ORIGINAL ARTICLE

Ultrasound guided fine needle aspiration cytology (FNAC): an assessment of the diagnostic potential in histologically proven thyroid nodules

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ABSTRACT

Aim Results of ultrasound guided fine needle aspiration cytology (FNAC) as the compatibility of cytological findings with histopathological diagnoses (the "gold standard") in the diagnosis of nodular thyroid lesions are inconsistent. The aim of this prospective study was to determine the validity of FNAC, as well as the compatibility of findings with histopathological diagnoses.

Methods The study included 92 patients who underwent FNAC and later surgery and histopathological assessment with a final diagnosis.

Results FNAC showed 95% specificity, 78% sensitivity and 90% accuracy. The compatibility of the cytological and histopathological findings was good (Kappa coefficient of 0.756; 95% CI). The cytology results proved to be very good at predicting malignant histopathological findings, (OR=72.33; p<0.001). Also, the result of ROC analysis (AUC=0.866) confirmed FNAC as a very good method of distinguishing benign and malignant thyroid nodules.

Conclusion The results confirmed the correctness of the algorithm in which, following clinical or ultrasound confirmation of nodular thyroid lesions with suspicious changes, FNAC is indicated. The FNAC results should guide a clinician to further diagnostic and therapeutic procedures. Certainly, in case of suspected follicular/Hurthle cell lesions one should be vigilant and aware of the fact that in these cases malignancy is defined by the invasion of blood vessels and/or the capsule, which FNAC is unable to detect.

Key words: biopsy, cytopathology, fine-needle, histopathology

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INTRODUCTION

A thyroid nodule, solitary or multiple, is a frequent finding in adults, with an estimated prevalence of 3-7%, based on clinical examination (1,2). Widespread use of ultrasound has led to an increase in the detection clinically invisible thyroid nodules and the prevalence in the general population is estimated at 19-67% (3-6). Data from numerous studies of thyroid nodules detected by ultrasound show a nearly linear increase in the prevalence of thyroid nodules according to age: less than 1% among people under the age of 15 and about 50% in people over the age of 60 (7,8).

Clinical significance of thyroid nodules is related to the necessity of excluding thyroid cancer, which is found in about 5% of cases to 12% in palpable thyroid nodules, as well as non-palpable incidentalomas (4,9,10). Therefore, it would be ideal to have a diagnostic method which would, with certainty, be able to preoperatively distinguish malignant from benign thyroid nodules and thus in most cases avoid the often unnecessary surgical procedures. The need for such a method is particularly reflected in the fact that there has been an increase in the incidence of malignant thyroid tumours in the last 50 years (11-13).

Clinical studies have shown a slight correlation between certain medical history data and clinical signs of the presence of cancer in the node. Ultrasound characteristics such as the irregular edges of the node, microcalcifications, hypoechogenicity of the node, the absence of haloes and increased vascularization of the node have traditionally been associated with an increased risk of malignancy (14). Unfortunately, none of these characteristics are sufficient to differentiate benign from malignant nodes. Diagnostic sensitivity for hypoechogenicity is 26.5-87.1%, for microcalcifications 26.1-59.1%, and 54.3-74.3% for intranodular blood supply, while the specificity in the series is 43.4-94.3%, 78.6-80.8% and 85.8-95%, respectively (1, 14-16). Thyroid scintigraphy is not able to distinguish malignant from benign nodes with certainty, it can only conclude that the vast majority of malignant nodes are "cold nodules" (17).

Ultrasound guided fine needle aspiration cytology (FNAC) of thyroid nodules is a simple, inexpensive, relatively painless and minimally invasive method that provides fast results and the results are comparable with those based on histopathological analysis as the "gold standard" in the diagnosis of thyroid nodules (7, 14-16).

Although there is a significant number studies in the world that evaluate the validity of ultrasound-guided cytological puncture in the diagnosis of nodular thyroid changes, we have not found data on similar, more significant studies in Bosnia and Herzegovina.

The aim of this study was to evaluate the validity of ultrasound-guided cytological puncture of thyroid nodules and their compatibility with histopathological findings as the gold standard in differentiating malignant and benign nodules, in specific conditions of lack of human and material resources.

PATIENTS AND METHODS

Patients and study design

This prospective study included 92 consecutive patients attended to the Department of Otorhinolaryngology, Head and Neck Surgery, County Hospital Livno, during the period 2016-2021, who were, after clinical examination, subjected to an ultrasound examination of the thyroid with FNAC, and after a certain period of time, surgical extirpation with histopathologic analysis.

The Ethics Committee of the County hospital Livno approved the investigation. All patients signed an informed consent.

Methods

The FNA was performed in an outpatient setting of the Department of Otorhinolaryngology, Head and Neck Surgery, County Hospital Livno, under ultrasound control with a 23 G needle attached to a 20mL syringe. No distinction was made in taking the sample from hypoechoic, anechoic or hyperechoic node areas. The aspirated material was spattered over the glass slide, air-dried and then dyed according to the May-Grünwald-Giemsa method. Cytological findings were divided into two groups: malignant lesions and benign lesions.

After a particular time period, all patients included in the study underwent surgical resection, and the resulting biopsy material was fixed in 10% buffered solution for 24 hours, set in pa-

raffin and stained using the standard staining method (hemalaun-eosin). The histopathological analysis was performed at the Department of Pathology, Cytology and Forensic Medicine, University Hospital Mostar. The results of the histopathological analysis were retrogradely compared with cytology findings in order to estimate the compatibility of findings.

Statistical analysis

Age was presented as the mean ±standard deviation (SD). One-way analysis of variance (one-way ANOVA) was used to test the differences between malignant and benign lesions groups according to the age. The analysis of the presence and type of various tumour was performed using Pearsonχ^2 -test. The ROC (receiver operating characteristic) analysis was used to compare diagnostic performance of cytological and histopathologic diagnostic tests. All statistical values were considered significant at $p<0.05$.

RESULTS

The mean age of all patients was 51.1±14.6. The youngest patient was 20 years old, while the oldest one was 83. Patients with malignant changes (determined histologically) were significantly older than patients with benign changes (p=0.001) (Table 1). There were no significant differences according to gender and thyroid status determined histologically (p=0.069). Females were predominant in both groups, with benign and malignant changes (p<0.001) (Table 1).

Table 1. Age and gender distribution of the study population according to type of lesion

Variable	Benign lesions	Malignant lesions	Total	p
	65 (70.6)	27 (29.4)	92 (100.0)	
Mean± SD of age (range) (years)	47.9 ± 13.7 (20 - 75)	58.8 ± 14.1 (30 - 83)	51.1 ± 14.6 (20 - 83)	p=0.001
Gender (No; %)				p=0.069
Females	61 (66.3)	22 (23.9)		
Males	4 (4.4)	5 (5.4)		

The sensitivity of the diagnostic procedure of 78%, specificity of 95% and accuracy of 90% were found (Table 2).

In 62 (67%) cases of benign cytological changes, results were confirmed by histopathologic diagnosis, while in 21 (23%) cases of malignant findings FNAC was confirmed histologically. In six (6.5%) cases of benign cytological changes malignant changes were determined, while in three (3.5%) cases malignant cytological diagnosis was determined as benign by histopathology (Table 3).

Table 2.Comparison of fine needle aspiration cytology (FNAC) and histopathological findings

FNAC	No (%) of histopathological findings		Total
	Malignant lesions	Benign lesions	
Malignant lesions	21(87.5)	3(12.5)	24
Benign lesions	6 (8.8)	62(91.2)	68
Total	27(29.4)	65(70.6)	92

Sensitivity (21/27) = 78%; Specificity(62/65) = 95%; Accuracy (83/92) = 90%

Table 3. Incompatibility of cytological and histopathological findings

Cytological findings	Histopathological findings
Benign lesion	Ca papillare
Adenoma folliculare	Hurthle cell carcinoma
Adenoma folliculare	Ca folliculare
Benign lesion	Ca medullare
Benign lesion	Ca medullare
Benign lesion	Ca folliculare
Ca medullare	Thyroiditis chr Hashioto
Ca folliculare	Adenoma folliculare
Ca medullare	Struma nodosa gl. thyroideae

The calculated Kappa coefficient was 0.756 (95% Cl; 0.605- 0.907 overall showing good agreement between cytological and histopathological analysis (Table 4). Logistic regression analysis of the predictive value of cytological findings, age and gender on histopathologic findings proved cytological findings could predict malignant histological findings (OR=72.33; 95%CI=16.60-315.11; p<0.001). The likelihood or probability of malignant histopathologic findings being found in those patients who had malignant cytologic findings was 72.33 times greater than not being found and that OR is statistically significant (p<0,001). Age proved to be statistically insignificant (OR=1.06; p=0.068), as was gender (OR = 3.47; p=0.082) (Table 5)

Table 4. The compatibility of the cytology and histopathological finding

Histopathological finding	No (%) of lesions according to cytological findings		
	Benign	Malignant	Total
Benign lesions	62 (67.4)	3 (3.5)	65 (70.7)
Malignant lesions	6 (6.5)	21 (22.8)	27 (29.3)
Total	68 (73.9)	24 (26.1)	92 (100)
Kappa coefficient (95% CI)	0.756 (0.605 to 0.907)		

Table 5. Predictor value of cytological findings, age and gender on histopathological findings

Variable	β	Sp	OR (95% CI)	p
Cytological finding	4.281	0.751	72.33 (16.60 – 315.11)	<0.001
Age	0.059	0.019	1.06 (0.98 – 1.10)	0.068
Gender	1.243	0.715	3.47 (0.85 – 14.09)	0.082

β, beta regression coefficient; S_p, standard error; OR, odds ratio; CI, confidence interval;

DISCUSSION

Our results showing the sensitivity of 78%, specificity 95% and accuracy of 90% are in line with those published in other studies where these values varied in the range of 43% -99%, 72% -100%, and80, 3-98%, respectively (2,25,28,29).

Benign cytological change in 6% patients was not confirmed after histopathological analysis. This prevalence of false negative results is in accordance with the results of other similar studies ranging from 1.5% to 11% (27-31).

Follicular carcinoma was the most frequently noticed (67%) and in one case Hurthle cell carcinoma. This phenomenon is not surprising since it is difficult to distinguish follicular cytology/Hurthle cell adenoma cancer because a cytologist cannot evaluate vascular criteria and capsular infiltration, as well as intrathyroidal expansion (2,25,29). In Graveset et al. study, in 63 out of 92 cases of follicular thyroid lesions, they were unable to be cytologically differentiated, and these follicular lesions were called the "grey zone" of the cytological diagnosis (32). Other authors, in addition to other restrictions relating to the adequacy of the sample, sampling techniques, the experience of staff sampling and experience of the cytopathologist, have particularly emphasized overlapping cytological benign and malignant follicular/Hurthle cell lesions (33,34). It should be noted that negative cytological findings should not exclude malignancy, if a distinct clinical suspicion is present; follicular and Hurthle cell lesions will continue to be a diagnostic challenge (2,32,34). The results of our study have shown falsely positive findings in 3% cases referring to a follicular adenoma, lymphocyte and thyroid nodule. The result is comparable with the results of other studies where the percentage of falsely positive results ranged from 1-11% (35-39). Lymphocytic thyroiditis, papillary hyperplasia and hyperplastic nodules, as well as samples full of oncocytic cells may be responsible for that cyto-histopathological disagreement (2,25,29). The correlation between cytological and histopathological findings showed 95% agreement. Also, we have found statistical significance of cytological results in predicting whether the patients will have malignant or benign histopathologic findings. The results were in accordance with reports published earlier (28,36).

In conclusion, we can confirm the correctness of the algorithm in the diagnosis of thyroid nodules after clinical or ultrasound confirmation of nodular thyroid lesions with suspicious changes, FNAC is indicated. The result of FNAC should direct the clinician for further diagnostic and therapeutic procedures. In case of suspected follicular/Hurthle cell lesions one should keep in mind that FNAC is not an adequate method of distinguishing between a malignant and a benign lesion.

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TRANSPARENCY DECLARATION

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