Vol. 46 (2021) No. 2 TIMOK MEDICAL GAZETTE Review article

ULTRASOUND CHARACTERISTICS OF NODULES IN THE THYROID GLAND

Aleksandar Aleksić, Vlada Mitov, Aleksandar Jolić, Vanja Antić, Nataša Savić

(1) SPECIALIST INTERNAL MEDICINE PRACTICE ALEKMED ZAJEČAR; (2) ZAJECAR HEALTH CENTER, DEPARTMENT OF INTERNAL MEDICINE; (3) ĆUPRIJA HEALTH CENTER, DEPARTMENT OF PNEUMOPHTHISIOLOGY; (4) ACADEMY OF EDUCATIONAL AND MEDICAL VOCATIONAL STUDIES, ĆUPRIJA DEPARTMENT

Summary: Nodules in the thyroid gland are very common and can be found in 50-68% of adults in the general population. Only about 5% of these nodules are malignant and require treatment. They usually do not give any discomfort. When they are discovered, they should be assessed on the basis of clinical, echosonographic and cytological findings, and if necessary, using additional diagnostic methods, and make a decision on the need for treatment. Based on the ultrasound characteristics of the nodule, it is decided whether further diagnosis is needed, in terms of aspiration puncture with a thin needle (FNA) and cytological examination, after which a decision is made on further procedure. Ultrasound is the initial diagnostic method for the detection of thyroid nodules. In addition to the presence of nodules, it accurately determines the size, location and number of nodules in the thyroid gland (thyroid). This non-invasive screening method is safe, harmless and can be repeated. FNA is a very important diagnostic method, but its performance must be selective, since systematic puncture of all nodes, regardless of size or appearance, is not recommended. It is important that the indications for FNA be based on clinical characteristics, as well as on echosonographic stratification of the risk of malignancy.

Key words: thyroid nodules, ultrasound examination, thin needle puncture.

INTRODUCTION

Nodules in the thyroid gland are very common and can be found in 50-68% of adults in the general population. Only about 5% of these nodules are malignant and require treatment. They usually do not give any discomfort. When they are discovered, they should be assessed on the basis of clinical, echosonographic and cytological findings, and, if necessary, using additional diagnostic methods, and make a decision on the need for treatment. Based on the ultrasound characteristics of the nodule, it is decided whether further diagnosis is needed, in terms of thin needle aspiration puncture (FNA) and cytological examination, after which a decision is made on further procedure [1-5].

Currently, FNA is the most effective method for determining the nature of the node. However, many nodules are benign, and even malignant nodules, especially those smaller than 1 cm, often show indolent and non-aggressive behavior. Therefore, not all detected nodes require FNA. A reliable non-invasive method to detect nodes indicated for FNA would be highly desirable [6]. Ultrasound is the initial diagnostic method for the detection of thyroid nodules. In addition to the presence of nodules, it accurately determines the size, location and number of nodules in the thyroid gland (thyroid).

This non-invasive screening method is safe, harmless and can be repeated [7]. Assessing the risk of malignancy is very important in patients with glandular nodules in order to identify those nodules that need to be punctured with a thin needle. The main disadvantage of this examination is that it largely depends on the doctor performing the examination [8]. Therefore, an attempt was made to find a formula for risk assessment in relation to ultrasound characteristics and standardization of ultrasound description, in order to reduce the subjectivity of the examiner. Koike E. et al. from the Noguchi Thyroid Clinic and Hospital Foundation from Japan in 2001. set the formula for the prediction of thyroid nodule malignancy based on 5 ultrasound characteristics of the nodule: margins, shape, echogenicity, echostructure and calcification [9,10]. As no characteristic can reliably predict malignancy, the use and combination of several traits or characteristics is advised. One such

system, that is, a way of combining and scoring several properties of a node in the thyroid gland, was published in 2009 by Horvath et al. as the Thyroid Imaging Reporting and Data System (TIRADS). It consists of a scale of 6 characteristics for stratification of malignancy risk. Subsequently, similar recommendations were issued by the Korean Thyroid Radiology Society, the American Thyroid Association, the American Association of Clinical Endocrinologists, the American College of Endocrinology, and the Italian Association of Clinical Endocrinologists [8].

In 2015, the American College of Radiology (ACR) issued instructions for access to the most common thyroid nodules and gave instructions for standardizing the ultrasound examination of the thyroid gland. Thyroid Imaging Reporting and Data System (ACR TI-RADS) [6].

Based on a review of the literature, the American Association of Clinical Endocrinologists, the American Thyroid Association and Korean guides, in 2017 a new EU-TI RADS (European Thyroid Imaging Reporting and Data System) classification was formed to assess thyroid nodules and decide on a possible FNA nodule [7]. .

In the following, the European Thyroid Imaging Reporting and Data System (EU-TI RADS) and the American College of Radiology (ACR), Thyroid Imaging Reporting and Data System (TI-RADS), ACR TI-RADS will be described.

GUIDELINES FOR STANDARDIZATION OF ULTRASOUND EXAMINATION OF THE THYROID GLAND EU-TI RADS

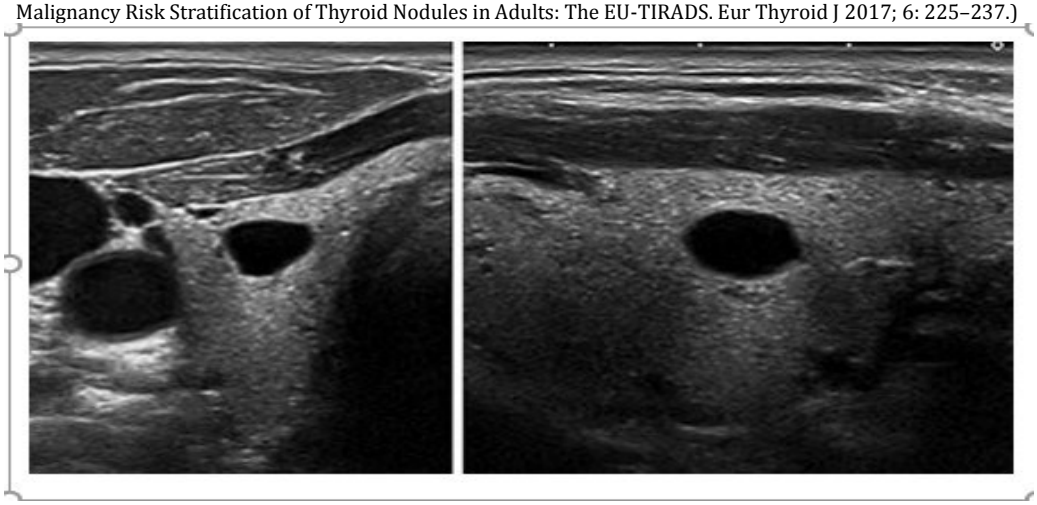
Category EU-TIRADS 1, is a category, ie thyroid gland (thyroid) that does not contain nodules.

Benign category (EU-TIRADS 2), risk of malignancy close to 0%.

This category includes completely anechoic nodules (cysts) and completely spongiform nodules.

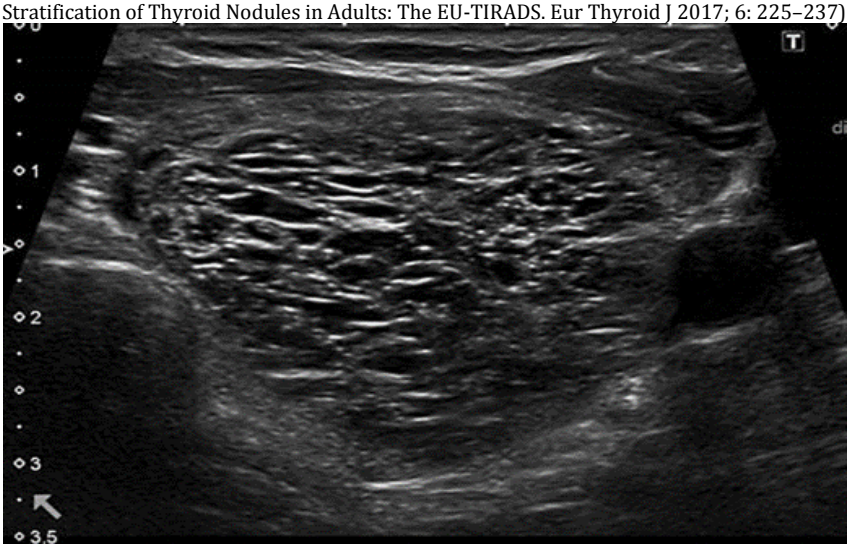
Pure cystic changes, cysts, are characterized by the absence of wall thickening, posterior signal amplification as well as the absence of a solid component, regardless of their size. Figure 1.

Figure 1. Completely cystic nodule (From: Gilles R. et all. European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: The EU-TIRADS. Eur Thyroid J 2017; 6: 225–237.)



This category also includes cysts that are divided into separate sections by fibrous septa. The presence of echogenic material within the cyst is often encountered and may correspond to either a clot of fibrin, a colloid, or a true solid component, which may be distinguished by the use of Doppler. If there is a suspicion regarding the existence of a solid component inside the cyst, such a node should be classified as low risk. Spongiform nodules are composed of tiny cystic spaces that cover the entire nodule, with the size of the nodule not playing a role in assessing the risk of malignancy. Small cystic spaces are separated by numerous isoechoic septa. Figure 2. If cystic spaces do not fill the entire node, the node should be classified as a low-risk node. Pure cystic changes and completely spongy nodules should be considered benign. FNA is not recommended for these changes, regardless of their size, and even for such benign cystic nodules, ablation with ethanol is recommended as the therapy of first choice [8,11].

Figure 2. Spongiform node. (From: Gilles R. et all. European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: The EU-TIRADS. Eur Thyroid J 2017; 6: 225–237)



Low risk category (EU-TIRADS 3), where the risk of malignancy is 2-4%.

These nodes are characterized by an oval shape, smooth edges (margins), as far as echogenicity is concerned, these nodes are isoechoic or hyperechoic, without any high-risk characteristics. Figure 3, isoechoic nodule, Figure 4 hyperechoic nodule. Nodes with these characteristics have a low risk of malignancy and FNA for nodes> 20mm should be considered. The 20 mm threshold was chosen based on the argument that distant metastases are rarely found in follicular carcinomas <2 cm [12]. Grouped and associated nodes (polynodose goiters) of these characteristics should be included in this category, and FNA should be considered if one or more nodes are> 20 mm. It should be noted that a completely homogeneous isoechoic nodule may correspond in less than 4% of cases to follicular carcinoma or follicular variant PTC [13,14]. However, even minimal cystic changes in the nodule favor benignity [15]. So oval-shaped nodules, which are isoechoic or hyperechogenic with smooth margins and without high-risk characteristics, should be classified as low-risk. FNA is usually only recommended for nodes> 20 mm [8].

Figure 3. Isoechogenic nodule. (From: Gilles R. et all. European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: The EU-TIRADS. Eur Thyroid J 2017; 6: 225–237)

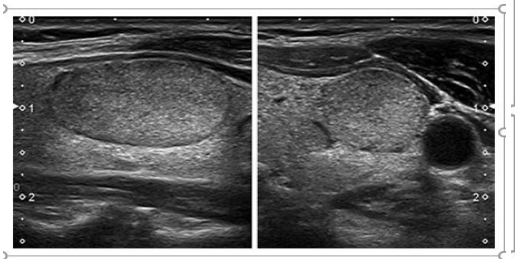
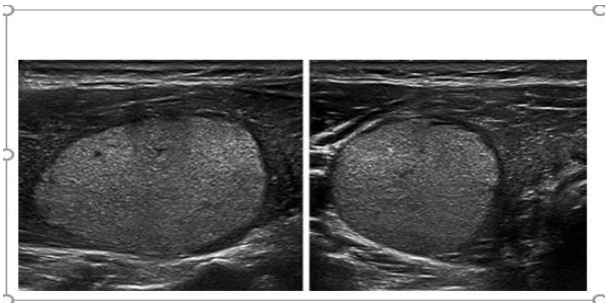


Figure 4. Hyperechogenic nodule. (From: Gilles R. et all. European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: The EU-TIRADS. Eur Thyroid J 2017; 6: 225–237)

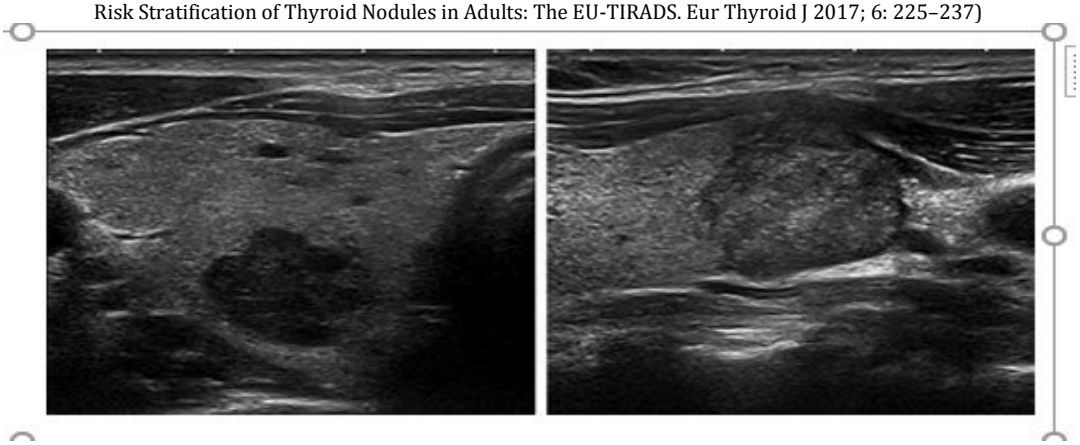


Medium risk category (EU-TIRADS 4) where the risk of malignancy is 6–17%.

These nodules are characterized by an oval shape, smooth edges, mild to moderate hypoechoicity, without other high-risk features. Figure 5. The difference between the low and medium risk category lies in the echogenicity of the solid component of the node. In the case of heterogeneous echogenicity of a solid component, the presence of any hypoechoic change classifies the node into a medium-risk category. The presence of a thin halo, partially cystic changes, comet-type artifact, peripheral vascularity, reduce the risk of malignancy.

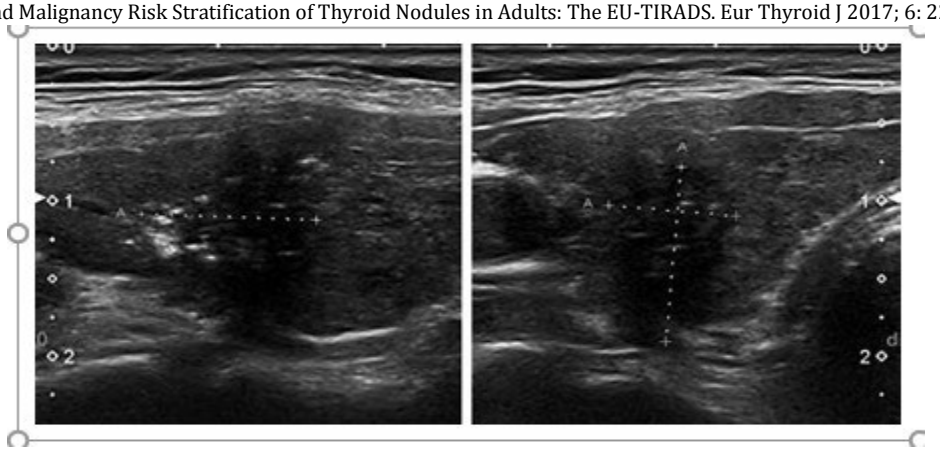
Hypoechoic nodes should be classified as moderate risk, including those with cystic areas, bearing in mind that the risk is lower in partially cystic nodes than in completely compact nodes. Characteristics such as discontinuous peripheral margins, peripheral macrocalcifications, dense halo, predominantly central vascularization may increase the risk of malignancy. In this group, the threshold for FNA is recommended for nodes larger than 15mm [8].

Figure 5. Hypoechogenic nodule. (From: Gilles R. et all. European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: The EU-TIRADS. Eur Thyroid J 2017; 6: 225–237)



High risk category (EU-TIRADS 5), where the risk of malignancy is 26–87% The characteristic of these nodes is the presence of at least one of the following characteristics, which belong to the characteristics (features) of high risk: not oval shape (higher than wider), irregular edges, microcalcifications and marked hypoechoicity. Figure 6.

Figure 6. Nodus from the high risk category. (From: Gilles R. et all. European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: The EU-TIRADS. Eur Thyroid J 2017; 6: 225–237)



All these characteristics show high rates of specificity (83–84%), but also low rates of sensitivity (26–59%). Pronounced hypoechoicity has the lowest sensitivity of the four described characteristics and is specific only if the node is compact, because a highly hypoechoic node may be the remnant of a previous cyst. In a partially cystic node, microcalcifications are the best predictor of malignancy, while other features appear less significant. At the same time, the presence of several anomalies, jagged intermittent, edges with spicules, lobulations, dotted echogenic foci, non-oval shape, increase the risk of malignancy. Nodes with such properties that are larger than 10 mm should undergo FNA, except in inoperable patients for any reason or a short lifespan is expected, due to the existence of other comorbidities [8]. In case of a benign cytological result, FNA of such a node, the puncture should be repeated within 3 months in order to reduce the number of false negative findings. In the case of nodules smaller than one centimeter with high-risk ultrasound characteristics, it is recommended to actively monitor the nodules as well as to treat pathological lymph nodes in the neck and the symptoms and signs that the patient himself reports. It is known that few or none of these patients will develop distant metastases, ie that mortality is negligible even if the nodule corresponds to cancer, in the case of subsantimetric dimensions of the nodules [8]. Patients with subcentimeter nodules and very suspicious ultrasound characteristics but without abnormal lymph nodes in the neck should be presented with the possibility of active surveillance as one option or FNA under ultrasound control.

EU-TIRADS scoring is also useful in multinodular thyroid gland for selecting nodes that are candidates for FNA. During the echosonographic examination, ultrasound high-risk nodes should be identified, observed, described, and FNA suggested if the node is larger than 10 mm.

Identify medium risk nodes; describe only those nodes larger than 5 mm and for FNA suggest those larger than 15 mm. Identify low-risk nodes; describe only those larger than 10 mm and suggest for FNA for those larger than 20 mm. If there are more nodes, more than three, describe in detail only those that are suspicious (according to the previous risk and size criteria), record the others [8].

SIGNIFICANCE OF OTHER ULTRASOUND CHARACTERISTICS

Shape, margins, echogenicity, composition and microcalcifications are the basic characteristics that enable EU TIRADS classification. However, some of the ultrasound features can be used to further assess and classify risks and modulate indications for FNA.

Suspicious lymphadenopathy

Ultrasound assessment of cervical lymph nodes should be performed in all patients with thyroid nodules, especially in those with medium and high risk.

In suspected lymph nodes, lymph node FNA should be performed for cytological analysis as well as for determination of thyroglobulin and calcitonin [8].

Extrathyroid propagation, proliferation and invasion of surrounding tissue

Propagation into adjacent structures and disruption of thyroid capsule continuity may be considered a specific feature for invasive

malignancy. Adherence to the capsule, ie close contact with the capsule, has less specificity for macroscopic extrathyroid invasion and spread, through the capsule. The presence of an unaltered thyroid parenchyma, 2 mm between the nodule and the continuous, compact thyroid capsule, indicates that there is almost no macroscopic extrathyroid expansion and invasion while reducing the risk of microscopic capsule invasion and extrathyroid expansion. The discontinuity of the capsule, the adhesion of the capsule and the bulge of the capsule must be emphasized in the report, ie the ultrasound description, due to the possible invasion of the capsule and extrathyroid expansion [8].

Macrocalcifications and hyperechoic points (foci)

Macrocalcificationscan be defined as echogenic foci (points) larger than 1 mm with the existence of posterior shading (acoustic window).

1. Isolated central intranodularmacrocalcifications are not necessarily associated with malignancy, ie they do not inevitably indicate malignancy.
2. Isolated macrocalcification, which almost completely fills the calcified node, has a low risk of malignancy.
3. Calcifications on the periphery, peripheral calcifications (peripheral or curvilinear) or (picture of broken egg shell) along the periphery of the node, increase the risk of malignancy if their continuity is interrupted [8].

Hyperechoic points (foci, spots)

These changes correspond to perimilimeter hyperechoic changes and can be caused by:

1. Colloidal crystals or remnants of fibrin that create artifacts (reverberations), comet tails and are almost always a sign of benign change.
2. Posterior acoustic amplification (posterior, posterior wall of the cyst, iemicrocystic area) is mainly seen in high-frequency probes and is a feature that indicates benignity.
3. True microcalcifications correspond to psammomic bodies around which there are multiple round echogenic foci up to 1 mm in size without the existence of posterior shading (acoustic headlight) and they are always placed in a solid, homogeneous component of the node. Microcalcifications largely suggest malignancy.
4. Hyperechogenic spots of indeterminate significance that cannot be classified with certainty in the previous three categories. Rather linear than round and without microcystic cavities and comet tail artefacts.

Isolated macrocalcifications are not specific for malignancy. Their presence should be correlated with other ultrasound characteristics. Echogenic spots of comet tail appearance suggest benignity. True microcalcificationsshould be distinguished from other echogenic spots and such nodules should be subjected to FNA [8].

Halo

The halo is thought to correspond to the nodule capsule or surrounding blood vessels, or to sometimes correspond to the surrounding compressed parenchyma. A thin halo reduces the risk of malignancy (0.3mm), while a thick halo or absence of halo increases the risk of malignancy. However, a clear definition of thin and thick halo cannot be given [8].

Vascularization

As for vascularity, the description of vascularity with the help of color Doppler is often used in clinical practice. Malignant nodules are more likely to have type III vascularity, while benign nodules show type I and II vascularity. Type I vascularity, denotes absent or scarce vascularity. Type II, denotes present perinodal and scarce intranodal vascularization and type III denotes scarce perinodal and pronounced intranodal vascularization.

However, it is very important that the intranodular signal increases with the size of the benign nodule. Vascularity as a criterion remains for the assessment of nodules remains controversial, mainly because the assessment of vascularity largely depends on the equipment and settings of the ultrasound apparatus and because it largely depends on the subjective assessment of the examiner. Therefore, the ETA working group does not recommend the inclusion of vascularity in the assessment in the TIRADS score [8].

Node growth

Regarding the growth of thyroid nodules, the published results suggest that the growth of nodules cannot accurately distinguish between benign and malignant lesions. Thus, determining the growth of nodules is not recommended as a criterion for distinguishing malignant and benign nodules [8].

The EU-TIRADS scoring system is based on the presence of ultrasound characteristics that are highly suspected of malignancy. This system includes five categories, ultrasound findings. The first category involves the absence

of thyroid nodules, the other four include benign, low-suspicion, moderate-suspicion, and high-suspicion categories. Compared to other risk scoring systems, the main advantage of EU-TIRADS is the facilitation of scoring in the use of specific ultrasound features to detect high-sensitivity thyroid cancer which should allow for the reduction of unnecessary FNA procedures [8].

Very few nodules will require invasive processing that includes cytology and molecular testing (FNA). An ultrasound examination with an assessment of clinical risk factors will be sufficient for an initial monitoring and diagnostic strategy. This is especially important for weak, elderly people, with comorbidities, because they are unlikely to be endangered by the thyroid tumor itself, and excessive diagnosis and interventions can do more harm than good. The goal is to identify the best strategy for the individual in terms of disease outcome and quality of life, avoiding the pitfalls of over-diagnosis and over-treatment [16].

ACR TI-RADS
THYROID IMAGING REPORTING AND DATA SYSTEM ACR TI-RADS

In this system, when evaluating the node, it is necessary to determine (score) each of the characteristics or ultrasonic properties of the node, which will be listed later, after which points are added. The total number of points determines the level of ACR TI-RADS score, which ranges from TR1 which is benign to TR5 which is a highly suspicious finding for malignancy. Recommendations for FNA and ultrasound monitoring of the node are based on the level of the number of points and its maximum diameter. Ultrasound, characteristics or properties to be scored are the composition of the node (composition), the echogenicity of the node, the shape of the node, the margins or edges of the node and the echogenic points or foci [6].

Composition

Nodes that are cystic or almost completely cystic do not bring any points, because they are almost always benign. Similarly, spongy material is highly associated with benign characteristics, regardless of other characteristics. However, the spongy node must be composed of at least 50% of small cystic spaces. Nodes should not be characterized as spongy only on the basis of the presence of several scattered cystic elements in a solid node. Mixed cystic solid nodules are categorized as predominantly solid and predominantly cystic. A solid component that is eccentrically placed and has a sharp angle in relation to the wall of the node is suspicious as well as a solid component that is hypoechoic, with lobulations and point echogenic foci. Completely cystic, predominantly cystic and spongy nodes are scored from zero points. Mixed, cystically solid nodes are scored with one point, and predominantly, ie mostly solid with two points [6].

Echogenicity

This feature refers to the reflectivity of the nodule in relation to the surrounding thyroid tissue, except for very hypoechoic nodules where muscles attached to the hyoid bone are used as a basis for comparing echogenicity. This category also includes anechoic changes with zero points, which refers to cystic or almost cystic nodes, and extremely hypoechoic nodes to which three points would be awarded due to their very hypoechoic picture. Anechoic nodes get zero points, isoechoic and hyperechoic one point, and hypoechoic two points, while highly hypoechoic nodes get three points [6].

Shape

Higher than wider (ovoid) is a non-sensitive but highly specific indicator of malignancy. This property is estimated in the axial plane by comparing the height and width of the node measured horizontally and vertically in the transverse section. A higher than broader configuration is usually obvious and rarely requires formal measurements. This shape got three points, the oval shape zero points [6].

Edges

Smooth and clear edges of the node reduce the risk of malignancy, the edges (margins of the node) with such characteristics get zero points. For nodes where we cannot estimate the edges, we classify them in the category of nodes with a poorly defined edge of the node, and that category gets zero points. A lobed or irregular margin refers to a serrated or needle-like edge, with or without protrusions in the surrounding parenchyma, and this characteristic of the node is scored with two points. Propagation beyond the thyroid gland is classified as extensive or minimal and is scored with three points. Extensive extrathyroid spread, which is characterized by invasion of the surrounding soft tissue or vascular structures, is a highly reliable sign of malignancy and is one of

the unfavorable prognostic signs. Minimal invasion may be echosonographically suspicious if we have little thyroid parenchyma between the nodule and the thyroid capsule or there is swelling (bulge) of the contours and loss of echogenicity of the thyroid border [6].

Echogenic foci

The comet's tail artifact is an echogenic focus with V-shaped echoes whose depth is greater than 1mm. They are found in cystic components and are characteristic of benignity, so that for this characteristic the node received zero points. Macrocalcifications are rough echogenic foci accompanied by acoustic shadows. For their existence, one point was awarded. Peripheral calcifications located along the entire margin or along one part of the margin receive two points. Some authors have drawn attention to intermittent peripheral calcifications with bulging soft tissue, as suspected malignancies. For nodes with calcifications that cause a strong acoustic shadow that prevents or limits the assessment of internal characteristics, especially echogenicity and composition, it is best to assume that the node is solid and assign 2 points for composition and one point for echogenicity [6].

Point (punctiform) echogenic foci are smaller than macrocalcifications and they are without acoustic shadow. For their existence, the node received three points. In solid constituents of thyroid nodules, they may correspond to psammomatous bodies (calcifications) that are associated with papillary carcinomas, and are therefore considered highly suspicious, especially in combination with other suspicious properties. This category includes echogenic foci that are associated with small comet tail artifacts in solid node components, as opposed to the large comet tail artifacts listed earlier. Significantly, small echogenic foci can be seen in spongy nodules, where they probably represent the posterior walls of small cysts. They are not suspicious in this case and should not be given any points [6].

Additional benign phenomena

Several ultrasound findings have been described as characteristic of benign changes with a high degree of reliability. These findings include the existence of uniform hyperechogenicity (white knight), as well as the variegated appearance of hyperechogenic areas, divided by hypoechoic bands resembling giraffe skin, both present in Hashimoto's thyroiditis.

Node size as an indication for FNA

In a 2005 publication, Machens et al. [17] reported that the cumulative risk for distant metastases for papillary and follicular thyroid cancers increased significantly for nodules larger than 2 cm. So he suggested a biopsy of nodules larger than 2 cm. Machens et al. Based their analysis on tumor size in resected samples rather than ultrasound. Subsequent studies have shown a significant lack of concordance between sonographic and pathohistological sizing, with the tendency of ultrasound toresult in larger measurements [18].

ACR TI-RADS is in accordance with most other guidelines in the recommended FNA for highly suspicious nodes of 1 cm or larger. That is, for slightly suspicious and moderately suspicious nodules larger than 2.5 and 1.5 cm. Biopsy is usually not indicated in a gland that is interspersed with multiple confluent nodules of similar characteristics [6].

Ultrasound report

For the ultrasound report, the exact dimension of the thyroid nodules is very important, since the maximum dimension of the nodule determines whether a given node should be biopsied or monitored.

Nodes should be measured in three planes. Maximum dimension in axial projection, maximum dimension in perpendicular projection in relation to the previous measurement, maximum longitudinal dimension in sagittal plane. The measurement should include a halo node if present. A calculation can also be used, which determines the volume. In addition to the dimensions, it is necessary to describe the ultrasonic characteristics, previously listed, on the basis of which the scoring is performed. It should be described whether the node touches the trachea or whether it is close to the tracheoesophageal groove (the place of the recurrent laryngeal nerve). An accurate description of the location of the nodes on the sonograms is equally important, especially when the gland is heteroechoic or multiple nodes are present. In the polynodose gland, describe accurately and in detail only the nodes that meet the criteria for FNA, only the others. As far as FNA is concerned, a biopsy of more than two nodes is not recommended, puncturing the most successful nodes. The decision to repeat a biopsy is usually made by physicians who monitor the patient

based on previous FNA results from the Bethesda system for thyroid cytopathology [18].

Definition of growth

Criteria for significant growth depend on the size of the node, which must also take into account the variability of measurements.
Significant magnification is defined as a 20% increase in at least two node dimensions and a minimum increase of 2mm, or a 50% or greater volume increase [6].

Tracking time

There is little agreement in the literature about the optimal time to monitor nodules, since the degree of growth does not reliably distinguish benign from malignant nodules. Examination intervals shorter than one year are not recommended, except for proven malignancies under active supervision, which may require more frequent monitoring. It is advisable to determine the monitoring intervals in relation to the number of points assigned to the node. For a TR5 lesion, we recommend monitoring once a year for 5 years. The first, second, third and fifth years should be done for TR4 controls. For TR3 controls can be performed in the first, third and fifth years.
Monitoring can be stopped after five years, if there are no changes in size, because stability in this time interval reliably indicates that the node behaves benignly, which is valid for all categories of nodes [6].

There are no published data for the treatment of nodules that increase significantly, if their size is still below the threshold for FNA and remain in the same number of ACR TI-RADS points for almost five years, but their monitoring is still necessary. If the ACR of the TI-RADS node increases during monitoring, the next control should be done in one year, regardless of its initial level [6].

Assessment of cervical lymph nodes

The suspicious finding is suggestive in spherical lymph glands, hyperechoic glands, loss of normal echogenic hilus, presence of more pronounced peripheral flow or vascularization than hilus. Heteroechogenicity with cystic components and point echogenic foci that may represent microcalcificationsis also a suspicious finding [6].

Categorization (scoring) of nodes after scoring

After scoring the ultrasonic properties of the nodes, the nodes are categorized as, TR1-TR5. TR1, benign nodules with 0 points TR2, non-suspicious nodes with 2 points, where FNA is not recommended for these nodes, TR3 minimally suspicious nodes with 3 points, where FNA is advised for nodes larger than 2.5 cm and for nodes larger than 1.5cm tracking, TR4 moderately suspicious nodes with 4-6 points, with FNA recommended for nodes larger than 1.5cm and for nodes larger than 1cm tracking and TR5 highly suspicious nodes having more than 7 points, with FNA is advised for nodes larger than 1 cm and monitoring for larger than 0.5 cm [6].

In addition to the ultrasound appearance of the nodule, other factors must be taken into account when deciding on FNA. TSH should be measured in all patients to rule out the possibility of a hyperfunctional node. Such lesions do not require a biopsy, because they are practically always benign. Risk factors for malignancy are exposure to ionizing radiation during childhood accidentally or for medical reasons, positive family history of thyroid malignancy, occurrence of nodules in children and the elderly, clinical features, nodules that are firm, hard, fixed to the substrate and the environment, grow rapidly. It has recently been confirmed that node location is also an independent risk factor for malignancy. Nodes located in the isthmus carry a higher risk of malignancy, while those located in the lower third of the lobe carry the lowest risk compared to those from the middle or upper lobes. These factors are not usually classified as a stratification algorithm, but may influence a definitive attitude in joint decision-making with patients about further diagnostic and therapeutic procedures [19].

Conclusion

Certain ultrasound properties, the characteristics of nodules in the thyroid gland, can significantly indicate malignancy and are used as criteria for FNA. The features with the greatest diagnostic significance for predicting malignancy are the shape of the nodule, higher than wider in the transverse section, ie ovoid appearance, the presence of small calcifications in the nodule, irregular margins, while the spongy and cystic appearance of the nodule and the presence of halo around the nodule significantly indicate benignity. Node size is an unreliable parameter for estimating nodes. These ultrasound properties have different sensitivity and specificity, but unfortunately

none of them is enough for certain rejection or confirmation of malignancy. FNA is a very important diagnostic method, but its performance must be selective since systematic puncture of all nodes, regardless of size or appearance, is not recommended. It is important that the indications for FNA be based on clinical characteristics, as well as on echosonographic stratification of the risk of malignancy.

REFERENCES:

1. Gharib H, Papini E, Garber JR, Duick DS, Harrell RM, Hegedüs L, at al.; American Association Of Clinical Endocrinologists, American College Of Endocrinology, And Associazione Medici Endocrinologi Medical Guidelines For Clinical Practice For The Diagnosis And Management Of Thyroid Nodules - 2016 UPDATE. Endocr Pract. 2016;22(5):622-39. doi: 10.4158/EP161208.GL.
2. Liénart F.Thyroid nodule: benign or malignant? Rev Med Brux. 2012;33(4):254-62.
3. Frates MC, Benson CB, Doubilet PM, Kunreuther E, Contreras M, Cibas ES, Orcutt J, Moore FD Jr, Larsen PR, Marqusee E, Alexander EK. Prevalence and distribution of carcinoma in patients with solitary and multiple thyroid nodules on sonography. J Clin Endocrinol Metab. 2006;91(9):3411-7.
4. Gharib H, Papini E. Thyroid nodules: clinical importance, assessment, and treatment. Endocrinol Metab Clin North Am. 2007;36:707-735.
5. Hegedüs L. Clinical practice. The thyroid nodule. N Engl J Med. 2004;351:1764-1771.
6. Franklin N. Tessler, MD, CMa , William D. Middleton, MDb, at al. ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White Paper of the ACR TI-RADS Committee Franklin N. Tessler, MD, CMa , William D. Middleton, MDb , Edward G. Grant, M. J Am Coll Radiol 2017;14:587-595.
7. Merima R. Goran. Značaj određivanja prediktivnih faktora za prisustvo limfonodalnih metastaza kod papilarnog tiroidnog mikrokarcinoma. Doktorska disertacija. Univerzitet u Beogradu, Medicinski fakultet 2018. Beograd.
8. Gilles Russa Steen J. Bonnemab Murat Faik Erdoganc Cosimo Duranted Rose Ngue Laurence Leenhardta aThyroid and Endocrine Tumors, Institute of Endocrinology, Pitié Salpêtrière H. European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: The EU-TIRADS. Eur Thyroid J 2017;6:225–237
9. Koike E, Noguchi S, Yamashita H, Murakami T, Ohshima A, Kawamoto H, et al. Ultrasonographic characteristics of thyroid nodules: prediction of malignancy. Arch Surg. 2001; 136(3):334-7.
10. Oh EM, Chung YS, Song WJ, Lee YD. The pattern and significance of the calcifications of papillary thyroid microcarcinoma presented in preoperative neck ultrasonography. Ann Surg Treat Res. 2014; 86(3):115-21.
11. Enrico P, Herve M, Andrea F, Laszlo H. 2020 European Thyroid Association Clinical Practice Guideline for the Use of Image-Guided Ablation in Benign Thyroid Nodules. Eur Thyroid J 2020;9:172–185.
12. Machens A, Holzhausen HJ, Dralle H: The prognostic value of primary tumor size in papillary and follicular thyroid carcinoma. Cancer 2005; 103:2269–2273.
13. Yoon JH, Kim EK, Hong SW, Kwak JY, Kim MJ: Sonographic features of the follicular variant of papillary thyroid carcinoma. J Ultrasound Med 2008; 27:1431–1437.
14. Kim DS, Kim JH, Na DG, Park SH, Kim E, Chang KH, Sohn CH, Choi YH: Sonographic features of follicular variant papillary thyroid carcinomas in comparison with conventional papillary thyroid carcinomas. J Ultrasound Med 2009;28(12):1685-92.
15. Na DG, Kim JH, Kim DS, Kim SJ: Thyroid nodules with minimal cystic changes have a low risk of malignancy. Ultrasonography 2016; 35:153–158.
16. Giorgio Grani, Marialuisa Sponziello, Valeria Pecce, Valeria Ramundo, and Cosimo Durante. Contemporary Thyroid Nodule Evaluation and Management. J Clin Endocrinol Metab, 2020; 105(9):2869–2883.
17. Machens A, Holzhausen HJ, Dralle H. The prognostic value of primary tumor size in papillary and follicular thyroid carcinoma. Cancer 2005;103:2269-73.
18. Deveci MS, Deveci G, LiVolsi VA, Gupta PK, Baloch ZW. Concordance between thyroid nodule sizes measured by ultrasound and gross pathology examination: effect on patient management. Diagn Cytopathol 2007;35:579-83.
19. Giorgio G, Marialuisa S, Valeria P, Valeria R, Cosimo D. Contemporary Thyroid Nodule Evaluation and Management. J Clin Endocrinol Metab, September 2020; 105(9):2869–2883.