectively. Additionally, pathology results were benign and malignant in 150 (66.7%) and 75 (33.3%) patients, respectively.

**CONCLUSION:** FNA was comparatively effective in diagnosis of thyroid nodules.

**KEY WORDS:** Fine Needle Aspiration, Thyroid, Pathology.

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## Introduction

Thyroid nodules are prevalent clinical problems which are detectable in 3-7% of people through physical examination. In more than 25% of cases, they are recognized by dint of diagnostic methods such as ultrasonography (1). Thyroid nodules are very critical in terms of probability of malignancy. Thyroid gland cancer is the most common endocrine malignancy. Approximately, 5-10% of the examined thyroid nodules are malignant (2). According to the obtained results of previous studies, between 10-20% of resected nodules were malignant. The high prevalence of malignancy in selected patients demonstrates the inefficiency of preoperative efforts for screening patients. The number of thyroid nodules cannot be estimated accurately in the general population (3). The chance of being a benign tumor is almost one in five cases. Therefore, correct preoperative differentiation between benign and malignant tumors is mandatory (4). As a result, using accurate methods for distinguishing benign tumors from malignant tumors is necessary in order for proper selection of treatment approach (5). Simple, safe and accurate methods of assessment and diagnosis of thyroid nodules include radionuclide (isotope) scan, ultrasonography and assessment of response to suppression therapy and FNA. The assessment of sensitivity, specificity and accuracy of FNA is necessary to increase the reliability of diagnostic results of thyroid nodules, especially when relying on the results leads to administering non-surgical therapies. According to American Association of Clinical Endocrinologists (ACCE), the sensitivity and specificity of FNA in the diagnosis of thyroid nodules ranged between 65-98% (mean: 83%) and 72-100% (mean: 92%), respectively.

Also, positive predictive value, false negative and false positive rates of FNA were 50-96% (mean 75%), 1-11% (mean 5%) and 0-7% mean (5%), respectively (1). On the other hand, some studies have shown that about one-third of palpable thyroid malignancies may not be detectable via FNA (6). Given the fact that biopsy is an invasive procedure with a significant impact on patients' outcomes, using a safe standard method can partially alleviate

procedural distress in patients. This study aimed to determine the diagnostic value of FNA as compared to pathology results in diagnosis of thyroid nodules in Shahid Beheshti Hospital at Babol city, north of Iran, within 22 years.

## Methods

This cross-sectional study was performed on cytology samples of 225 patients who were undergoing thyroidectomy at Shahid Beheshti Hospital of Babol, Iran, during 1990-2012. Patients' age and gender, physician's experience in performing FNA, type and location of surgery as well as FNA and pathology results were obtained. According to the pathology reports, FNA results were divided into four groups i.e. inadequate, benign, malignant and suspicious.

1) Inadequate group: in this group, either the samples did not have the defined criteria for cell efficiency or contained insufficient follicular cells for inclusion in this group. The existence of at least six clusters of well-preserved cells (10 to 20) was sufficient for assessment of thyroid FNA samples. Physician's experience in sampling was also critical.

2) Benign group: this group included colloid, adenomatous or nontoxic nodular goiter, thyroid cysts and thyroiditis.

3) Malignant group: papillary carcinoma (PTC), medullary thyroid cancer (MTC), anaplastic carcinoma of the thyroid (ATC), metastatic tumors, lymphomas, sarcoma and in a few cases, follicular carcinoma with a high degree of malignancy, which are detectable by cytology, were included in this group.

4) Suspicious group: this group included the following:

- Follicular neoplasms and Hurthle cells containing tissue samples in order to observe invading the capsule or peripheral blood vessels.
- Follicular lesions for differential diagnosis of adenomatous goiter and follicular neoplasm.
- Cases suspected to papillary carcinomas in which cytology results were not sufficient for definitive diagnosis.

•Cases suspected to malignancy with suspicious cytology reports without diagnosis of the type of tumor.

The pathology results were divided into two categories: benign and malignant. Colloid, adenomatous and follicular goiter, Hurthle cell, thyroiditis and thyroid cysts were placed in the benign group. Different types of thyroid cancers including papillary carcinoma, follicular carcinoma, medullary carcinoma, anaplastic carcinoma and in some rare cases lymphoma, sarcoma and metastasis were placed in the malignant group (1). The obtained data were collected and coded. Then they were categorized in the designed tables and consequently, the data were entered into SPSS software, version 18. Chi-square test was performed at the significance level of 0.05. Additionally, sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of FNA in diagnosis of malignant thyroid nodules were evaluated.

## Results

Among 225 patients who entered this study, 38 (16.9%) cases were male and 187 (83.1%) cases were female. The mean age of the participants was  $40.37 \pm 13.34$  (their age ranged between 11 and 77 years). In 73.8% of cases, FNA was performed by an endocrinologist and in 26.2% of cases, it was performed by a radiologist. Moreover, lobectomy was performed on 115 patients. Total and subtotal thyroidectomies were performed on 98 and 11 patients, respectively and partial thyroidectomy was performed on one case. The nodules were located in the right and left lobes of 98 and 92 cases, respectively, and they were bilateral in 19 patients. Additionally, the nodules were placed in isthmus in 16 cases. Based on the FNA results, among the 225 cytology samples, 127, 47, 27 and 24 samples were benign, malignant, suspicious and insufficient, respectively. Moreover, based on the final diagnostic pathology, 150 patients (66.7%) had benign tumors and 75 patients (33.3%) had malignant tumors (table 1). According to the obtained results, the sensitivity and specificity of

FNA in diagnosis of thyroid nodules were 60% (CI 95%, 41-79) and 96% (CI 95%, 94-99), respectively. The positive and negative predictive values were 65% (CI 95%, 46-85) and 95% (CI 95%, 92-98), respectively. Additionally, the positive and negative likelihood ratios of FNA were 15.75 (CI 95%, 7.43-33.38) and 0.42 (CI 95%, 0.26-0.67), respectively.

**Table 1. Cytology and pathology in patients with thyroid nodules.**

Groups		FNA N(%)	Pathology N(%)
Benign	Adenomatous goiter	63(49.6)	70(46.7)
	Colloid goiter	49(38.6)	59(39.3)
	Hashimoto's thyroiditis	6(4.7)	9(6)
	Follicular adenomas	9(7.1)	11(7.3)
	Graves	-	1(0.7)
Suspected	Suspected PTC	25(53.2)	-
	Hurthle cell neoplasms	3(6.4)	-
	Without specifying the type of cancer	14(29.8)	-
	Atypia (Non-diagnostic)	5(10.6)	-
Malignant	Papillary carcinomas	26(96.3)	59(78.7)
	Micropapillary carcinomas	-	8(10.6)
	Medullary carcinoma	-	3(4)
	Hurthle cell carcinoma	-	2(2.7)
	Follicular carcinoma	1(3.7)	2(2.7)
Anaplastic carcinoma	-	1(1.3)	

## Discussion

According to our findings, the sensitivity and specificity of FNA in diagnosis of malignant thyroid nodules were 60% and 96% with positive and negative predictive values of 65% and 95%, respectively. Based on the results provided by ACCE the sensitivity and specificity of FNA were reported to be between 56-98% and 72-100%, respectively, with positive predictive value of 50-96% (1). In studies conducted in Iran, the sensitivity and specificity of thyroid FNA ranged between 53.8-94% and 67-100%, respectively. Also, positive and negative predictive values and diagnostic accuracy were reported to be between 58-95.5%, 75-98.4% and 75-97.8%, respectively

(1-10). Results of the previous studies were in agreement with our findings. In diagnosis of thyroid malignancy, several factors can lead to low FNA diagnostic value, i.e., 1) sampling error: in some cases the sampled cells cannot be identified from thyroid nodules; 2) heterogeneity in the index nodule: the foci of malignancy can be located in large index nodules, if so, the cancer cells may be undetectable even in numerous aspirations; 3) the presence of false negative in FNA or suboptimal slide preparation.

Given physicians' skill in sampling and interpretation of results, diverse ranges of FNA sensitivity have been reported in various studies. This discrepancy might be due to different approaches for dealing with cases of suspected malignancy in FNA results. In other words, if suspected cases of malignancy in cytology specimens are considered as positive, the sensitivity increases and specificity decreases, otherwise, it would be the opposite. There are many techniques for decreasing false negative results in diagnosis of malignant thyroid nodules.

These techniques include ultrasound-guided fine needle aspiration biopsy (USFNA), multiple aspiration of nodules, setting priorities for nodules that should be sampled based on ultrasonography findings, reviewing the slides by an expert cytopathologist, cytological follow-up of patients with benign nodules, sampling of solid areas of cystic lesions, cyst fluid analysis and repeating FNA under ultrasound guidance in benign nodules at the time of follow-up (1). USFNA is a proper method for decreasing false negative results and increasing sensitivity (7).

For this reason, current guidelines have emphasized on the role of ultrasonography findings in identification and assessment of thyroid nodules. It is recommended that ultrasonography findings demonstrate the apparent hypoechogenicity, the presence of microcalcification or macrocalcification and type of nodules (nodule's length greater than its width) which are significantly related to malignancy and must be considered in treatment of thyroid nodules (8). In cases of suspected malignancy, cytological

diagnosis is not valuable, since there are no accurate cancer indicators in their FNA thyroid samples. Given the fact that cytological features of benign Hurthle cell tumors and benign follicular nodules are similar to Hurthle cell carcinomas and low grade follicular carcinomas, further investigation is required in this area. (10). To avoid unnecessary surgery, correct diagnosis of follicular thyroid lesions and accuracy in reporting them are of utmost importance. In our study, the sensitivity and specificity of FNA in diagnosis of malignant thyroid nodules were 60% and 96%, respectively, with positive and negative predictive values of 65% and 95%, respectively. Also, its diagnostic accuracy was 81.8%. Therefore, efficiency of FNA seems enough in diagnosis of thyroid nodules as compared to histopathology examination.

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