

EARLY AND DIFFERENTIAL DIAGNOSIS OF THYROID NODULAR LESIONS IN WOMEN LIVING IN THE ARAL SEA REGION USING ULTRASOUND ELASTOGRAPHY AND THE TI-RADS SYSTEM

Bekniyazova Sh.T.

Basic Doctoral Student

Scientific Supervisor: **Ismailova M.Kh.**

Tashkent State Medical University, Tashkent, Uzbekistan

Abstract

Background

Thyroid nodular disease is one of the most common structural abnormalities of the thyroid gland and represents an important diagnostic problem in modern endocrinology and radiology. Although the majority of thyroid nodules are benign, a clinically significant proportion may be malignant. Therefore, the principal challenge is not merely to detect thyroid nodules but to distinguish lesions with a high probability of malignancy from those that can be safely monitored. This issue is of particular importance among women living in environmentally vulnerable areas of the Aral Sea region, where thyroid dysfunction and other environmental health problems have previously been documented.

Objective

The aim of this study was to substantiate the clinical and diagnostic significance of combining conventional thyroid ultrasonography, the Thyroid Imaging Reporting and Data System (TI-RADS), and ultrasound elastography for early detection and differential diagnosis of thyroid nodular lesions in women living in the Aral Sea region.

Materials and Methods

A literature-based analytical approach was used. International clinical guidelines, systematic reviews, meta-analyses and original diagnostic studies addressing thyroid ultrasound, ACR TI-RADS and ultrasound elastography were analyzed. Particular attention was paid to the diagnostic characteristics of suspicious ultrasound findings, tissue stiffness parameters and the potential clinical value of combining morphological and elastographic criteria. Available evidence concerning thyroid dysfunction among women living in the environmentally unfavorable Aral Sea region was also considered.

Results

Conventional ultrasound remains the primary imaging method for the detection and characterization of thyroid nodules. The ACR TI-RADS system provides a standardized framework based on composition, echogenicity, shape, margins and echogenic foci and allows nodules to be stratified according to their estimated risk of malignancy. Published evidence demonstrates good diagnostic performance of ACR TI-RADS and its potential to reduce unnecessary biopsy procedures.

Ultrasound elastography provides complementary information by assessing the mechanical properties of thyroid tissue. Malignant nodules frequently demonstrate increased stiffness compared with normal thyroid tissue and many benign lesions. However, elastographic parameters may vary depending on the technique, equipment, measurement protocol and operator experience. Therefore, elastography

should be interpreted together with B-mode ultrasound and TI-RADS rather than used as an independent diagnostic criterion.

Conclusion

The combination of conventional ultrasound, TI-RADS and elastography represents a promising multimodal strategy for early and differential diagnosis of thyroid nodular lesions in women living in the Aral Sea region. The proposed approach may improve risk stratification, facilitate appropriate selection of patients for fine-needle aspiration biopsy and decrease unnecessary invasive procedures. Regional prospective studies are required to validate elastographic thresholds and determine the diagnostic accuracy of the combined algorithm in the population of the Aral Sea region.

Keywords: thyroid gland, thyroid nodule, women, Aral Sea region, ultrasonography, elastography, shear-wave elastography, TI-RADS, thyroid cancer, differential diagnosis, early diagnosis.

Introduction

Thyroid nodules are among the most frequently encountered abnormalities in clinical endocrinology. With the widespread availability of high-resolution ultrasonography, the detection rate of focal thyroid lesions has increased considerably. Many of these lesions are clinically insignificant and benign; however, a proportion represents differentiated thyroid carcinoma or other malignant neoplasms. The clinical challenge is therefore to identify suspicious lesions at an early stage while avoiding unnecessary invasive diagnostic procedures in patients with benign disease.

Thyroid pathology has particular significance in women. Epidemiological studies consistently demonstrate a higher prevalence of thyroid disorders among women compared with men. The female predominance is observed in autoimmune thyroid diseases, functional thyroid disorders and thyroid nodular pathology. Consequently, women represent an important target population for thyroid screening and diagnostic monitoring. The situation deserves special attention in the Aral Sea region. The ecological consequences of the Aral Sea disaster have created a complex environmental and public health context. Changes in environmental conditions, nutritional factors and micronutrient availability may influence thyroid function and general health. Previous research conducted among women of reproductive age living in the environmentally unfavorable Aral Sea region has reported a substantial prevalence of thyroid functional abnormalities, including subclinical and overt hypothyroidism.

It is important to distinguish between functional and structural thyroid disease. An abnormal thyroid-stimulating hormone concentration does not by itself indicate the presence of a malignant thyroid nodule. Conversely, a patient with normal thyroid function may have a clinically significant thyroid malignancy. Therefore, laboratory evaluation and structural imaging should be regarded as complementary diagnostic components.

High-resolution ultrasonography is the preferred first-line imaging method for thyroid nodules. It allows visualization of the gland in real time and provides detailed information about nodule size, composition, echogenicity, shape, margins and echogenic foci. Nevertheless, the interpretation of individual ultrasound signs may vary between observers. Furthermore, several benign lesions can demonstrate suspicious ultrasound characteristics, while some malignant nodules may lack classical high-risk features.

To improve reproducibility and standardization, several ultrasound-based risk stratification systems have been developed. Among them, the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) has become one of the most widely used approaches. The system assigns points to specific ultrasound characteristics and categorizes nodules according to their estimated malignancy risk.

Despite the advantages of TI-RADS, some nodules remain diagnostically indeterminate. In such cases, additional information regarding the physical properties of the lesion may be useful. Ultrasound elastography has emerged as an important complementary technique because it assesses tissue stiffness, a parameter that may differ between benign and malignant lesions.

The combination of morphological information obtained by TI-RADS and biomechanical information obtained by elastography may therefore provide a more comprehensive characterization of thyroid nodules.

The present article discusses the scientific rationale, diagnostic advantages and limitations of this combined approach, with particular consideration of women living in the Aral Sea region.

Aim of the Study

The aim of the study was to develop a scientifically justified approach to the early detection and differential diagnosis of thyroid nodular lesions in women living in the Aral Sea region using conventional ultrasound, the TI-RADS classification system and ultrasound elastography.

The specific objectives were:

- to characterize the diagnostic role of conventional thyroid ultrasonography;
- to assess the clinical value of TI-RADS-based risk stratification;
- to analyze the diagnostic potential and limitations of ultrasound elastography;
- to determine the potential advantages of combining TI-RADS and elastographic parameters;
- to propose a practical diagnostic algorithm suitable for women living in the Aral Sea region.

Materials and Methods

The present work was designed as an analytical literature-based study. Published scientific literature concerning thyroid nodules, thyroid ultrasonography, TI-RADS, ultrasound elastography and thyroid malignancy was reviewed.

Priority was given to clinical guidelines, systematic reviews, meta-analyses and diagnostic studies published in peer-reviewed medical journals. International recommendations concerning thyroid nodule evaluation were also considered.

The main analytical domains included:

- conventional B-mode ultrasonographic characteristics of thyroid nodules;
- ACR TI-RADS risk stratification;
- strain and shear-wave elastography;
- correlation between ultrasound and elastographic findings;
- clinical indications for fine-needle aspiration;
- potential applicability of the combined diagnostic approach in the Aral Sea region.

The literature analysis was supplemented by consideration of published regional evidence regarding thyroid functional status among women residing in the Aral Sea region.

Multidisciplinary research and Innovation (SICMRI 2026)

Because individual patient-level clinical, cytological and histological data were not available for the present manuscript, original sensitivity, specificity, predictive values and ROC-derived thresholds were not calculated. Consequently, no artificial clinical results were introduced.

Results

1. Ultrasound as the basis of thyroid nodule evaluation

Ultrasound is currently the cornerstone of thyroid nodule assessment. Its advantages include absence of ionizing radiation, relatively low cost, high spatial resolution and the possibility of repeated examinations.

A comprehensive examination should include evaluation of both thyroid lobes and the isthmus. The echogenicity and homogeneity of the thyroid parenchyma should be described, and focal lesions should be measured in three dimensions.

Once a nodule is identified, its morphology should be systematically assessed.

The most clinically relevant characteristics include: composition; echogenicity; shape; margins; echogenic foci; calcification; vascular pattern; relationship to the thyroid capsule; presence of suspicious cervical lymph nodes. The combination of these characteristics provides substantially more information than nodule size alone. A common diagnostic error is to consider a large nodule automatically more suspicious than a small nodule. In reality, certain small nodules may demonstrate a substantially higher risk profile because of their morphology. Therefore, ultrasound risk stratification should be based on the complete set of sonographic features.

2. Clinical significance of TI-RADS

The development of TI-RADS represented an important step toward standardization of thyroid ultrasound reporting. The ACR TI-RADS system evaluates five major domains: composition, echogenicity, shape, margins and echogenic foci. Points are assigned according to the characteristics of each nodule, after which the total score determines the final TI-RADS category. The categories range from TR1 to TR5, representing progressively increasing suspicion. The practical value of TI-RADS lies in its ability to transform a descriptive ultrasound examination into a structured risk assessment.

According to the ACR approach, biopsy thresholds are determined not solely by malignancy risk but also by nodule size. This strategy is intended to reduce the number of unnecessary fine-needle aspiration procedures while maintaining an appropriate level of cancer detection.

A systematic review and meta-analysis of ACR TI-RADS demonstrated favorable pooled diagnostic performance, supporting its use as a standardized ultrasound-based risk stratification system.

However, TI-RADS does not eliminate all diagnostic uncertainty. Nodules classified within intermediate-risk categories may demonstrate overlapping characteristics, and some benign lesions may have suspicious morphology. These circumstances create a potential role for additional imaging techniques.

3. Ultrasound Elastography in Thyroid Nodule Assessment

Elastography is a relatively modern ultrasound technique that evaluates the mechanical properties of tissues.

Two principal approaches are used in thyroid imaging.

Strain elastography

Strain elastography evaluates tissue deformation in response to an applied force. The relative stiffness of a thyroid nodule can be compared with adjacent normal thyroid tissue.

Shear-wave elastography

Multidisciplinary research and Innovation (SICMRI 2026)

Shear-wave elastography generates and measures shear waves within the tissue. Tissue stiffness can be expressed quantitatively in meters per second or kilopascals.

The biological rationale for elastography is based on differences in tissue architecture. Malignant lesions may contain increased cellularity, fibrosis and altered extracellular matrix, resulting in greater tissue stiffness.

However, increased stiffness is not synonymous with malignancy. Fibrotic benign nodules, chronic inflammatory lesions and lesions containing calcifications may also demonstrate high stiffness.

Consequently, elastographic findings must always be interpreted in clinical and morphological context.

Published meta-analyses indicate that elastography can provide clinically useful diagnostic information. A systematic review of multiple elastography studies demonstrated generally favorable sensitivity and specificity, although considerable heterogeneity was observed between studies and techniques.

This heterogeneity is clinically important. Elastographic values depend on the ultrasound platform, transducer frequency, acquisition technique, compression, region of interest and operator experience.

For this reason, the development of universally applicable stiffness cut-off values remains difficult.

4. Complementary Value of TI-RADS and Elastography

The principal theoretical advantage of combining TI-RADS with elastography is that the two techniques evaluate different characteristics of a lesion.

TI-RADS primarily evaluates morphology. Elastography evaluates mechanical properties. The integration of these two dimensions may therefore improve the overall characterization of indeterminate nodules. A nodule demonstrating multiple suspicious TI-RADS features and marked stiffness on elastography may deserve a higher level of clinical attention than a lesion with low-risk morphology and low stiffness.

Conversely, a nodule with low-risk morphology and favorable elastographic characteristics may be considered for surveillance if its size and clinical context do not justify biopsy.

Importantly, elastography should not be used to override a clearly suspicious ultrasound examination. Instead, it should provide additional information when the morphological assessment leaves residual uncertainty.

Recent evidence has investigated the potential benefit of adding elastography to ACR TI-RADS. Such studies suggest that elastography may provide additional diagnostic value, particularly in nodules where the conventional ultrasound assessment results in an intermediate level of suspicion.

5. Relevance to Women Living in the Aral Sea Region

The application of advanced ultrasound techniques may be particularly relevant in environmentally vulnerable populations.

Previous studies among women living in the Aral Sea region have demonstrated a considerable prevalence of thyroid functional disorders.

Although thyroid dysfunction and thyroid malignancy are distinct clinical entities, the high prevalence of thyroid abnormalities supports the need for appropriate structural evaluation.

The use of a standardized diagnostic protocol may be particularly valuable in regional healthcare settings where access to highly specialized diagnostic services can be limited.

A practical approach could involve the following sequence:

Multidisciplinary research and Innovation (SICMRI 2026)

Clinical assessment → thyroid function testing → high-resolution ultrasound → TI-RADS classification → selective elastography → FNA when indicated → cytological/histological verification.

Such a pathway would allow the initial evaluation to remain non-invasive while reserving invasive procedures for appropriately selected patients. Discussion The early detection of thyroid nodular lesions is an important component of preventive medicine. The objective is not to identify every thyroid nodule and immediately biopsy it, but to identify lesions that carry a clinically meaningful risk of malignancy. This principle is especially important because modern ultrasound has made the detection of very small thyroid nodules increasingly common. Without an appropriate risk-stratification system, increased detection could result in overdiagnosis and overtreatment.

TI-RADS addresses this problem by introducing standardized risk categories. Its use can improve communication between radiologists, endocrinologists, surgeons and cytologists.

Nevertheless, ultrasound morphology alone cannot resolve every diagnostic problem.

Elastography addresses this limitation by providing an additional parameter. The mechanical properties of tissue may help characterize nodules that appear equivocal on B-mode ultrasound.

However, several limitations should be acknowledged.

First, elastography is technique-dependent. Different ultrasound systems may produce different numerical measurements. Second, there is no universally accepted stiffness threshold that can be applied to every thyroid nodule. Third, operator experience affects image acquisition and interpretation. Fourth, inflammatory and fibrotic benign lesions can demonstrate increased stiffness and produce false-positive findings. Therefore, elastography should be regarded as an adjunct rather than a replacement for conventional ultrasound and TI-RADS. Another important issue is the need for regional validation. Most published elastography data originate from populations outside Central Asia. Differences in patient characteristics, disease prevalence, equipment and examination protocols mean that published thresholds cannot necessarily be transferred directly to the population of the Aral Sea region. This creates an important research opportunity. A prospective study involving women from Karakalpakstan and other territories affected by the Aral Sea ecological crisis could establish a regional database of thyroid ultrasound and elastography findings.

Such a study should include: demographic characteristics; age and reproductive status; thyroid-stimulating hormone levels; free thyroxine levels; thyroid autoantibodies when clinically indicated; ultrasound morphology; TI-RADS category; elastographic measurements; cytological results according to the Bethesda system; histological diagnosis when surgery is performed. Statistical analysis should include sensitivity, specificity, positive and negative predictive values and receiver operating characteristic analysis. The resulting area under the ROC curve would allow objective comparison of conventional ultrasound, TI-RADS, elastography and their combination. Such research could ultimately lead to the development of a regional diagnostic model specifically adapted to women living in the Aral Sea region.

Proposed Diagnostic Algorithm Based on the available evidence, the following practical algorithm can be proposed:

Stage 1 — Clinical assessment

Women with suspected thyroid disease should undergo clinical evaluation, including examination of the thyroid gland and assessment of relevant risk factors.

Stage 2 — Laboratory evaluation

TSH should be assessed as the principal biochemical indicator of thyroid function. Free T4 and thyroid antibodies may be added according to clinical indications.

Stage 3 — Standardized ultrasound

High-resolution ultrasound should document the size, composition, echogenicity, shape, margins and echogenic foci of each relevant nodule.

Stage 4 — TI-RADS classification

Each nodule should be assigned an appropriate TI-RADS category.

Stage 5 — Elastography

Elastography should be considered particularly for nodules with indeterminate or intermediate-risk morphology.

Stage 6 — Cytological verification

FNA should be performed according to the TI-RADS category, lesion size and clinical risk factors.

Stage 7 — Follow-up

Nodules not meeting biopsy criteria should undergo follow-up according to their risk category and clinical circumstances. Scientific and Practical Significance The proposed multimodal approach has several potential advantages. First, it improves the standardization of thyroid ultrasound reporting. Second, it provides additional information regarding tissue stiffness. Third, it may improve characterization of indeterminate nodules. Fourth, it may reduce unnecessary invasive procedures. Fifth, it provides a framework for developing a regional thyroid screening and diagnostic program for women living in the Aral Sea region. The approach is particularly attractive because both ultrasound and elastography are non-invasive and do not expose patients to ionizing radiation.

Limitations

The main limitation of the present article is that it is an analytical literature-based work rather than a prospective clinical study with an original patient cohort. Therefore, the article does not provide original sensitivity, specificity or ROC-derived elastographic thresholds for women living in the Aral Sea region. Another limitation is heterogeneity among published elastography studies. Differences in equipment and methodology complicate direct comparison of numerical stiffness values. These limitations emphasize the need for future prospective regional studies.

Conclusion

Thyroid nodular disease represents an important diagnostic problem among women and requires a systematic approach to early detection and risk assessment.

High-resolution ultrasound remains the foundation of thyroid nodule evaluation. The ACR TI-RADS system improves diagnostic standardization by categorizing nodules according to established sonographic risk features. Ultrasound elastography provides complementary information concerning tissue mechanical properties and may improve differential diagnosis, particularly in nodules with indeterminate conventional ultrasound characteristics. The combination of TI-RADS and elastography is therefore a promising multimodal approach for women living in the Aral Sea region. It may facilitate early identification of suspicious lesions, improve selection of patients for FNA and decrease unnecessary invasive procedures. At the same time, elastography should not replace conventional ultrasound, TI-RADS or cytological verification. Its results must be interpreted within the overall clinical and imaging context. The next important step is the development of a prospective regional study involving women from the Aral Sea region. Such research should establish locally applicable

elastographic thresholds and determine the diagnostic accuracy of the combined ultrasound–TI-RADS–elastography algorithm. The implementation of a standardized diagnostic pathway could contribute to earlier detection of clinically significant thyroid pathology and improve the quality of thyroid disease management in environmentally vulnerable populations.

References

1. Tessler F.N., Middleton W.D., Grant E.G., et al. ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White Paper of the ACR TI-RADS Committee. *Journal of the American College of Radiology*. 2017;14(5):587–595.
2. Li W., Wang Y., Wen J., Zhang L., Sun Y. Diagnostic Performance of American College of Radiology TI-RADS: A Systematic Review and Meta-Analysis. *American Journal of Roentgenology*. 2021;216(1):38–47.
3. Haugen B.R., Alexander E.K., Bible K.C., et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid*. 2016;26(1):1–133.
4. Russ G., Bonnema S.J., Erdogan M.F., Durante C., Ngu R., Leenhardt L. European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: EU-TIRADS. *European Thyroid Journal*. 2017;6:225–237.
5. Cantisani V., De Silvestri A., Scotti V., et al. US-Elastography With Different Techniques for Thyroid Nodule Characterization: Systematic Review and Meta-analysis. *Frontiers in Oncology*. 2022;12:845549.
6. Zhan J., Diao X.H., Jin J.M., et al. Real-time ultrasound elastography for differentiation of benign and malignant thyroid nodules: a meta-analysis. *Ultrasound in Medicine & Biology*. 2014.
7. Kubaev A.B., Kultanov B.Z., Tauesheva Z.B., et al. Evaluation of the functional state of the thyroid gland in women residing in the ecologically unfavorable Aral Sea region. *Gigiena i Sanitariya*. 2017;96(2):131–133.
8. Middleton W.D., Teefey S.A., Reading C.C., et al. Multiinstitutional comparison of the performance of ultrasound risk stratification systems for thyroid nodules. *Radiology*. 2017.
9. Angelopoulos N., Goulis D.G., Chrisogonidis I., et al. Elastography Enhances Diagnostic Accuracy of ACR TI-RADS in Thyroid Nodule Evaluation. *Journal of Clinical Endocrinology & Metabolism*. 2026;111(6):e1616–e1625.