



# Consistency analysis of ultrasound-guided fine-needle aspiration and histopathology results in thyroid nodules

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## Abstract

**Introduction:** Thyroid nodules are considered as a frequent clinical problem. The great majority of thyroid nodules are benign; however malignancy probability is predicted to be 5-10%. The inconsistency between ultrasonography and fine-needle aspiration (FNA) findings is one of important problems in management of thyroid nodules.

**Objectives:** This study was designed to investigate the consistency of ultrasonography, FNA and histopathology findings in thyroid nodules.

**Patients and Methods:** In this descriptive study, 93 patients who were candidate for thyroid surgery were included. Data on ultrasound-guided fine-needle aspiration of the thyroid and histopathologic results before and after surgery were considered. The Cramér's V and Fisher's exact tests were conducted for this study.

**Results:** In patients whose ultrasound (US) results were low-suspicious, we observed a significant correlation between FNA and pathology results (Cramér's V = 0.574, P = 0.037). However, relationship between FNA and pathology was not accessible among patients whose ultrasonography results were intermediate suspicious or high-suspicious due to insufficient number of samples.

**Conclusion:** In our study, a significant correlation was observed between FNA and pathology results in low-suspicious nodules.

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## Introduction

Thyroid nodules are considered as discrete lesions in the thyroid gland which may or may not be palpable and radiology are distinct from thyroid parenchyma (1). The frequency of palpable thyroid nodule is higher among women and older patients in developing societies and iodine-decreasing intake (2,3). Based on the epidemiological data, the frequency of nodules varies in different discovery methods, 19% to 68% ultrasonography, 2%-6% (palpation) and 8%-65% (autopsy) (4,5). In recent years, the diagnosis of thyroid nodules was increased, which is largely due to more availability and widespread use of imaging methods such as ultrasonography to examine patients' symptoms (6). Although most of the nodules are benign, the risk of thyroid cancer is estimated at 7%-15% in all cases. Moreover, different factors like family history, gender, age and history of radiation exposure are

## Key point

Thyroid nodules are considered as a frequent clinical problem. The great majority of thyroid nodules are benign, however malignancy probability is predicted to be 5%-10%. Around 93 patients who were candidate for thyroid surgery were studied. Data on ultrasound-guided fine-needle aspiration of the thyroid and histopathologic results before and after surgery, were evaluated. Based on our findings, when a nodule is classified in low-suspicious category, a significant correlation was seen between fine-needle aspiration and pathology results.

considered the clinical significance for nodules malignancy (7,8). Since 1966, thyroid ultrasound (US) has been conducted to confirm the presence of nodules and detect thyroid disorders at early stages. Ultrasonography findings can evaluate the shape, composition, margin and type of calcification of nodules (9,10). Nodules that need to be further examined based on imaging



finding are subjected to fine needle aspiration (FNA) biopsy. Fine-needle aspiration is the most appropriate, safe, and affordable method. However, the inadequate sample and the similarities between benign and malignant cytology in some cases are the limitations of this method, which has led to reconsideration of the ultrasonographic features of the nodules in planning the surgery (11-13). Furthermore, determination of sonographical findings in malignant nodules may be more effective and practical in evaluation of thyroid nodules (14). Thyroidectomy is used for malignant or suspicious for malignancy cytology or molecular-based finding and includes (a) a near-total or total thyroidectomy should be considered for patients with thyroid cancer >4 cm, or with gross extra-thyroidal extension (clinical T4), or clinically apparent metastatic disease to nodes (clinical N1) or distant sites (clinical M1), (b) bilateral (near-total or total thyroidectomy) or a unilateral (lobectomy) procedure should be considered for patients with thyroid cancer >1 cm and <4 cm without extra-thyroidal extension, and without clinical evidence of any lymph node metastases (cN0), (c) initial surgical procedure should be lobectomy in patients with thyroid cancer <1 cm without extra-thyroid invasion; unless there is a clear indication to remove another loop (14). One of the important problems in managing the diagnostic and therapeutic process of thyroid nodules is the discrepancy between the ultrasonography and FNA cytology. In such cases, post-surgical pathology will confirm correctness of each of the findings prior to surgery (ultrasonography and FNA cytology) as a definitive method.

### Objectives

Therefore, the aim of this study was to determine the consistency between ultrasonography, FNA cytology and histopathology findings in thyroid nodules. Findings of this study can be helpful in the determination of predicting and diagnosing the nature of thyroid nodules before surgery.

### Patients and Methods

#### Study design

Out of 1000 referred patients, 93 cases were selected. Patients who were referred to the endocrinology clinic of Imam Reza hospital in Tabriz, Iran during 12 months for performing of FNA of thyroid nodule, were evaluated. For these patients, ultrasonography and FNA were conducted by an experienced radiologist and endocrinologist, respectively. Then the fine-needle aspiration (FNA) specimens were examined by a skilled pathologist. Thyroid nodules were assessed by sonography (Affiniti 50, Philips) based on American Thyroid Association (ATA) guidelines by localization, size, calcification, shape, margins, echogenicity, contents and vascular patents in ultrasonography with high-resolution and then were divided into five classifications based on these results: benign, very low-suspicion, low-suspicion, intermediate

suspicion and high suspicion. FNA was conducted from thyroid nodules according to ATA sonographic criteria and size cutoff. In addition, sampling was repeated for patients who had insufficient FNA samples. Based on the Bethesda system, thyroid nodules in FNA procedure grouping was determined non-diagnostic or unsatisfactory, benign, atypia of undetermined significance, follicular neoplasm/suspicious for follicular neoplasm (FN/SFN), suspicious for malignancy and malignant (14).

During the study, considering the existence of an indication, 93 patients underwent surgery. Subjects with prior history of thyroid cancer or prior FNA were excluded from the study. Finally, the obtained reports from the ultrasonography, FNA cytology and histopathology were compared with each other.

#### Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 16. Variables were analyzed for normality by Kolmogorov-Smirnov test. The results were reported as number (percent) for qualitative variables and mean  $\pm$  SD (standard deviation) for quantitative variables. Fisher's exact test was used for assessment of independence between the results of ultrasonography, FNA and histopathology procedures. Cramér's V coefficient test was used for analyzing the correlation between reported results of these three procedures.  $P \leq 0.05$  was considered for statistically significant outcomes.

### Results

#### Clinical profile of the subjects

Among enrolled patients in this study, 73.1% (68) were female. The mean age of the subjects was  $42.98 \pm 11.51$  (22-71 years old). After surgery, the thyroid nodule of 19.4% (18 cases) of patients was diagnosed as benign and the others, 80.6% (75 cases), were diagnosed as malignant. Additionally, it was reported that the malignancy in women was higher than men (Table 1).

#### Correlation analysis between ultrasonography and FNA diagnostic methods

Table 2 shows the correlation between two diagnostic methods of ultrasonography and FNA. Accordingly, 36 patients were diagnosed as low-suspicious from the viewpoint of ultrasonography. However, according to FNA results, 5.6%, 63.9%, 8.3%, 2.8%, 8.3% and 11.1% were diagnosed as non-diagnostic or unsatisfactory, benign, atypia of undetermined significance, follicular neoplasm, suspected to be malignant and malignant, respectively. In addition, 19 and 38 subjects were diagnosed to be intermediate suspicious and high-suspicious based on the ultrasonography findings. According to FNA for the first group, 5.3%, 5.3%, 47.4% and 42.1% were diagnosed as atypia of undetermined significance, follicular neoplasm, suspected to be malignant and malignant, respectively. According to FNA for the second group,

**Table 1.** Clinical Characteristics of patients

Characteristics	
Gender	
Female	68 (73.1%)
Male	25 (26.9%)
Age (year)	42.98±11.51
Pathologic findings	
Malignant pathology	75 (80.6%)
Malignancy	
Male	18 (73.9%)
Female	57 (82.4%)

Data are presented as mean ± SD or number (percent).

2.6%, 7.9%, 7.9%, 13.2% and 68.4% were diagnosed as atypia of undetermined significance, follicular neoplasm, suspected to be malignant and malignant, respectively. The correlation coefficient Cramér's V of FNA and ultrasonography results was estimated as 0.578, which was statistically significant ( $P < 0.0001$ ).

#### Evaluation of correlation between ultrasonography and pathologic diagnostic methods

Table 3 shows the correlation between ultrasonography

and pathologic as diagnostic methods. According to ultrasonography results, 36, 19 and 38 patients were diagnosed as low-suspicious, intermediate suspicious and high-suspicious, respectively. After pathological examination, 50% of the subjects were diagnosed as malignant in the first group since, 100% of the second and third groups were malignant. The correlation coefficient Cramér's V of these two methods was 0.616 was statistically significant ( $P < 0.0001$ ).

#### Evaluation of correlation between FNA and pathologic diagnostic methods

The correlation between two diagnostic methods of FNA and pathology was measured based on Table 4. According to this table, based on FNA findings, 2, 24, 7, 5, 17 and 38 patients were diagnosed as non-diagnostic or unsatisfactory, atypia of undetermined significance, follicular neoplasm, suspected to be malignant and malignant, respectively. After pathologic analysis, 50%, 33.3%, 85.7%, 100%, 100% and 100% of our six groups in this table were diagnosed as malignant. According to the obtained data, the correlation coefficient of these two methods was determined as 0.734, which was statistically significant ( $P < 0.0001$ ).

**Table 2.** Correlation of US and FNA diagnostic methods

US	Number	FNA	Number (%)	Cramer's v	P value <sup>a</sup>
Low suspicious	36	Non-diagnostic or dissatisfied	2 (5.6%)	0.584	<0.0001
		Benign	23 (63.9%)		
		Atypia of undetermined significance	3 (8.3%)		
		Follicular neoplasm	1 (2.8%)		
		Suspected malignancy	3 (8.3%)		
		Malignant	4 (11.1%)		
Intermediate suspicious	19	Atypia of undetermined significance	1 (5.3%)		
		Follicular neoplasm	1 (5.3%)		
		Suspected malignancy	9 (47.4%)		
High suspicious	38	Malignant	8 (42.1%)		
		Benign	1 (2.6%)		
		Atypia of undetermined significance	3 (7.9%)		
		Follicular neoplasm	3 (7.9%)		
		Suspected malignancy	5 (13.2%)		
		Malignant	26 (68.4%)		
US		FNA		0.584	<0.0001

Data are presented as number or percent.  $P \leq 0.05$  was considered as statistically significant. Fisher exact test, FNA: fine needle aspiration.

**Table 3.** Correlation of US and pathology diagnostic methods

US	Number	Pathology		Cramér's V	P value <sup>a</sup>
		Benign No. (%)	Malignant No. (%)		
Low suspicious	36	18 (50%)	18 (50%)	0.616	<0.0001
Intermediate suspicious	19	0	19 (100%)		
High suspicious	38	0	38 (100%)		
US				0.616	<0.0001

Data are presented as number or percent.  $P \leq 0.05$  was considered as statistically significant. <sup>a</sup>Fisher exact test.

### Evaluation of correlation between ultrasonography, FNA and pathology diagnostic methods

Table 5 shows the correlation between three ultrasonography, FNA and pathology diagnostic methods. About 36 patients were diagnosed as low-suspicious from the viewpoint of ultrasonography results. However, according to the FNA and pathologic findings, two patients were non-diagnostic or unsatisfactory of which one patient (50%) was post-surgery diagnosed malignant and the other was diagnosed benign. In addition, 23 patients were benign, which after surgery 16 (69.6%) were determined as benign and the remained were malignant in seven (30.4%) patients. Three patients were atypia of undetermined significance, which 1 (33.3%) of them was benign and 2 (66.7%) cases were malignant. In addition, patients who were diagnosed as follicular neoplasm,

individuals suspected to be malignant (three patients) and malignant (four patients), 100% were postoperatively determined as malignant lesions. The *P* value was 0.006 based on Fisher's exact test and 0.037 according to the Cramér's V test. The correlation coefficient of these three methods in low-suspicious group was calculated as 0.574, which was statistically significant ( $P < 0.0001$ ). In other groups, the correlation coefficient was not assessable.

### Discussion

Ultrasonography features are utilized to detect risk of malignancy in thyroid nodules (7,18). In addition, FNA method has high sensitivity and specificity in diagnosis of papillary and medullary carcinomas (19,20). Herein, thyroid nodules of 93 patients were assessed by ultrasonography, FNA and histopathological procedures

Table 4. Correlation of FNA and pathology diagnostic methods

FNA	Number	Pathology		Cramér's V	P value <sup>a</sup>
		Malignant No. (%)	Benign No. (%)		
Non-diagnostic or dissatisfied	2	1 (50)	1 (50)		
Benign	24	8 (33.3)	16 (66.7)		
Atypia of undetermined significance	7	6 (85.7)	1 (14.3)		
Follicular neoplasm	5	5 (100)	0 (0)		
Suspected malignancy	17	17 (100)	0 (0)		
Malignant	38	38 (100)	0 (0)		
<b>Ultrasonography</b>				<b>0.734</b>	<b>&lt;0.0001</b>

$P \leq 0.05$  was considered as statistically significant, <sup>a</sup> Fisher exact test ; FNA: fine needle aspiration

Table 5. Correlation between US, FNA and pathology diagnostic methods

US	Number	FNA	Pathology		P value
			Benign No. (%)	Malignant No. (%)	
Low suspicious	36	Non-diagnostic or dissatisfied	1 (50)	1 (50)	The <i>P</i> value based on Fisher Exact Test was 0.006 and according to Cramér's V was 0.037 (Cramér's V = 0.574).
		Benign	16 (69.6)	7 (30.4)	
		Atypia of undetermined significance	1 (33.3)	2 (66.7)	
		Follicular neoplasm	0 (0)	1 (100)	
		Suspected malignancy	0 (0)	3 (100)	
		Malignant	0 (0)	4 (100)	
Intermediate suspicious	19	Non-diagnostic or dissatisfied	0 (0)	0 (0)	Not assessable
		Benign	0 (0)	0 (0)	
		Atypia of undetermined significance	0 (0)	1 (100)	
		Follicular neoplasm	0 (0)	1 (100)	
		Suspected malignancy	0 (0)	9 (100)	
		Malignant	0 (0)	8 (100)	
High suspicious	38	Non-diagnostic or dissatisfied	0 (0)	0 (0)	Not assessable
		Benign	0 (0)	1 (100)	
		Atypia of undetermined significance	0 (0)	3 (100)	
		Follicular neoplasm	0 (0)	3 (100)	
		Suspected malignancy	0 (0)	5 (100)	
		Malignant	0 (0)	26 (100)	

$P \leq 0.05$  was considered as statistically significant. FNA: fine needle aspiration.

and it was compared the gathered findings from these three methods and discordance between them was evaluated in diagnosis of malignancy of thyroid nodule.

So far, various studies have been conducted to identify benign and malignant features of thyroid nodules (11, 13,21-24). Kwak et al classified thyroid nodules into four groups based on their ultrasonographic features; malignant, suspicious to be malignant, undetermined and benign cases. Some of the ultrasonographic features that predict an increased risk of malignancy include hypoechogenicity, existence of micro-calcification, irregular margin or lobular and longer shape or pattern of taller than wide (11). Additionally, Kwak et al declared that malignancy rate was 84% for malignancy suspicious nodules based on FNA biopsy. When the thyroid nodules had suspicious ultrasonographic features, the malignancy rate was significantly high (96.4%) compared to that of thyroid nodules with no suspicious ultrasonographic features (25.5%). Hassan et al reported that the combination of ultrasonography and cytopathology greatly reduces the false negative reports of FNA, prevents cancer diagnosis delay and leads to rapid treatment of possible cancer cases (21). In addition, Prasad et al emphasized the diagnostic value and importance of FNA in the diagnosis of benign nodules (13). They also suggested that FNA could be a support for ultrasonography in detecting malignancies. Although FNA could also be conducted in some cases (including some types of follicular cancers), researchers have not been able to overlook the importance of ultrasonography in detecting malignancies.

The diagnosis of thyroid nodules is conducted with ultrasonography in 19-68% of patients, while there is higher frequency among women and elderly individuals. As discussed before, thyroid nodules of >1 cm in diameter have potential to become malignant and they should be further examined. Further evaluation should be considered in nodules of <1 cm if there are clinical signs or lymphadenopathy (13, 25).

On the other hand, other studies have pointed to the cancer probability in FNA results as suspicious for malignancy and it was recommended for thyroidectomy procedures regardless of the ultrasonography results. According to FNA results, Sclabas et al reported thyroid nodules of 240 patients as malignant (32%), benign (22%), undetermined in terms of malignancy (42%) and non-diagnostic (5%) (22). However, 4% of FNA results in postoperative pathology results of tissue samples were reported as false positive since 4% were reported as false negative. In addition, after pathology procedure, 27% of atypia of undetermined significance in terms of FNA diagnosis were determined as malignant among which 15%, 20% and 82% were reported as follicular neoplasms, Hurthle cell neoplasms and suspicious for papillary carcinoma, respectively (23,24). Likewise, Lee et al demonstrated a lower diagnostic value in ultrasonography than cytology (26). Additionally, the obtained results from

Marqusee et al suggested that ultrasonography should be considered for thyroid nodules that are suspicious of malignancy (18). Moreover, a decrease in discordance was observed in US-guided FNAs compared to pathologist-performed palpation-guided FNA in the study by Conrad et al (27).

The obtained results from this study showed that 19.4% of patients were diagnosed benign and 80.6% were diagnosed as malignant among 93 studied patients. Based on ultrasonographic features, diagnosis results of 36 patients were low-suspicious, 19 patients were intermediate suspicious and 38 patients were high suspicious. Around half of patients in the first group and whole patients in the second and third groups were diagnosed with malignant lesions after pathological assessment. In addition, Cramér's V correlation coefficient showed a statistically significant correlation between FNA and pathology results in patients with ultrasonography results of low- suspicious.

During the current study, we observed a discordance between diagnosis results of ultrasonography and pathology in some cases. Thyroid nodules of 36 patients were diagnosed as low-suspicious by ultrasonography method, however among these patients 1 patient (2.8%) was diagnosed follicular neoplasm, 3 patients (8.3%) were diagnosed suspicious for malignancy and 4 patients (11.1%) were diagnosed malignant by FNA test. Totally, 22.2% thyroid nodules of patients were diagnosed low-suspicious.

Around, 50% of our patients diagnosed as low-suspicious in ultrasonography were detected to be malignant after histopathological examination. This figure suggests the need for further examination of thyroid nodules by complementary methods.

In our study also, an inconsistency in thyroid nodules of 50% of patients with low-suspicious nodules who were diagnosed malignant after surgery by histopathology was seen. It can be justified by two reasons. First, the presence of small malignant nodules adjacent to the nodules that were interpreted as low-suspicious in the ultrasonography, has changed the pathology results (including 15 patients). The second reason was lack of clear radiology reports and simultaneous reporting features of low and high-suspicious criteria that have made the possible interpretation error in the nodule characteristics (including three cases of patients). Since, the nature of the nodules in multinodular goiter was not reported separately in pathology, therefore, the pathology result did not necessarily indicate the nodule that was aspirated before surgery.

## Conclusion

Based on this study, a significant relationship was observed between FNA and pathology results among patients whose ultrasonography findings were reported to be low-suspicious. However this condition, maybe due to insufficient number of samples. We found, among patients whose results of sonography were intermediate and highly



suspicious, the relationship between FNA and pathology could not be determined, which may be due to insufficient number of samples. It seems that ultrasonography and FNA cannot lonely help for accurate diagnosis of thyroid nodules since it is necessary to combine obtained results of these two methods. In addition, histopathological examination of thyroid nodules as a definitive method can largely compensate the limitations (shortcomings) of both previous methods.

### Recommendations

Considering the small sample size of the study, it is suggested that a study with large sample size be conducted, in addition, a careful investigation of the consistency between the aspirated nodule and the pathologic report should be done.

### Limitations of the study

Limitations of the study our sample size was relatively low as we excluded some patients because of missing hospital records.

### Authors' contribution

JH designed and directed the whole project. SV carried out the experiments. JH, SV and FN wrote the manuscript. SV analyzed the data. MH and RJR and JJ contributed to sample preparation. AB and NA helped supervise the projec. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

### Conflicts of interest

The authors declare that they have no competing interests.

### Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Tabriz University of Medical Sciences approved this study. The institutional ethical committee at Tabriz University of Medical Sciences approved all study protocols (IR.TBZMED.REC.1397.061). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from M.D., thesis of Soheila Valizadeh at this university. Besides, ethical issues (including plagiarism, data fabrication and double publication) have been completely observed by the authors.

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### References

- Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2006;16:109-42. doi: 10.1089/thy.2006.16.109.
- Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinol (Oxf)*. 1977;7:481-93. doi: 10.1111/j.1365-2265.1977.tb01340.x.
- Vander JB, Gaston EA, Dawber TR. The significance of nontoxic thyroid nodules. Final report of a 15-year study of the incidence of thyroid malignancy. *Ann Intern Med*. 1968;69:537-40. doi: 10.7326/0003-4819-69-3-537.
- Dean DS, Gharib H. Epidemiology of thyroid nodules. *Best Pract Res Clin Endocrinol Metab*. 2008;22:901-11. doi: 10.1016/j.beem.2008.09.019.
- Guth S, Theune U, Aberle J, Galach A, Bamberger CM. Very high prevalence of thyroid nodules detected by high frequency (13 MHz) ultrasound examination. *Eur J Clin Invest*. 2009;39:699-706. doi: 10.1111/j.1365-2362.2009.02162.x.
- Leenhardt L, Bernier MO, Boin-Pineau MH, Conte Devolx B, Maréchaud R, Niccoli-Sire P, et al. Advances in diagnostic practices affect thyroid cancer incidence in France. *Eur J Endocrinol*. 2004;150:133-9. doi: 10.1530/eje.0.1500133.
- Hegedüs L. Clinical practice. The thyroid nodule. *N Engl J Med*. 2004;351:1764-71. doi: 10.1056/NEJMcp031436.
- Mandel SJ. A 64-year-old woman with a thyroid nodule. *JAMA*. 2004;292:2632-42. doi: 10.1001/jama.292.21.2632.
- Smith-Bindman R, Lebda P, Feldstein VA, Sellami D, Goldstein RB, Brasic N, et al. Risk of thyroid cancer based on thyroid ultrasound imaging characteristics: results of a population-based study. *JAMA Intern Med*. 2013;173:1788-96. doi: 10.1001/jamainternmed.2013.9245.
- Brito JP, Gionfriddo MR, Al Nofal A, Boehmer KR, Leppin AL, Reading C, et al. The accuracy of thyroid nodule ultrasound to predict thyroid cancer: systematic review and meta-analysis. *J Clin Endocrinol Metab*. 2014;99:1253-63. doi: 10.1210/jc.2013-2928.
- Kwak JY, Kim EK, Kim MJ, Hong SW, Choi SH, Son EJ, et al. The role of ultrasound in thyroid nodules with a cytology reading of "suspicious for papillary thyroid carcinoma". *Thyroid*. 2008;18:517-22. doi: 10.1089/thy.2007.0271.
- Gardiner GW, de Souza FM, Carydis B, Seemann C. Fine-needle aspiration biopsy of the thyroid gland: results of a five-year experience and discussion of its clinical limitations. *J Otolaryngol*. 1986;15:161-5.
- Prasad CV. Evaluation of correlation between ultrasonography and FNAC of thyroid nodules. *Int Arch Integr Med*. 2016;3:92-7.
- Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2016;26:1-133. doi: 10.1089/thy.2015.0020.
- Mehta RS, Carty SE, Otori NP, Hodak SP, Coyne C, LeBeau SO, et al. Nodule size is an independent predictor of malignancy in mutation-negative nodules with follicular lesion of undetermined significance cytology. *Surgery*. 2013;154:730-6; discussion 6-8. doi: 10.1016/j.surg.2013.05.015.
- Yoo WS, Choi HS, Cho SW, Moon JH, Kim KW, Park HJ, et al. The role of ultrasound findings in the management of thyroid nodules with atypia or follicular lesions of undetermined significance. *Clin Endocrinol (Oxf)*. 2014;80:735-42. doi: 10.1111/cen.12348.
- Goldstein RE, Nettekville JL, Burkey B, Johnson JE. Implications of follicular neoplasms, atypia, and lesions suspicious for malignancy diagnosed by fine-needle aspiration of thyroid nodules. *Ann Surg*. 2002;235:656-62. doi: 10.1097/0000658-200205000-00007.
- Marqusee E, Benson CB, Frates MC, Doubilet PM, Larsen PR, Cibas ES, et al. Usefulness of ultrasonography in the management of nodular thyroid disease. *Ann Intern Med*. 2000;133:696-700. doi: 10.7326/0003-4819-133-9-200011070-00011.
- Carmeci C, Jeffrey RB, McDougall IR, Nowels KW, Weigel RJ. Ultrasound-guided fine-needle aspiration biopsy of thyroid masses. *Thyroid*. 1998;8:283-9. doi: 10.1089/thy.1998.8.283.

20. Danese D, Sciacchitano S, Farsetti A, Andreoli M, Pontecorvi A. Diagnostic accuracy of conventional versus sonography-guided fine-needle aspiration biopsy of thyroid nodules. *Thyroid*. 1998;8:15-21. doi: 10.1089/thy.1998.8.15.
21. Hassan QA, Asghar AA, Hadi MA. Sonographic-pathologic correlation in an ultrasound-guided fine needle aspiration of a thyroid nodule: concordant or discordant? *Int J Med Res Health Sci*. 2018;5:148-58.
22. Sclabas GM, Staerke GA, Shapiro SE, Fornage BD, Sherman SI, Vassilopoulos-Sellin R, et al. Fine-needle aspiration of the thyroid and correlation with histopathology in a contemporary series of 240 patients. *Am J Surg*. 2003;186:702-10. doi: 10.1016/j.amjsurg.2003.08.015.
23. Bakhos R, Selvaggi SM, DeJong S, Gordon DL, Pitale SU, Herrmann M, et al. Fine-needle aspiration of the thyroid: rate and causes of cytohistopathologic discordance. *Diagn Cytopathol*. 2000;23:233-7. doi: 10.1002/1097-0339(200010)23:4<233::aid-dc3>3.0.co;2-l.
24. Blansfield JA, Sack MJ, Kukora JS. Recent experience with preoperative fine-needle aspiration biopsy of thyroid nodules in a community hospital. *Arch Surg*. 2002;137:818-21. doi: 10.1001/archsurg.137.7.818.
25. Mortensen JD, Woolner LB, Bennett WA. Gross and microscopic findings in clinically normal thyroid glands. *J Clin Endocrinol Metab*. 1955;15:1270-80. doi: 10.1210/jcem-15-10-1270.
26. Lee YJ, Kim DW, Park YM, Park HK, Jung SJ, Kim DH, et al. Comparison of sonographic and cytological diagnoses of solid thyroid nodules: Emphasis on the discordant cases. *Diagn Cytopathol*. 2015;43:953-9. doi: 10.1002/dc.23363.
27. Conrad R, Yang SE, Chang S, Bhasin M, Sullivan PS, Moatamed NA, et al. Comparison of cytopathologist-performed ultrasound-guided fine-needle aspiration with cytopathologist-performed palpation-guided fine-needle aspiration: a single institutional experience. *Arch Pathol Lab Med*. 2018;142:1260-7. doi: 10.5858/arpa.2017-0123-OA.