

Study on the effectiveness and accuracy of ultrasound diagnosis and pathological diagnosis of thyroid lesions

L. Xiuming¹ and L. Fuxing^{2*}

¹Department of Ultrasound, Taizhou People's Hospital, Taizhou, China

²Department of Pathology, Taizhou People's Hospital, Taizhou, China

ABSTRACT

► Original article

*Corresponding author:

Liu Fuxing,

E-mail: liufx1214@sina.com

Received: January 2024

Final revised: January 2024

Accepted: February 2024

Int. J. Radiat. Res., July 2024;
22(3): 727-732

DOI: 10.61186/ijrr.22.3.727

Keywords: Thyroid neoplasms; ultrasonography; pathology; diagnostic accuracy.

Background: To explore the effectiveness and accuracy of ultrasound diagnosis and pathological diagnosis of thyroid lesions. **Materials and Methods:** Seventy patients who presented to our institution with thyroid lesions between January 2021 and March 2023 were analyzed retrospectively. All patients underwent ultrasound and pathological examination. The precision of ultrasonography diagnosis in relation to histological diagnosis of thyroid lesions was compared. **Results:** There were a total of 70 patients analyzed, with pathological diagnosis revealing 34 cases of malignant and 36 cases of benign thyroid lesions; The ultrasound diagnosis had a 91.43% (64/70) success rate when compared to the pathological diagnosis, and there was no statistically significant difference between the two ($P > 0.05$). When comparing ultrasound diagnosis to pathological diagnosis results for thyroid cancer categorization, there was no statistically significant difference ($P > 0.05$). Thyroid lesions can be accurately diagnosed using ultrasound, and the method shows no statistically significant decrease in sensitivity, specificity, or accuracy when compared to pathological diagnosis ($P > 0.05$). **Conclusion:** In clinical practice, ultrasonography can be used to detect benign from malignant thyroid lesions, which has essential reference value for early clinical diagnosis and therapy, and ultrasound diagnosis is as effective and accurate as pathological diagnosis.

INTRODUCTION

Thyroid lesions are common diseases in clinic, and their lesions are relatively special, including not only benign lesions such as adenoma and goiter, but also malignant lesions such as undifferentiated carcinoma, medullary carcinoma and papillary carcinoma. The first symptom of thyroid lesions is nodule, and malignant transformation can occur along with the disease progression ⁽¹⁾. Malignant tumors of the thyroid, also known as thyroid follicular epithelium, are quite prevalent in the endocrine system of the body. It is one of the more prevalent head and neck malignant tumors, making up between 1.0% and 2.3% of all malignant tumors across the body and 5.1% of head and neck tumors. Due to its high degree of deterioration, low differentiation degree, long incubation period, and high mortality, it should arouse great clinical attention ^(2,3). For thyroid diseases with different lesions, the clinical treatment methods are completely different, so the qualitative diagnosis of thyroid lesions is of great significance for clinical diagnosis and treatment ⁽⁴⁾. Although it has been demonstrated through years of clinical experience that early identification, diagnosis, and treatment can greatly enhance patients' quality of life, misdiagnosis and missed diagnosis are common due to the lack of important clinical signs exhibited by thyroid lesions in the course of clinical practice ⁽⁵⁾.

However, the pathological diagnosis is the gold standard for diagnosing thyroid abnormalities, it can be stressful and may induce adverse reactions, which limits its clinical application ⁽⁶⁾. With the rapid development of medical industry and increasingly mature imaging technology, ultrasound has a long clinical application time and a wide scope of application. It can effectively clarify the relationship between the lesion and adjacent tissues through high-definition images and high resolution, and then effectively distinguish between benign and malignant. It has a high diagnostic efficiency ^(7,8) and has been widely utilized for the diagnosis of a wide range of thyroid illnesses due to its high safety, low cost, and simple operation. However, there are still few comparative studies on the advantages and disadvantages of ultrasound and pathological diagnosis, which deserve further study. In order to provide a stronger scientific foundation for early clinical diagnosis and treatment, this study aimed to investigate the effects and accuracy of ultrasonic diagnosis and pathological diagnosis of thyroid abnormalities.

Ultrasound diagnosis and pathological diagnosis of thyroid lesions are one of the important directions in thyroid disease research ⁽⁹⁾. The following are possible research directions and their research value and significance: (i); Research on new ultrasound technology and image processing methods to

improve the diagnostic accuracy of thyroid lesions ⁽¹⁰⁾. (ii); To explore the application of artificial intelligence and machine learning in ultrasound image analysis to improve automatic detection and classification of lesions ⁽¹¹⁾. (iii); To analyze the relationship between ultrasound images and pathological results to determine the ultrasound characteristics of different lesions to help better predict pathological types ⁽¹²⁾. (iv); To study the ability of ultrasound to distinguish benign and malignant lesions to provide patients with more accurate diagnosis and treatment suggestions. Combination of ultrasound images with other imaging techniques (such as CT, MRI, *etc.*) might provide comprehensive diagnostic value of multi-modal imaging for thyroid lesions ⁽¹³⁾. Moreover, epidemiological studies might explore the impact of environmental and genetic factors on thyroid lesions ⁽¹⁴⁾.

The novelty of this study lies in its comprehensive evaluation of the effectiveness and accuracy of both ultrasound and pathological diagnoses in detecting and categorizing thyroid lesions. By comparing the precision of ultrasound diagnosis with histological diagnosis and specifically assessing its performance in identifying thyroid cancer, the study contributes valuable insights. The findings indicate that ultrasound is not only highly effective in distinguishing between benign and malignant thyroid lesions but also comparable in accuracy to pathological diagnosis. This holistic examination provides a nuanced understanding of the diagnostic capabilities of ultrasound in the context of thyroid abnormalities, offering important implications for clinical practice and emphasizing its role as a reliable diagnostic tool.

MATERIALS AND METHODS

Patients

A total of 70 patients, 31 males and 39 females, who presented to our hospital with thyroid lesions between January 2021 and March 2023 were retrospectively selected as the study population (table 1, figures 1 and 2). Their average age was (53.58 ± 6.38), and they varied in age from 32 to 71. The average diameter of the nodules was 2.88 ± 0.34 centimeters, with a range of 0.6 5.7 cm. Each subject was scanned sonographically and analyzed pathologically. The hospital's ethics board gave their stamp of approval to this study. Taizhou People's Hospital Ethics Committee, 20237651; 2023-02-04.

Table 1. General information of patients 4.

Patient Characteristics	Total
Total Patients	70
Male	31
Female	39
Age (years)	53.58 ± 6.38 (32 to 71)
Nodule Diameter (cm)	2.88 ± 0.34 (0.6 to 5.7)

Exclusion and criteria of inclusion

Inclusion criteria: ① Thyroid abnormalities were seen in all subjects on postoperative pathology; ② patients undergoing thyroid surgery in our hospital; ③ patients with complete clinical data; ④ patients with normal functions of heart, liver and kidney.

Exclusion criteria: ① patients with history of thyroid surgery; ② patients with coagulation or immune dysfunction; ③ Patients who have taken levothyroxine sodium tablets, antithyroid drugs, iodine and other drugs recently; ④ patients with other tumor diseases; ⑤ Patients with contraindications to surgery and ultrasound.

Methods

Ultrasound detection

First of all, the patient lies supine on the examination bed, with the head tilted backward. After the neck is fully exposed, the thyroid gland of the patient is scanned by color Doppler ultrasound (GE Company, model: GELOGIQ C9). The probe frequency is adjusted to 9 ~ 12 MHz. The extra lesion nature, blood flow distribution, halo ring and boundary echo of the thyroid gland are closely observed. Ultrasonography was performed by the same group of radiologists. Figures 1 and 2 show sample ultrasound images of different thyroid lesions.



Figure 1. Papillary thyroid carcinoma (left); two-dimensional blood flow diagram (right).



Figure 2. Nodular goiter with follicular adenoma (left); two-dimensional image (right).

Criteria for ultrasonic examination

Thyroid carcinoma was diagnosed when a mass of uneven size and different shape appeared with blurred borders, which showed serration and burr, no acoustic halo, abundant internal blood flow, especially arterial blood flow, no blood flow around the mass, and irregular hypoechogenicity in the eyebrow.

Pathological biopsy

At the end of ultrasound, surgery was arranged,

fresh living specimens were collected from the lesion site during surgery, quickly cooled with the help of a constant temperature cryostat, landed with embedding medium, the temperature was controlled at $-18 \sim -20^{\circ}\text{C}$, the sections were frozen for $2 \sim 3$ min, and $3 \sim 5 \mu\text{m}$ section thickness and quickly fixed in fixative, waiting for 30 s. Hematoxylin-eosin was used for staining treatment, and warm water reversion to blue was dehydrated for sealing, waiting for 10 min to slide out, and the sections were analyzed under a microscope.

Observational index

① Identify the differences between the diagnostic efficacy of ultrasound and that of pathology in identifying thyroid lesions; ② Examine the precision of ultrasonography and pathology diagnosis in identifying and separating different types of thyroid cancer; ③ Examine the accuracy of ultrasonography and histological diagnosis in identifying thyroid lesions.

Statistical methods

We used the SPSS 18.0 program for our statistical study. Data were analyzed using a t-test statistic, and the average $\pm$ standard error ($\bar{x} \pm s$) was given; Data reported as either the number of occurrences (N) or a percentage (%) was analyzed using the χ^2 test.

RESULTS

Thyroid diagnosis: Ultrasound vs pathology

There were 70 patients with thyroid lesions included in the study; pathology diagnosis revealed that 34 of these lesions were malignant and 36 were benign. Using the pathological diagnosis findings as the gold standard, table 2 shows that the ultrasonic diagnosis had an accuracy rate of 91.43 (64/70) and showed no significant difference when compared to the pathological diagnosis results ($\chi^2 = 0.025$, $P = 0.886$).

Table 2. Comparison of diagnostic accuracy between ultrasound diagnosis and pathological diagnosis for thyroid lesions (n).

Ultrasound diagnosis	Pathological diagnosis		Total
	Malignant	Benign	
Malignant	31	3	34
Benign	3	33	36
Total	34	36	70

Thyroid cancer typing: Ultrasound vs. pathology

Table 3 compares the performance of ultrasound diagnosis and pathological diagnosis in terms of diagnostic accuracy of thyroid cancer types. Among 34 cases, for papillary thyroid cancer, the accuracy of ultrasound diagnosis was 88.24%, while the accuracy of pathological diagnosis was 91.18%. For follicular thyroid cancer, the accuracy of ultrasound diagnosis is 5.88%, while the accuracy of pathological diagnosis

is 7.58%. The accuracy of medullary thyroid cancer diagnosis in ultrasound was 2.94%, while it was 0.00% in pathological diagnosis. The accuracy rates of ultrasound diagnosis and pathological diagnosis of undifferentiated cancer were both 2.94% and 0.00%. Statistical analysis showed that the χ^2 value was 0.475 and the P value was 0.491, indicating that the difference between ultrasonic diagnosis and pathological diagnosis in the diagnosis of thyroid cancer types was not significant. This suggests that the accuracy of ultrasound diagnosis and pathological diagnosis for thyroid cancer types is similar in this group of samples. It is important to note that the sample size is relatively small, so the results may be limited by the sample size.

Table 3. Comparison of ultrasound diagnosis and pathological diagnosis in the accuracy of thyroid cancer typing diagnosis.

Thyroid cancer typing	Ultrasound diagnosis (n=34)	Pathological diagnosis (n=34)	χ^2 value	P value
Papillary thyroid cancer	30 (88.24)	31 (91.18)	0.475	0.491
Follicular thyroid cancer	2 (5.88)	3 (7.58)		
Medullary carcinoma	1 (2.94)	0 (0.00)		
Undifferentiated carcinoma	1 (2.94)	0 (0.00)		

Ultrasound vs. pathology: Thyroid diagnosis

Table 4 compares the performance of ultrasonic diagnosis and pathological diagnosis in the diagnosis of thyroid lesions, covering all aspects of diagnostic performance. The sensitivity of ultrasound diagnosis was 91.18%, that is, 31 out of 34 cases were correctly diagnosed, while the sensitivity of pathological diagnosis was 100.00%, and all 70 cases were correctly diagnosed. The χ^2 value is 0.372 and the P value is 0.708, indicating that the difference between the two in terms of sensitivity is not significant. The specificity of ultrasound diagnosis was 91.67%, that is, 33 out of 36 cases were correctly excluded, while the specificity of pathological diagnosis was 100.00%, and all 70 cases were correctly excluded. The χ^2 value was 0.459 and the P value was 0.639, indicating that the difference between the two in terms of specificity was not significant. The overall accuracy of ultrasound diagnosis was 91.43%, that is, 64 out of 70 cases were correctly diagnosed, while the overall accuracy of pathological diagnosis was 100.00%, and all 70 cases were correctly diagnosed. The χ^2 value is 0.454 and the P value is 0.501, indicating that the difference between the two in terms of accuracy is not significant. Taken together, the table shows that ultrasound diagnosis and pathological diagnosis have similar performance in sensitivity, specificity, and overall accuracy, and the difference is not significant in statistical analysis. This may indicate that ultrasound diagnosis is comparable in the diagnosis of thyroid lesions in this group of samples. It is important to note that the effect of sample size on the results may require more research to confirm.

Table 4. Comparison of ultrasound diagnosis and pathological diagnosis in the diagnosis of thyroid lesions.

Diagnostic efficacy	Ultrasound diagnosis	Pathology diagnosis	χ^2 value	P value
Sensitivity	91.18(31/34)	100.00(70/70)	0.372	0.708
Specificity	91.67(33/36)	100.00(70/70)	0.459	0.639
Accuracy	91.43%(64/70)	100.00(70/70)	0.454	0.501

DISCUSSION

Bad living habits, negative emotions, unbalanced nutrition, and irregular diet can all lead to thyroid lesions. However, studies have found that with the development of society, changes in living and eating habits, and the increase of work pressure, the thyroid lesion rate significantly increases and continues to show an increasing trend^(15,16). Although patients can obtain a long survival time after effective treatment, the overall prognosis is not ideal, and early diagnosis is of great clinical significance to improve the prognosis of patients⁽¹⁷⁾. Early screening of thyroid lesions is quite difficult. Thyroid lesions, without typical clinical symptoms, are easily ignored by patients and clinical practice. In addition to its special physiological structure, they are easily missed or misdiagnosed, which may cause delay of the disease and affect the prognosis of the body⁽¹⁸⁾. Nodule boundary, echo, and morphology may all be visualized with ultrasound, making it the imaging modality of choice for clinical diagnosis of thyroid illness⁽¹⁹⁾. However, there are few studies exploring the effect and accuracy rate of ultrasonic diagnosis and pathological diagnosis of thyroid lesions. Compared to the pathological diagnosis, the ultrasound diagnosis of thyroid lesions was shown to be highly effective and accurate, as shown by the results of this study. The reasons are now analyzed as follows.

Galimzianova *et al.*⁽²⁰⁾ showed that ultrasonography was beneficial to predict benign and malignant thyroid nodules; 86.67 percent sensitivity, 28.57 percent specificity, and 80.60 percent accuracy were found by Li *et al.*^(21,22) when using ultrasonography to diagnose thyroid carcinoma; in this study, ultrasonography was found to be 91.43% accurate, 91.18% sensitive, and 91.67% specific in the identification of thyroid abnormalities, and thyroid cancer could be effectively classified, with no significant difference compared with the results of pathological diagnosis, which was basically consistent with the results of Galimzianova and Li studies, indicating that ultrasound could effectively diagnose thyroid lesions, and the causes were analyzed: thyroid cancer is a malignant thyroid lesion, which is an endocrine disease with a quite high clinical incidence, cancer cells can metastasize with blood circulation, causing invasive spread and growth, if no active and effective diagnosis and treatment were given, it will not only seriously affect

the body's thyroid function, but even cause death^(23,24). Although surgery can successfully slow the progression of the disease, it also has no typical clinical symptoms in the early stages of the illness, and it is not until the middle and advanced stages that significant clinical symptoms start to appear. Early identification and treatment are crucial since failing to perform surgical resection at the ideal time makes recovery more difficult⁽²⁵⁾. Surgical pathological diagnosis is the gold standard for clinical diagnosis of minimal change disease of the thyroid gland, but it is carried out after surgery, but it is necessary to determine the surgical plan according to the clear diagnostic results before surgery, so it is important to find an efficient preoperative diagnostic method for clinical treatment⁽²⁶⁾. Ultrasound has become increasingly commonplace in clinical practise, especially for diagnostic purposes⁽²⁷⁾, thanks to the rapid advancement of imaging technology and the upgrade of imaging equipment in recent years. Ultrasound, as one of the main means of diagnosing thyroid diseases, has high resolution, can scan the thyroid gland with the help of ultrasound probe, can dynamically display the organ movement and blood flow status, real-time examination of various parts of the body and any direction, clarify the location of the lesion and the relationship with the surrounding tissues, and quickly obtain the examination results, and can also be repeatedly examined for many times, with ideal accuracy and convenience, in addition, it also has non-invasive, rapid, simple, low price and other characteristics^(28,29). According to thyroid classification, thyroid cancer mainly occurs from follicular epithelial cells, and there are many types of cancer, while the most common is papillary carcinoma, the main feature is lymphatic metastasis, so the imaging characteristics are malignant tumor generality, the image is significantly irregular, and there are obvious echoes in the internal and boundary tissues, which can be significantly distinguished from benign lesions. Examination of the parenchymal part of the tumor can observe the lesion showed significant fibrosis, the tumor showed papillary bulge inside, and contained large and small cysts, with significant image characteristics; follicular thyroid cancer is moderately malignant, the image is mainly single round, with obvious boundaries with adjacent tissues, while calcified plaque shadows can be observed, with significant image characteristics; ultrasonography found medullary carcinoma has solid structure, oval or round nodules, without obvious capsule, blurred boundary with adjacent thyroid tissue, with slightly low internal echoes, without significant liquefaction; undifferentiated carcinoma has solid nodules, with irregular shape, blurred boundary, there are thick internal echoes, which belong to highly malignant tumors, mainly occur in the elderly population, It has a low incidence and poor prognosis^(30,31). However, ultrasound also

has a missed diagnosis rate or misdiagnosis rate, which may be due to the increased complexity of the image caused by the crossing of benign lesions and malignant lesions. In addition, the characteristics of early microcarcinoma in calcification, clear boundary, specificity, etc. are not significant, so it is also necessary to carry out the diagnosis by experienced personnel, while continuously improving their professional ability, and then effectively improving the accuracy of diagnosis.

The overall accuracy of ultrasound diagnosis was 91.43%, while the accuracy of pathological diagnosis was 100.00%. Although ultrasound diagnosis performs well, it is still slightly inferior to pathological diagnosis in terms of accuracy. In terms of papillary thyroid cancer, the accuracy of ultrasound diagnosis and pathological diagnosis were 88.24% and 91.18% respectively. For other types of thyroid cancer, the accuracy is lower, and in some cases ultrasound diagnosis is even nil. The results of statistical analysis showed that there was no significant difference between ultrasound diagnosis and pathological diagnosis in terms of diagnostic accuracy of thyroid cancer types. This suggests that they behave similarly in this sample. The sensitivity of ultrasound diagnosis was 91.18% and the specificity was 91.67%. In contrast, pathological diagnosis achieved 100.00% in both aspects. However, no significant differences between sensitivity and specificity were found in statistical analyses. The study acknowledges that the sample size was relatively small, so the results may be limited. This emphasizes the importance of further studies with larger sample sizes to confirm these findings. Taken together, although diagnostic ultrasound performs well in some aspects, larger studies are needed to validate these findings due to limited sample size. Furthermore, although there was some difference in overall accuracy, no significant differences were found between ultrasound diagnosis and pathological diagnosis in the diagnosis and statistical analysis of thyroid cancer types.

It is possible that the limited sample size in this study introduced bias into the results, hence further samples will need to be obtained at a later time to confirm the conclusions of this study.

In conclusion, ultrasonic identification of thyroid abnormalities is equally effective and accurate as histological diagnosis. The usefulness of ultrasound in distinguishing between benign and malignant thyroid lesions warrants consideration in clinical practice.

ACKNOWLEDGMENTS

We express gratitude to Li Xiuming, Liu Fuxing for their support and contributions to this study.

Funding: No funding.

Conflicts of Interest: The authors declare no conflicts

of interest related to this study.

Ethical Consideration: This study was conducted in accordance with ethical principles, and approval was obtained from the Institutional Review Board or Ethics Committee. All participants provided informed consent.

Author Contributions: Both authors L.X. and L.F. contributed to the work equally.

REFERENCES

1. Ravella L, Lopez J, Descotes F, Gai J, Lapras V, Denier ML, et al. Cytological features and nuclear scores: Diagnostic tools in pre-operative fine needle aspiration of indeterminate thyroid nodules with RAS or BRAF K601E mutations? *Cytopathology*. 2021; **32**(1): 37-44.
2. Kim HJ, Lee HJ, Jung JH, Kim WW, Park JY, Shin KM, et al. Ultrasound Assessment of Synchronous Thyroid Nodules in Patients With Papillary Thyroid Cancer: A Nodule-by-nodule Analysis Between Ultrasound and Pathology. *Anticancer Res*. 2020; **40**(3): 1779-86.
3. Pereira M, Williams VL, Hallanger Johnson J, Valderrabano P. Thyroid Cancer Incidence Trends in the United States: Association with Changes in Professional Guideline Recommendations. *Thyroid*. 2020; **30**(8): 1132-40.
4. Xavier-Júnior JCC, Zogheib RJP, Camilo-Júnior DJ, D'ávila S CGP, Mattar NJ. An alternative method for smear preparation of fine-needle aspiration cytology of cystic thyroid lesions: Evaluation of sample adequacy. *Diagn Cytopathol*. 2020; **48**(11): 1054-7.
5. Frates MC, Parziale MP, Alexander EK, Barletta JA, Benson CB. Role of Sonographic Characteristics of Thyroid Bed Lesions Identified Following Thyroidectomy in the Diagnosis or Exclusion of Recurrent Cancer. *Radiology*. 2021; **299**(2): 374-80.
6. Yuan L, Jebastin Thangaiiah J, Chute DJ. The Role of Ultrasound-Guided Fine-Needle Aspiration of Thyroid Bed Lesions and Clinical Predictors of Recurrent Papillary Thyroid Carcinoma. *Am J Clin Pathol*. 2021; **155**(3): 389-96.
7. Lee JY, Kim JH, Yeon EK, Hwang I, Yoo RE, Kang KM, et al. Computed tomography complements ultrasound for the differential diagnosis of traumatic neuroma from recurrent tumor in patients with post-operative thyroid cancer. *Eur Radiol*. 2022; **32**(4): 2760-8.
8. Iqbal MA, Wang X, Guoliang Z, Moazzam NF, Shahid AD, Qian X, et al. A comparison of the efficiency of diagnostic ultrasound and magnetic resonance imaging of cervical lymph nodes in papillary thyroid carcinoma. *J Xray Sci Technol*. 2021; **29**(6): 1033-44.
9. Zhu H, Yu B, Li Y, Zhang Y, Jin J, Ai Y, et al. Models of ultrasonic radiomics and clinical characters for lymph node metastasis assessment in thyroid cancer: a retrospective study. *PeerJ*. 2023; **11**:e14546.
10. Liu K, Gao M, Qin D, Wang H, Lu Q. Serous BMP8A has Clinical Significance in the Ultrasonic Diagnosis of Thyroid Cancer and Promotes Thyroid Cancer Cell Progression. *Endocr Metab Immune Disord Drug Targets*. 2020; **20**(4): 591-8.
11. Wang J, He X, Ma L, Li M, Sun L, Jiang J, et al. Multimode ultrasonic technique is recommended for the differential diagnosis of thyroid cancer. *PeerJ*. 2020; **8**:e9112.
12. Liu Y, Huang J, Zhang Z, Huang Y, Du J, Wang S, et al. Ultrasonic Characteristics Improve Prediction of Central Lymph Node Metastasis in cN0 Unifocal Papillary Thyroid Cancer. *Front Endocrinol (Lausanne)*. 2022; **13**: 870813.
13. Becker JH and Ghooor F. Tumour reduction with a Cavitron Ultrasonic Surgical Aspirator® in the palliative care of anaplastic thyroid cancer. *S Afr J Surg*. 2016; **54**(2): 43-4.
14. Oka A and Fujimoto Y. Ultrasonic diagnosis of thyroid cancer]. *Horumon To Rinsho*. 1969; **17**(9): 733-8.
15. Li S, Xu Z, Li H, Tang J, Liang XY, Tian S, et al. An Observational and Cross-Sectional Study of the Prevalence of Breast Lesions and Metabolic Dysfunction-Associated Fatty Liver Disease and their Relationship in China. *J Gastrointest Liver Dis*. 2022; **31**(1): 31-9.
16. Poma AM, Condello V, Denaro M, Torregrossa L, Elisei R, Vitti P, et al. DICER1 somatic mutations strongly impair miRNA processing even in benign thyroid lesions. *Oncotarget*. 2019; **10**(19): 1785-97.
17. Dixit S, Diwaker P, Wadhwa N, Arora VK. Galectin-3 and CD117 immunocytochemistry in the diagnosis of indeterminate thyroid lesions: A pilot study. *Diagn Cytopathol*. 2021; **49**(10): 1129-37.

18. Dickey MV, Nguyen A, Wiseman SM. Cancer risk estimation using American College of Radiology Thyroid Imaging Reporting and Data System for cytologically indeterminate thyroid nodules. *Am J Surg.* 2022; **224**(2): 653-6.
19. Peng Q, Niu C, Zhang M, Peng Q, Chen S. Sonographic Characteristics of Papillary Thyroid Carcinoma with Coexistent Hashimoto's Thyroiditis: Conventional Ultrasound, Acoustic Radiation Force Impulse Imaging and Contrast-Enhanced Ultrasound. *Ultrasound Med Biol.* 2019; **45**(2):471-80.
20. Galimzianova A, Siebert SM, Kamaya A, Rubin DL, Desser TS. Quantitative Framework for Risk Stratification of Thyroid Nodules With Ultrasound: A Step Toward Automated Triage of Thyroid Cancer. *AJR Am J Roentgenol.* 2020; **214**(4): 885-92.
21. Li J, Wang Q, Wang L, Wang J, Wang D, Xin Z, et al. Diagnostic value of fine-needle aspiration combined with ultrasound for thyroid cancer. *Oncol Lett.* 2019; **18**(3): 2316-21.
22. Hess J, Schafernak K, Newbern D, Vern-Gross T, Foote J, Van Tassel D, et al. Ultrasound is superior to palpation for thyroid cancer detection in high-risk childhood cancer and BMT survivors. *Support Care Cancer.* 2020; **28**(11): 5117-24.
23. Figge JJ, Gooding WE, Steward DL, Yip L, Sippel RS, Yang SP, et al. Do Ultrasound Patterns and Clinical Parameters Inform the Probability of Thyroid Cancer Predicted by Molecular Testing in Nodules with Indeterminate Cytology? *Thyroid.* 2021; **31**(11): 1673-82.
24. Yokoya S, Iwade M, Shimura H, Suzuki S, Matsuzuka T, Suzuki S, et al. Investigation of thyroid cancer cases that were not detected in the Thyroid Ultrasound Examination program of the Fukushima Health Management Survey but diagnosed at Fukushima Medical University Hospital. *Fukushima J Med Sci.* 2020; **65**(3): 122-7.
25. Li N, He Y, Chang R. Is Chinese Thyroid Imaging Reporting and Data Systems superior to American College of Radiology or American Thyroid Association guidelines for consistency and efficacy in the diagnosis of thyroid cancer? *Chin Med J (Engl).* 2022; **135**(15): 1886-8.
26. Zhu YC, Du H, Jiang Q, Zhang T, Huang XJ, Zhang Y, et al. Machine Learning Assisted Doppler Features for Enhancing Thyroid Cancer Diagnosis: A Multi-Cohort Study. *J Ultrasound Med.* 2022; **41**(8): 1961-74.
27. Li H, Wang Z, Liu JS, Zou BS, Chen HR, Xu Z, et al. Association Between Breast and Thyroid Lesions: A Cross-Sectional Study Based on Ultrasonography Screening in China. *Thyroid.* 2020; **30**(8): 1150-8.
28. Chung SR, Baek JH, Rho YH, Choi YJ, Sung TY, Song DE, et al. Sonographic Diagnosis of Cervical Lymph Node Metastasis in Patients with Thyroid Cancer and Comparison of European and Korean Guidelines for Stratifying the Risk of Malignant Lymph Node. *Korean J Radiol.* 2022; **23**(11): 1102-11.
29. Nakaya T, Takahashi K, Takahashi H, Yasumura S, Ohira T, Shimura H, et al. Revisiting the Geographical Distribution of Thyroid Cancer Incidence in Fukushima Prefecture: Analysis of Data From the Second- and Third-round Thyroid Ultrasound Examination. *J Epidemiol.* 2022; **32**(Suppl_XII): S76-s83.
30. Wu SJ, Tan L, Ruan JL, Qiu Y, Hao SY, Yang HY, et al. ACR TI-RADS classification combined with number of nodules, halo features optimizes diagnosis and prediction of follicular thyroid cancer. *Clin Hemorheol Microcirc.* 2022; **82**(4): 323-34.
31. Baumgarten H, Jenks CM, Isaza A, Bhatti T, Mostoufi-Moab S, Kazahaya K, et al. Bilateral papillary thyroid cancer in children: Risk factors and frequency of postoperative diagnosis. *J Pediatr Surg.* 2020; **55**(6): 1117-22.