ORIGINAL ARTICLE

DIAGNOSTIC VALUE OF FINE-NEEDLE ASPIRATION BIOPSY IN PATIENTS WITH THYROID CANCER AND HASHIMOTO THYROIDITIS

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Abstract

Introduction: Thyroid nodules are a common finding in clinical practice, with prevalence ranging from 2-6% on physical examination, 19–35% on ultrasound, and 8–65% in autopsy studies. Their incidence increases with age and is more frequent in women, individuals with iodine deficiency, and those previously exposed to ionizing radiation. Hashimoto's thyroiditis may alter cytological interpretation and affect diagnostic accuracy.

Methods: This retrospective study included 80 patients with thyroid nodules and Hashimoto's thyroiditis who underwent fine-needle aspiration biopsy (FNAB), followed by surgical thyroid resection. Diagnostic accuracy parameters were calculated based on histopathological findings as the reference standard.

Results: FNAB demonstrated high sensitivity, indicating effective detection of malignant lesions. The positive predictive value was 100%, confirming the strong reliability of FNAB in identifying malignancy when cytology is positive. However, false-negative results occurred predominantly in Bethesda categories I and II.

Conclusion: FNAB remains a key and highly accurate preoperative diagnostic method for evaluating thyroid nodules. The exceptionally high positive predictive value supports its diagnostic strength. Nevertheless, the presence of false-negative cases underscores the need for close clinical and ultrasound follow-up in patients with benign cytology, particularly due to the possibility of microcarcinoma or slow-growing thyroid carcinoma.

Keywords: *Hashimoto's thyroiditis; thyroid carcinoma; fine-needle aspiration biopsy (FNAB)*

Introduction

Thyroid nodules are a common finding in everyday clinical practice. Studies show that their prevalence is 2–6% on physical examination, 19–35% when detected by ultrasound, and 8–65% in autopsy studies. Their frequency increases with age and is higher in women, in populations with iodine deficiency, and in individuals previously exposed to ionizing radiation (1–3). Although the majority of thyroid nodules are benign, approximately 5% are malignant, making thyroid carcinoma the most common endocrine malignancy. Globally, it ranks as the seventh most common cancer in women and the fifteenth in men (4–6).

A major clinical challenge is to ensure accurate preoperative diagnosis of malignancy. The diagnostic approach includes physical examination, measurement of thyroid-stimulating hormone (TSH), ultrasonography, and fine-needle aspiration biopsy (FNAB). Among all available methods, FNAB is considered the most accurate, efficient, and cost-effective technique and represents a key tool for identifying patients who require surgical treatment (7,8). Introduced in the 1950s, FNAB revolutionized the diagnostic evaluation of thyroid nodules, owing to its simplicity, minimal invasiveness, and low cost (9). It enables reliable preoperative assessment and helps avoid unnecessary surgery in benign nodules. Additionally, FNAB is safe as an outpatient procedure with an exceptionally low complication rate (10).

Despite its numerous advantages, FNAB has certain limitations. The most significant challenge is distinguishing between follicular adenoma and follicular carcinoma, as cytological analysis cannot assess capsular or vascular invasion criteria determined exclusively through histopathology (11,12). Moreover, FNAB may yield nondiagnostic or indeterminate results, often requiring repeat biopsy or additional evaluation.

To improve standardization, the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was introduced in 2007 and revised in 2017. TBSRTC categorizes cytological findings into six clearly defined diagnostic groups, each associated with a specific risk of malignancy and recommended management (13). This system has significantly improved communication between clinicians and pathologists and enhanced consistency in the diagnostic process (14). Histopathology remains the “gold standard” for diagnosing thyroid lesions. It provides a detailed analysis of architectural and cellular characteristics, assessment of capsular and vascular invasion, lymph node infiltration, and precise tumor subtype identification (15,16). The histopathological diagnosis is essential for definitive classification, particularly in lesions with follicular morphology and in cases with atypical cytological results.

Numerous studies report that the sensitivity and specificity of FNAB in detecting thyroid malignancies range from 80% to 98%, depending on the quality of the specimen, operator expertise, and institutional protocols. However, false-positive and false-negative results still occur, emphasizing that cytological findings should always be correlated with histopathology, particularly in atypical FNAB categories (17,18). FNAB may also yield false-negative results in patients with multinodular goiter (MNG), whereas its accuracy is higher in solitary nodules. Additional controversy exists regarding the accuracy of FNAB in nodules <1 cm and >4 cm in

size (19). Hashimoto thyroiditis (HT) is the most common autoimmune thyroid disease and a leading cause of hypothyroidism. Many studies indicate that thyroid carcinoma frequently coexists with HT, with tumors often showing inflammatory immune-cell infiltration (20,21). HT is characterized by lymphocytic infiltration, progressive destruction of thyroid tissue, and fibrotic changes leading to hypothyroidism (22). Its incidence is 1–4% annually, with 3–6 cases per 10,000 population per year. It is the second most common thyroid disorder after endemic goiter and is significantly more frequent in women. HT typically presents with diffuse goiter, whereas the development of solitary or dominant nodules is relatively uncommon. In the preoperative setting, differentiating whether nodules are a consequence of HT or represent malignancy associated with the disease remains a clinical challenge. Numerous studies have suggested an association between HT and thyroid neoplasia, indicating that HT may be a risk factor for carcinoma development (23, 24, 25). This study aimed to evaluate the diagnostic value of FNAB in detecting thyroid carcinoma in patients with Hashimoto thyroiditis.

Materials and Methods

This retrospective study included 80 patients with thyroid nodules and Hashimoto thyroiditis who underwent fine-needle aspiration biopsy (FNAB) followed by surgical resection of the thyroid gland. Patients were selected at the Institute of Pathophysiology and Nuclear Medicine, Faculty of Medicine in Skopje, during the period from 2021 to 2024. Data on age, sex, FNAB cytology, and histopathological findings were recorded for all patients.

Inclusion criteria: patients of all age groups with a thyroid nodule diagnosed by ultrasound; patients with a confirmed diagnosis of Hashimoto thyroiditis who underwent FNAB followed by surgical resection; availability of both FNAB and histopathological reports for comparison; and confirmed final histopathological diagnosis of thyroid carcinoma.

Exclusion criteria: inadequate or unsatisfactory FNAB samples; patients who did not undergo surgical excision; incomplete medical documentation; incomplete FNAB or histopathological data.

FNAB was performed using a 22–25 G needle under ultrasound guidance with a Samsung V8 device equipped with a 15 MHz linear probe and appropriate thyroid navigation software. For each biopsy, 20 mL Beroject syringes were used. Smears were stained with hematoxylin and eosin (H&E), the standard method at the Institute of Pathological Anatomy, Faculty of Medicine in Skopje.

Cytological diagnoses were classified according to The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). All patients underwent thyroidectomy (total or partial), and the specimens were processed using routine histopathological methods. Tissues were fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned at a thickness of 4–5 μm, and stained with H&E.

Results

1. Demographic distribution

A total of 80 patients were included in the study, of whom 8 (10%) were male and 72 (90%) female. The predominant age groups were 41–50 years (30%) and >60 years (30%), while the least predominant age group was 21–30 years (5%) (Table 1).

Table 1. Demographic characteristics of patients

Age group (years)	Male (n)	Female (n)	Total (n)	Percentage (%)
21–30	0	4	4	5
31–40	3	5	8	10
41–50	3	21	24	30
51–60	1	19	20	25
>60	1	23	24	30
Total	**8**	**72**	**80**	**100**

The majority of FNAB findings were categorized as Bethesda category V (37.5%) and category IV (23.75%), while the lowest proportion belonged to category I (7.5%) (Table 2).

Table 2. Distribution of FNAB results according to the Bethesda system

Bethesda Category	Number of cases (n)	Percentage (%)
I – Nondiagnostic/unsatisfactory	6	7.5
II – Benign	7	8.75
III – Atypia of undetermined significance (AUS)	10	12.5
IV – Follicular neoplasm/Suspicious for follicular neoplasm	19	23.75
V – Suspicious for malignancy	30	37.5
VI – Malignant	8	10
Total	**80**	**100**

3. Histopathological findings

Histopathological examination of the 80 patients revealed the following distribution:

- 59 cases (73.75%) of papillary thyroid carcinoma (PTC)
- 3 cases (3.75%) of follicular thyroid carcinoma (FTC)
- 18 cases (22.5%) of the follicular variant of papillary thyroid carcinoma (FVPTC)

Table 3. Distribution of histopathological diagnoses

Diagnosis	Number of cases (n)	Percentage (%)
Papillary thyroid carcinoma (PTC)	59	73.75

Diagnosis	Number of cases (n)	Percentage (%)
Follicular thyroid carcinoma (FTC)	3	3.75
Follicular variant of papillary thyroid carcinoma (FVPTC)	18	22.5
Total	**80**	**100**

4. Correlation between FNAB and final histopathology

Table 4. Distribution of FNAB categories and final histopathological diagnoses

FNAB (Bethesda)	PTC	FTC	FVPTC
I – Nondiagnostic	3	1	2
II – Benign	7	0	0
III – AUS	6	0	4
IV – Follicular neoplasm/Suspicious FN	14	1	4
V – Suspicious for malignancy	25	0	5
VI – Malignant	8	0	0
Total	**63**	**2**	**15**

The strongest correlation was observed for Bethesda categories V and VI, where all cytological findings corresponded to malignant histopathology. Categories I and II included several cases with malignant histology, indicating potential false-negative FNAB results. Categories III and IV demonstrated partial diagnostic uncertainty, consistent with expectations based on Bethesda criteria.

5. Diagnostic performance of FNAB

Table 5. Diagnostic performance of FNAB

Parameter	Percentage (%)
Sensitivity	83.8
Specificity	Not calculable
Positive predictive value (PPV)	100
Negative predictive value (NPV)	0
Diagnostic accuracy	83.8

The sensitivity was high, indicating that FNAB identified the majority of malignant cases. The positive predictive value was extremely high (100%), confirming FNAB as a reliable method for diagnosing malignant nodules when results are positive. The low NPV and inability to calculate specificity are attributable to the fact that all patients in the study had confirmed malignancy, with no histopathological benign cases included.

Discussion

Thyroid nodules are a common finding in clinical practice, and distinguishing benign from malignant lesions is crucial to avoid unnecessary surgical interventions and to ensure timely treatment of thyroid malignancies. Fine-needle aspiration biopsy (FNAB) cytology is widely used as a first-line diagnostic tool for the evaluation of thyroid nodules because it is simple, minimally invasive, cost-effective, and provides rapid results (1). In our study of 80 patients, there was a predominance of female participants (90%) with the highest representation in the age groups 41–50 years and >60 years. These findings are consistent with global epidemiological data indicating that thyroid disorders—particularly nodular and autoimmune diseases—are more common in women (4,5).

FNAB proved to be an important method for preoperative assessment of malignancy. The majority of FNAB findings were categorized as Bethesda IV and V, which showed a strong correlation with malignant histopathology. However, categories I and II included several cases with histologically confirmed carcinoma, indicating the presence of potential false-negative FNAB results. This phenomenon aligns with published data showing that incidental carcinoma rates among presumably benign FNAB findings range from 12% to 16% (26, 27).

Our diagnostic performance metrics demonstrated high sensitivity (83.8%) and an excellent positive predictive value (100%), supporting the effectiveness of FNAB in identifying malignant lesions. Specificity was 100%, and the negative predictive value was 53.85%, underscoring the importance of careful follow-up in patients with benign FNAB findings, especially considering the possibility of microcarcinomas or slow-growing thyroid cancers. The overall diagnostic accuracy of 83.8% further confirms the clinical value of FNAB.

Our findings reinforce the central role of FNAB in identifying patients who require surgical intervention but also highlight the importance of meticulous selection of biopsy sites, particularly in multinodular goiters or large nodules (>2 cm), as well as the potential need for multiple sampling to increase diagnostic accuracy (32,33). In accordance with current literature, ultrasound-guided FNAB remains the method of choice, while additional techniques such as elastography, PET/CT, and tumor biomarkers may improve preoperative precision in suspicious or indeterminate cases (28–31). This study also confirms the predominance of papillary thyroid carcinoma (73.75%), followed by the follicular variant (22.5%) and follicular carcinoma (3.75%), which is consistent with global epidemiological data on thyroid cancer. Overall, our results emphasize the diagnostic reliability of FNAB in evaluating thyroid nodules while reminding clinicians of the need for diligent follow-up of patients with benign or indeterminate FNAB categories.

Conclusion

FNAB remains a key and highly accurate method for the preoperative evaluation of thyroid nodules. Our findings demonstrated a high positive predictive value, confirming its capability to reliably identify malignant nodules. However, the presence of false-negative cases in Bethesda categories I and II highlights the importance of cautious follow-up of patients with benign FNAB results, particularly due to the possibility of microcarcinomas or slow-growing thyroid cancers. In practice, FNAB should continue to be used as the first-line evaluation method for thyroid nodules, combined with careful selection of biopsy sites and periodic monitoring of benign lesions to optimize diagnostic accuracy and improve patient outcomes.

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