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CLINICAL ASPECTS OF EARLY DIAGNOSIS OF THYROID PATHOLOGY: THE ROLE OF ULTRASOUND IN THE DETECTION OF INFLAMMATORY, PRECANCEROUS DISEASES AND THYROID CANCER

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Abstract

This scientific and analytical work systematizes the clinical applications of ultrasound diagnostics for various thyroid diseases. Diffuse and focal changes, echogenicity variations, nodular and cystic lesions, inflammatory changes, and neoplastic processes in this organ are covered in detail. It is emphasized that ultrasound examination occupies a leading place both in the initial diagnosis and as part of a comprehensive patient examination. The article presents a detailed and comprehensive review of modern ultrasound diagnostic methods using various modes: B-mode only, Doppler techniques, microangiographic technologies, elastography, contrast-enhanced ultrasound, and digital analysis algorithms using artificial intelligence, as well as their features and informative value in the differential and early diagnosis of thyroid pathological conditions. Current recommendations for ultrasound diagnostic specialists in accordance with the TI-RADS standard are presented. The article presents clinical protocols for the diagnosis and treatment of various thyroid pathologies, and also describes in detail current international practices and trends in the field of oncological surveillance and early diagnosis of thyroid cancer using ultrasound examination.

Keywords: thyroid gland, thyroid, thyroid lesions, radiology, ultrasound, ultrasound diagnostics, region of interest, B-mode, color Doppler, ultra-microangiography, ultra-microvascular imaging technology, elastography, contrast ultrasonography, computer-assisted diagnosis, artificial intelligence, fine needle aspiration biopsy, oncology, thyroid cancer.

Today, ultrasound diagnostics of various thyroid gland pathologies, including diffuse changes, decreased and increased echogenicity, nodular and cystic lesions, inflammatory changes, and thyroid cancer, is a leading method for both primary diagnosis and comprehensive examination. According to current protocols for the diagnosis and treatment of thyroid pathology in the Republic of Kazakhstan, ultrasound diagnostics occupies a leading position both in diagnostics and for monitoring [1-4].

As noted by Zhou H. et al. [5] thyroid cancer is one of the most common malignant tumors of the endocrine system. Thyroid nodules in 5% ~ 15% thyroid cancer are malignant. The incidence rate of thyroid cancer is increasing year by year. The incidence rate in women is generally higher than that in men. Papillary thyroid carcinoma is the most common clinical feature of thyroid cancer. It has the characteristics of high differentiation, low malignancy, good prognosis, and long survival. However, local metastasis and distant metastasis can also occur. Studies have shown that the rate of lymph node metastasis in papillary thyroid carcinoma is 84.7%, of which two-thirds have 70% lymph node metastases to thyroid cancer, and the incidence rate of thyroid cancer ranges from 70% to 85%. Local invasion or distant metastasis of thyroid cancer may increase the chance of postoperative recurrence. Therefore, metastasis of thyroid cancer is one of the important factors affecting the prognosis of patients. Early detection of thyroid cancer metastasis can help clinicians to estimate the surgical conditions. Ultrasound is the most important imaging method for the diagnosis of thyroid cancer metastasis, which is not only convenient but also accurate and reliable. With the continuous improvement of instrument performance, high-frequency ultrasound can not only sensitively display the internal structure of lesions but also provide blood flow information or judge the quality of lesions. In 2009, the American Thyroid Association emphasized the significance of ultrasound in thyroid nodules in the diagnosis and treatment manual of thyroid nodules and differentiated thyroid cancer and evaluated the ultrasonic thyroid examination as Grade A. Ultrasound examination is of great significance for early detection of thyroid cancer metastasis, early treatment, and improving the survival rate and quality of life of patients and has an important impact on the prognosis of patients.

A very interesting study was conducted by Kennedy E. et al. [6]. Our colleagues investigated which indications most commonly prompt referral for thyroid ultrasound and the diagnostic utility by indication. Extractors categorized referral reasons into (1) suspected palpable nodule (SPN) on physical examination; (2) chronic symptoms (CS) - e.g., globus sensation and dysphagia; (3) metabolic symptoms (MS; e.g., fatigue, weight change, and heat intolerance); (4) screening due to high risk for thyroid cancer (e.g., multiple endocrine neoplasia, Pendred syndrome, and family history of thyroid cancer); (5) follow-up of incidental thyroid nodule detected on another imaging study; or (6) combination of aforementioned factors. Suspected cases of goiter were included in the physical examination findings of a palpable thyroid nodule or mass. Additional variables extracted included the date of ultrasound, maximum diameter of largest nodule identified, if a biopsy was recommended by the interpreting radiologist, and if fine needle aspiration biopsy (FNAB) was performed. Demographic variables extracted included patient age, sex, race/ethnicity (White, Black, Asian, and Hispanic), insurance status (Medicaid, Medicare, private insurance, and uninsured), and Charlson Comorbidity Index (CCI) - 0, 1, and 2+. The primary outcome of interest was the percentage of thyroid ultrasounds performed that had an identifiable nodule for each referral indication. The secondary outcome evaluated "biopsy-recommended" nodules specifically, which were defined as nodules that the radiologist recommended for biopsy. Radiologists at institution routinely utilize the Thyroid Imaging Reporting and Data System (TI-RADS), and recommendations for biopsy are based on nodule size and TI-RADS category; however, specific TI-RADS scores were not abstracted. The percentage of biopsy-recommended nodules among all ultrasounds performed was compared among each referral indication.

In all, 3459 discrete neck ultrasounds were identified between 2017 and 2019. Of these, 1739 (50%) met inclusion criteria. The majority of patients were female (76%), White (86%), privately insured (62%), and healthy (76% with CCI 0); the mean age was 53 years standard deviation (SD). The most common indication for thyroid ultrasound referral was an SPN on physical examination (40% of all ultrasounds performed). The next leading referral indication was follow-up of a nodule identified on incidental imaging (28%). Referral for CS and MS made up 13% and 6% of ultrasounds, respectively. Only 2% of patients were referred for thyroid ultrasound due to high-risk factors. Patients referred for a combined indications accounted for 11% of thyroid ultrasounds. The combined indication was most often (45%) due to a patient presenting with CS and an SPN on examination. Among all ultrasounds performed, 62% identified a thyroid nodule. Patients referred for incidental findings had the highest percentage of ultrasounds with thyroid nodules present at 94%. Several possible reasons exist for the 6% of incidental findings that lacked a thyroid ultrasound correlate. For example, some were imaging "suggestive" of a nodule, but not definitively a nodule. These findings typically derived from imaging that was not optimal for the thyroid (e.g., chest or cervical spine computed tomography scan and nuclear imaging); and the suggestive nodule was ultimately not detectable on dedicated thyroid ultrasound [6].

In comparison, patients referred because of an solid pseudopapillary neoplasm (SPN) on examination and for CS identified nodules on 55% and 39% of ultrasounds, respectively. Patients with MS had a nodule on ultrasound 43% of the time. Among those referred for high-risk factors, 57% had a nodule present. Patients referred for combined indications had nodules on 42% of ultrasounds. Analysis of variance (ANOVA) indicated the difference in nodule detection rate between indications was statistically significant ($p < 0.05$). Only 27% of ultrasounds identified a thyroid nodule that was recommended for biopsy. Those referred from incidental imaging had the highest percentage of biopsy-recommended nodules (55%). This was followed, in order, by patients referred for physical examination of a palpable thyroid nodule (21%), high-risk factors (20%), combined indications (16%), MS (10%), and CS (6%). The overall mean maximum diameter of identified thyroid nodules was 1.9 cm (SD 1.3 cm). Of note, 32 radiology reports identified a thyroid nodule but did not record size and were, therefore, excluded from this specific analysis. Patients referred for incidentally found thyroid nodules had the largest mean nodule size at

2.4 cm (SD 1.2 cm). All other groups had a mean nodule size between 1.2 and 1.8 cm. The difference in average size of nodule was statistically significant ($p < 0.05$). A logistic regression model evaluated the association of patient age, sex, ethnicity, CCI, insurance status, and referral indication with identification of a nodule on ultrasound. Compared with patients referred for an SPN on examination, those with incidental nodules were over 10 times more likely to have a nodule found on ultrasound (odds ratio [OR] = 10.6 [confidence interval (CI) 7.0–16.0]). Conversely, patients referred for CS were half as likely to have an identifiable nodule compared with those referred for physical examination findings (OR = 0.5 [CI 0.4–0.7]). In addition, the odds of finding a nodule increased with age, especially for those aged 65 years and above (vs. age <45 OR = 3.6 [CI 2.2–5.9]). Finally, females were twice as likely to have a nodule found on thyroid ultrasound (OR = 2.0 [CI 1.5–2.6]). Results were similar when evaluating only biopsy-recommended nodules. Compared with patients referred for an SPN on examination, those referred for incidental findings were significantly more likely to have a biopsy-recommended nodule (OR = 4.7 [CI 3.5–6.3]), while those referred for CS were significantly less likely to have a biopsy-recommended nodule on ultrasound (OR = 0.3 [CI 0.1–0.5]. There was no difference in identifying biopsy-recommended nodules between sexes (female vs. male OR = 1.2 [CI 0.9–1.6]). In conclusion, the authors emphasize that only a quarter of dedicated thyroid ultrasounds yielded a nodule recommended for biopsy, and 39% did not have a nodule present at all. Moreover, only half of ultrasounds performed to evaluate a suspected nodule on physical examination actually identified one. Ultrasound referrals for symptoms had the lowest diagnostic yield, with fewer than 10% identifying a biopsy-recommended nodule. These findings suggest that re-evaluation of guidelines on thyroid ultrasound referral may be necessary to decrease the overutilization of thyroid ultrasound and the downstream consequences of detection of small potentially irrelevant nodules [6].

Wu J. et al. [7] to study the application value of SMI technology (ultra-microvascular imaging technology) and contrast-enhanced ultrasound in the differential diagnosis of thyroid benign and malignant nodules. According to the authors, thyroid disease has always been a common and frequent disease in clinical medicine, and its disease detection rate has been increasing year by year. Thyroid diseases are mainly divided into two categories: thyroid diseases treated by medical treatment and thyroid diseases treated by surgery. Thyroid cancer has also become one of the most common malignant secretory tumor diseases today. Ultrasound examination is a commonly used method for diagnosing thyroid diseases. During the diagnosis process, doctors need to observe the characteristics of ultrasound images and combine professional knowledge and clinical experience to give the patient's disease status.

The thyroid is an important organ of the human body, and it plays an important role in maintaining the health of the human endocrine system and the physical and mental health of the human body. With the advancement of medical ultrasound technology, ultrasound examination has become one of the most commonly used early detection methods for diseases due to its advantages such as low price, safety, noninvasiveness, convenient use, and ability to reflect the actual situation of tissues. A thyroid nodule refers to a mass in normal thyroid tissue that is different from normal glandular tissue. Thyroid nodules can be divided into two categories according to their nature: benign nodules and malignant nodules. Among them, benign nodules can be divided into nodular goiter, thyroid adenoma, and Hashimoto's thyroiditis (HT); the main type of malignant nodules is thyroid papilloma, which is the most common pathological type with the highest incidence of malignant thyroid nodules, while other pathological types are relatively rare. Due to the superficial location of the thyroid, the boundary between the outer envelope and surrounding soft tissues is clear, which provides favorable conditions for ultrasound diagnosis. The self-regulation of thyroid function refers to the regulation of the secretion of thyroxine by the amount of iodine supplied by the thyroid itself in the absence of thyroid-stimulating hormone (TSH) or the concentration of TSH is unchanged. Therefore, for the identification and diagnosis of benign and malignant thyroid nodules, ultrasound has always been one of the preferred imaging methods. With the continuous improvement of the level of science and technology, ultrasound inspection technology has also improved. When using ultrasound to diagnose thyroid diseases, thyroid neoplastic lesions can be displayed more clearly on the ultrasound images, and the lesions can be found in time and medical measures can be taken to control the condition. However, thyroid diseases are complex and changeable, especially malignant thyroid nodules, which are difficult to diagnose and control. During an ultrasound examination, benign and malignant nodules overlap on the two-dimensional sound image, which makes the diagnosis more difficult. Especially when some nodules have both benign and malignant characteristics, it is difficult to distinguish and qualitatively diagnose their nature based on the sonogram alone, which directly affects the choice of clinical treatment and surgical methods. This puts forward higher requirements for the initial qualitative diagnosis of lesion formation for ultrasound diagnosticians. Therefore, medicine urgently needs more advanced ultrasound diagnostic technology to overcome the difficulties encountered when using conventional ultrasound examination methods to diagnose thyroid diseases so as to help clinicians better diagnose and treat thyroid diseases and protect the health of patients. There is a clinical need for an intelligent diagnosis technology of thyroid diseases based on ultrasound images, which can provide objective and reliable auxiliary diagnosis opinions for thyroid diseases through the texture, shape, and other information of the images, freeing doctors from heavy work [7].

The study states that SMI technology is a new ultrasound diagnostic imaging method proposed by Canon in Japan in 2014. The principle basis of SMI technology is the motion suppression technology used to isolate and eliminate clutter but retain the vulgar blood flow signal. It includes ultrasound diagnostics, ultrasound therapy, and biomedical ultrasound engineering. Therefore, ultrasound medicine has the characteristics of combining medicine, science, and engineering. It involves a wide range of contents and has a high value in the prevention, diagnosis, and treatment of diseases. In the motion suppression technology, the ultrasonic detection image subtracts the change of the structure position from one frame to another, leaving only the color imaging part. SMI technology uses an adaptive wall wave to suppress clutter noise and minimize the flash artifacts of the image. Ultrasound technology is a high-tech developed in the 20th century. It is an emerging, interdisciplinary, and borderline science, which has attracted extensive attention of scientific and technological workers in countries such as the United States, Germany, Canada, Japan, and China. Contrast-enhanced ultrasound technology is a very prominent technological development in the field of ultrasound imaging diagnostics in recent years, and it can also be called the third leapfrogging revolution in the history of ultrasound imaging. Contrast-enhanced ultrasound uses low mechanical index (MI0.2) pulse contrast sequence imaging technology for ultrasound inspection, so it reduces the damage to microbubbles and greatly improves the signal-to-noise ratio of the image. In the project of acquiring a dynamic image by contrast-enhanced ultrasound, although the detected object can hold the breath for a short time, the slight movement of the organs cannot be completely eliminated, and the organ movement may be more serious after the breath-hold is over. In order to comprehensively use multiple imaging modes or co-modal changes to provide more complete information, the ultrasound contrast motion correction algorithm often integrates all effective information to make up for information deficiencies and better serve clinical diagnosis and treatment. In the work of our colleagues, the experimental methods of this study are as follows: first, 40 cases of benign and malignant thyroid nodules in China in 2018 were randomly selected. Among them, there were 20 cases of benign and malignant nodules. The maximum diameter of the nodules was 0.6~3.9 cm, with an average of 2.10.3 cm. The pathological results of all nodules were obtained through fine-needle aspiration biopsy or surgical treatment. Then, according to the standard blood flow distribution pattern of thyroid nodules, SMI technology and contrast-enhanced ultrasound were used to judge, and two different selected nodule cases composed of 20 nodules in each group (10 benign and malignant nodules) compared the distribution pattern of blood flow and the morphological characteristics of blood vessels. According to the standard blood flow distribution pattern of thyroid nodules, in this experiment, SMI technology was used to judge the blood flow distribution pattern of nodules 4 times. That the analysis of the blood flow distribution pattern of SMI technical nodules in 20 cases of benign and malignant thyroid nodules in this group showed that the number of central and mixed nodules was the same, and the number of peripheral nodules was the least. After evaluation, through 4 repeated judgments, the blood flow distribution pattern of the nodules under SMI technology is completely consistent with the actual case. It shows that SMI technology has a high accuracy rate for displaying the blood flow distribution pattern of thyroid nodules. SMI angiography showed that the vascular morphology of malignant nodules was stump type and crab foot type, with more tortuous and chaotic directions, and more irregular small branches, which was in line with the actual situation. This shows that SMI technology has a good imaging effect on nodular blood vessels [7].

In conclusion, the authors come to the conclusion that with the improvement of medical technology in today's society and the enhancement of people's health awareness, people's attention to thyroid diseases continues to increase. However, thyroid diseases, such as malignant secretory tumor diseases, are more complex and changeable, especially for malignant thyroid nodules, which are difficult in clinical diagnosis and treatment. Conventional thyroid ultrasound examination methods also have certain limitations, such as: for benign and malignant thyroid lesions, two-dimensional detection images sometimes overlap, which can also lead to different images of the same disease, and the same frequency of different diseases; at the same time, the blood flow with a low flow rate will not be displayed. And usually, it can only clearly display the larger blood vessel images, but the new microvascular network of the tumor cannot show its full picture, which means that thyroid cancer with less blood supply is easy to be missed. These deficiencies in conventional ultrasound examinations will directly affect the clinical treatment of thyroid diseases. Therefore, the medical field of thyroid diseases urgently needs more advanced ultrasound diagnostic technology to overcome the difficulties encountered in the diagnosis of thyroid diseases so as to help clinicians better diagnose and treat thyroid diseases and protect the health of patients. With the improvement of science and technology, two more advanced ultrasound detection technologies, SMI technology and contrast-enhanced ultrasound, have emerged in medicine. SMI technology can detect very low blood flow in thyroid lesions and can noninvasively and truly reflect the blood perfusion state of the nodules; contrast-enhanced ultrasound can continuously and dynamically observe the vascular distribution and blood perfusion of thyroid nodules, showing that the possibility of tumor neovascularization has also been improved. Therefore, SMI technology and contrast-enhanced ultrasound technology can solve the current problems in the diagnosis and treatment of thyroid diseases to a certain extent by virtue of their own advantages and have begun to be used in the identification and diagnosis of thyroid benign and malignant nodules. The research in this article has proved through experiments that SMI technology and contrast-enhanced ultrasound have high diagnostic sensitivity for the identification and diagnosis of benign and malignant thyroid nodules, that is they have better diagnostic efficiency and application value. And from the comparison of sensitivity, the diagnostic sensitivity of SMI technology is slightly higher than that of contrast-enhanced ultrasound, which shows that SMI technology has slightly better diagnostic performance and application value than contrast-enhanced ultrasound. The findings of this article provide a meaningful reference for the medical community to better apply SMI technology and contrast-enhanced ultrasound in the diagnosis and treatment of thyroid diseases. The number of features extracted manually in the research of thyroid nodular disease in this article is relatively small. In the future, more features can be added to study the interaction between artificial features and neural network features to achieve better classification results [7].

Jacome C.S. et al. [8] провели познавательное исследование, посвященное эффективности пальпаторного выявления узлов в щитовидной железе и корреляции этих результатов с последующими ультразвуковыми исследованиями. The authors conducted a retrospective observational study and identified adult patients (>18 years old) who underwent thyroid or neck ultrasounds (TUS) for the first time between January 1, 2015, and September 30, 2017, from ultrasound database. An initial search identified 5,938 patients with a TUS, from which our colleagues randomly selected a cohort of 500 patients who had a TUS ordered for any reasons (e.g., screening, workup of thyroid dysfunction). Of these, 327 patients were found to have both a TUS ordered and documented physical examination of the thyroid, which was performed either as part of the thyroid-related workup (e.g., thyroid function test abnormalities, personal or family history of thyroid cancer) or as a routine neck examination. In all those instances, the TUS was ordered after the physical examination had been conducted.

The researchers piloted and applied an extraction form to collect patient demographics and the specialty of the clinician who conducted the physical exam. From the physical exam documentation, they extracted the types of findings (solitary nodule, multinodular goiter, enlargement without nodularity, normal thyroid, and an "other category" for patients with indeterminate findings such as thyroid asymmetry). Additionally, study's authors documented the precise locations (right lobe, left lobe, isthmus or bilateral) where these findings were encountered, whenever the data was accessible. In a similar fashion, researchers carefully extracted the TUS findings (solitary nodule, multinodular goiter, enlargement without nodularity, no finding, and "other category" to group patients who had thyroiditis without the presence of nodules or lymphadenopathy) and noted the corresponding locations of the described findings. When there was a nodular finding in the ultrasound, authors extracted the largest diameter from the largest nodule. Given that the accuracy of thyroid physical exam may be affected by previous knowledge of thyroid-related symptoms, our colleagues also documented whether there was presence of symptoms associated with thyroid nodules or masses (e.g., neck fullness, dysphagia, odynophagia, choking, etc). The authors summarized continuous variables using means and standard deviations, and categorical variables using frequencies and percentages. Using the TUS findings as the reference standard, they calculated the accuracy of the findings noted from the thyroid palpation. First, our colleagues calculated the sensitivity, specificity, accuracy, and positive predictive value (PPV) and negative predictive value (NPV) of the thyroid palpation in the identification of any abnormal thyroid findings (any abnormality yes/no in thyroid palpation compared with any abnormality yes/no in thyroid ultrasound). Then, study's authors estimated the accuracy of the physical exam in detecting thyroid nodules (single thyroid nodule [yes/no] detected by thyroid palpation compared to thyroid nodule [yes/no] detected on confirmatory thyroid ultrasound), and multinodular goiters (multiple nodules [yes/no] found by thyroid palpation compared to multiple nodules [yes/no] identified on a thyroid ultrasound). Additionally, they calculated the accuracy and PPV of the thyroid physical exam to determine the location (e.g., right lobe, left lobe, isthmus or bilateral) of the thyroid findings when data was available in the medical records. Finally, authors calculated the proportion of additionally findings derived from a positive thyroid palpation as 1) the number of patients who had a solitary nodule palpated and were found to have multiple nodules on the subsequent ultrasound, or 2) patients who had a thyroid enlargement in the physical exam and found to have one or more thyroid nodules on the subsequent ultrasound. When possible, researchers conducted subgroup analyses by patient sex, patient weight (obese or overweight vs. normal weight based on body mass index (BMI) categories), size of the thyroid nodule (≤2 cm or >2cm), symptoms of nodular disease (yes and no), and by clinician specialty (primary care vs. specialties). Scientific researchers conducted a test interaction to evaluate for statistically significant subgroup differences [8].

Our colleagues included 327 patients, the majority were female (213/327, 65.1%) and white (275/327, 84.1%) with a mean age [standard deviation – (SD)] of 50.8 years old (16.9). Most patients were obese or overweight (225/327, 71.2%) and had the thyroid physical exam performed by a primary care clinician (178/327, 54.4%). Additionally, most patients did not present any symptoms of thyroid nodular disease (231/327, 70.6%). Regarding finding any thyroid abnormality, the thyroid physical exam had a sensitivity of 71.8% (n= 189/263; 95% CI 66%-72.2%), specificity of 35.9% (n= 23/64; 95% CI 24.2%-49.9%), accuracy of 64.8% (212/327; 95% CI 59.4%-70.0%), NPV 23.7% (23/97; 95% 17.5%-31.3%) and PPV 82.1% (189/230; 95% CI 79.1%-84.9%). When the diagnostic accuracy was estimated by an individual thyroid palpation finding (thyroid nodule or multinodular goitre), the physical exam had a sensitivity of 20.3% (n=12/59; 95% CI 12.3%-36.2%), specificity of 79.1% (212/268; 95% CI 73.7%-83.2%), accuracy of 68.5% (n=224/327; 95% CI 59.4%-70.0%), NPV 81.8% (n=212/259; 95% 81.5%-85.8%) and PPV 17.6% (n=12/68;95% CI 11.1%-27.1%) in detecting a thyroid nodule; and a sensitivity of 10.8% (n-=17/157; 95% CI 6.4%-16.7%), specificity of 96.5% (n=164/170; 95% CI 92.4%-98.7%), accuracy of 55.4% (n=181/327; 95% CI 49.78%-60.8%), NPV 53.9% (n=164/304; 95% 52.4%-55.4%) and PPV 73.9% (n=17/23; 95% CI 53.4%-87.5%) in finding a multinodular goiter. Out of 327 patients, 60 physical exams included the side of the thyroid nodule. Among these, the overall accuracy, and the PPV of the physical examination in identifying the location (e.g., right lobe, left lobe, isthmus, or bilateral) of the thyroid finding were 46.6% and 37.5%, respectively. Physical exams among symptomatic patients demonstrated superior performance than those conducted among asymptomatic patients, with higher specificity (100% vs. 62%; p<0.01), accuracy (83% vs. 62%; p<0.01), and NPV (87% vs. 79%; p<0.01) for detection of solitary nodules, as well as a higher NPV for detection of multinodular disease (61% vs. 51%; p<0.01). In addition, higher PPV for detecting multinodular disease was observed when a specialist conducted the physical exam compared to a primary care provider (100% vs. 60%; p<0.01) and when the nodule detected by physical examination was greater than 2 cm (100% vs. 73% for nodules ≤2 cm; p=0.026). The study's authors found that out of 68 solitary nodules palpated, 37 (54%) were found to have additional findings such as, multinodular goiter on a subsequent TUS; similarly, out of 88 patients for whom the physical exam identified an enlarged thyroid, 56 (64%) of these were subsequently found to have a solitary nodule (16 cases) or a multinodular goiter (40 cases) on the TUS. The authors emphasize that in this retrospective observational study, scientific researchers found that, while a thyroid physical exam can detect thyroid abnormalities, these findings were rarely concordant with findings identified on a subsequent thyroid ultrasound. Furthermore, the diagnostic accuracy of specific thyroid physical exam findings was low, particularly for the PPV of solitary thyroid nodules. For instance, out of every 100 patients with a physical exam consistent with a solitary thyroid nodule, approximately 18 had a thyroid nodule, while out of every 100 patients with a physical exam consistent with multinodular goiter, about 74 had the same finding in the ultrasound. In the course of the study, the authors state that thyroid physical exam has limited diagnostic performance and leads to additional findings when followed by a thyroid ultrasound. As such, thyroid physical exams in asymptomatic patients may play an important role in the overdiagnosis and overtreatment of thyroid cancer. To determine if any patient subgroups derive some benefit from thyroid physical exams beyond their use as a diagnostic approach, further research is necessary. Additionally, potential interventions should be explored to improve the accuracy of thyroid physical exams [8].

Next, we consider a study aimed to examine the potential associations between Doppler parameters and clinical characteristics of hypothyroid patients, such as the autoimmune nature of the disease and adequacy of LT4 replacement [9]. Angelopoulos N. et al. in their work note that While hormonal assays are commonly used for thyroid function assessment, Doppler sonography provides valuable information on vascularization and blood flow.

A total of 400 consecutive patients with hypothyroidism attending an Endocrinology outpatient clinic for annual follow-up visit were evaluated for eligibility. Autoimmune thyroiditis was considered the underlying disease of hypothyroidism based on high serum concentrations of antithyroid antibodies [thyroid peroxidase (anti-TPO) and/or thyroglobulin (anti-Tg) antibodies]. Exclusion criteria were history of Graves' disease or subacute thyroiditis, malignancies, pregnancy, previous use of medications that can affect thyroid stiffness (amiodarone, tamoxifen, anti-neoplastic) and nodular abnormalities of the thyroid gland (nodules > 3 mm detected by conventional B-mode ultrasound. A total of 338 patients treated for hypothyroidism [females: n = 292 (86.4%); males: n = 46 (13.6%)] were enrolled in the study. Demographic characteristics (age, sex, BMI), treatment parameters (LT4 daily dose) were recorded and thyroid hormones [TSH, free thyroxin (fT4)] were measured. All included subjects were residents of a geographical area of low-prevalence iodine deficiency disorders. The study protocol was conducted by the tenets of the Declaration of Helsinki and all patients agreed to participate in the study, which was approved by the Bioethics Committee of the Aristotle University of Thessaloniki, Greece. Conventional B-mode thyroid ultrasound and strain elastography [(real-time elastography (RTE)] were performed on a General Electric P9 machine (LOGIQ-P9; GE Medical Systems, Milwaukee, WI, USA) with an 8–12 multifrequency linear probe. Conventional grey-scale ultrasound was initially performed to measure transverse (two dimensions) and longitudinal (one-dimension) diameters and thyroid volume. Three linear dimensions were measured for each lobe: the length (L) was assessed on the sagittal view and the anterior–posterior (A-P) and width (W) diameters of each lobe were assessed on the transverse view. Given that the normal thyroid shape is ellipsoid, the volume of each lobe was automatically calculated by recording the abovementioned three linear dimensions (ellipsoid equation with a correction factor: V (ml) = L (cm) × A-P (cm) × W (cm) × 0.523). Thyroid vascularity was examined with color Doppler and patients were classified into four patterns: Pattern I (normal thyroid vascularity, blood flow limited to the peripheral thyroid arteries, absent parenchymal flow); Pattern II (minimally increased thyroid vascularity, mildly increased parenchymal flow); Pattern III (increased blood flow with a diffuse homogenous distribution, increased parenchymal flow with a diffuse homogenous distribution pattern) and Pattern IV (markedly increased parenchymal flow with a homogenous distribution, including the “thyroid inferno”). The probe was placed perpendicularly to the skin for RTE examination, and repetitive light compression was applied in the longitudinal plane. The ideal pressure on the target lesion was confirmed based on the cine-memory data. A cine-memory stores data obtained through the transmission and reception of ultrasound. A cine-memory generally has a storage capacity allowing storage of multiple numbers of frames obtained in time sequence. In a cine-memory, the newest input data overwrites the oldest data which is already stored in the memory, and this process is repeated. The patients held their breath while the images were obtained to avoid respiratory motion artifacts. The strain index (elastography ratio, E2/E1) was used that represents the ratio of the strain of thyroid parenchyma (E2) to that of sternocleidomastoid muscles (E1). Region of interest (ROI) for E2 was free-handed and designed at the peripheral edge of the gland to include the whole longitudinal image of each lobe; ROI for E1 was the sternocleidomastoid muscle in front of the ipsilateral thyroid parenchyma [9].

An endocrinologist with twenty years of experience in sonography, who was blinded to the clinical status, performed all thyroid ultrasound examinations. The

Doppler spectral analysis was of the right and left inferior thyroid arteries in the transverse scanning, in which the vessels crossed the common carotid arteries posteriorly, or in the longitudinal scanning of the ascending parts of the arteries, in which the vessels lie parallel to the common carotid arteries for the superior thyroid arteries. The superior thyroid artery was assessed with the probe positioned in the oblique sagittal plane, close to the superior thyroid pole. The inferior thyroid artery was assessed in the oblique transversal plane, close to the transition between the mid and inferior third of the thyroid. The cursor for evaluating the inferior thyroid artery was set close to the trachea to avoid artifacts from the common carotid artery and the internal jugular vein. Parameters for color Doppler are frequency 4.4–6.6 MHz, Gn 40%, pulse-repetition frequency (PRF) 2–8 kHz and Wall Filter (WF) 25–80 Hz. The angle correction cursor was parallel to the flow direction and the Doppler angle was kept at or below 60°. The sampling gate was set to 2 mm. The peak systolic velocity (PSV), end-diastolic velocity (EDV), and pulsatility indices (PI) and the resistive index (RI) values in the superior and the inferior thyroid arteries were obtained in both thyroid lobes. The mean value of the right and left lobes was used as the outcome parameter. Serum TSH and fT4 concentrations were measured by the immunochemistry method with enzyme chemiluminescence immunoassay (reference range: 0.27–4.5 mUI/ml and 0.8–1.5 ng/dl, respectively). Measurements were performed on the Cobas 8000 platform by Roche (Basel, Switzerland). Data were presented as mean ± SD or range (min—max). The Kolmogorov–Smirnov test was used to evaluate data distribution. The Student's t-test was used for group comparisons of continuous variables with a normal distribution (age, BMI, weight) and Mann–Whitney test was used for variables with a nonparametric distribution. Spearman and Pearson correlation coefficients were used to investigate correlations between variables. The Chi-squared test ($\chi 2$-test) was used for group comparisons of categorical variables. Predictive models were compared using Receiver Operating Characteristic (ROC) – Area Under the Curve (AUC) statistics. The optimal threshold values were determined from the ROC curve analysis and the Youden Index and its associated criterion values. The sensitivity, specificity, positive likelihood ratio and negative likelihood ratio values were calculated. A p-value < 0.05 was considered statistically significant [9].

In total, 288 patients (85.2%) had autoimmune thyroiditis, while 50 (14.8%) had no history of increased thyroid autoantibodies. A total of 68 patients (20.1%) had TSH concentrations ≥ 4 mIU/l (50 with autoimmune thyroiditis and 10 without autoimmune disease) and were considered suboptimally treated at the time of the enrolment, while 270 (79.9%) had TSH concentrations within the reference range (< 4 mIU/l) and were considered optimally treated (230 with autoimmune disease and 40 without). In patients with autoimmune thyroiditis, the LT4 dose (expressed as dose/weight) needed to achieve optimal thyroid treatment was higher (1.1 ± 0.4 vs. 0.8 ± 0.4 mcg/kg, p < 0.001). The elastography ratio was increased in patients with autoimmune thyroiditis (0.86 ± 0.52 vs. 0.77 ± 0.54, p = 0.026) compared with patients without autoimmune thyroiditis. There was a positive association between autoimmune thyroiditis and vascularity [$\chi 2(3) = 13.28$, p = 0.004, Cramér's V = 0.2]. In patients with no autoimmune thyroiditis, the total thyroid volume was lower in those with suboptimal LT4 replacement (5.3 ± 3.0 vs. 6.3 ± 3.7 ml, p = 0.032) compared with those with optimal replacement. There was no association between suboptimal LT4 replacement and vascularity [$\chi 2(3) = 2.11$, p = 0.551, Cramér's V = 0.08]. PSV and EDV of the inferior thyroid artery were higher in patients with suboptimal LT4 replacement compared with those with optimal replacement (PSV: 41.9 ± 17.0 vs. 35.1 ± 11.2, p = 0.004 and EDV 18.5 ± 9.0 vs. 14.7 ± 6.0, p = 0.004, respectively). RI was lower in patients with suboptimal LT4 replacement compared with those with optimal replacement (0.63 ± 0.08 vs. 0.66 ± 0.09, p = 0.024). The severity of hypothyroidism, as expressed by LT4 dose/BMI, was negatively correlated with thyroid volume (r = – 0.190, p < 0.001) and EDV values of superior (r = – 0.16, p = 0.009) and inferior thyroid arteries (r = – 0.17, p = 0.008). A weak positive correlation was found between LT4 dose/BMI with elastography ratio (r = 0.180, p < 0.001). This correlation was significant only in patients with autoimmune thyroiditis (r = 0.156, p = 0.007) but not in those without it (r = 0.255, p = 0.07). A positive correlation was found between dose/BMI and PI and RI of both arteries (PI superior: r = 0.130, p = 0.031; PI inferior: r = 0.140, p = 0.023; RI superior: r = 0.140, p = 0.024; RI inferior: r = 0.150, p = 0.014). A backward stepwise logistic regression analysis was performed to identify possible predictors of suboptimal LT4 replacement. All ultrasound indices (PSV, EDV, PI, RI, elastography ratio) were included as independent variables. Only RI and PSV of the inferior thyroid artery remained in the final model, [$\chi 2(2) = 14.93$, df = 2, p = 0.001). ROC curve analysis was performed for PSV of the inferior thyroid artery to define the optimal threshold for predicting suboptimal LT4 replacement (defined as TSH > 4 or > 5 mIU/ml). The AUC for TSH > 4 mIU/ml was 0.625 (p = 0.002, Youden Index: 0.238, associated criterion: > 31.2, sensitivity 81.8%, specificity 42%). For TSH > 5 mIU/ml, the corresponding AUC was 0.672 (p < 0.001, Youden Index: 0.305, associated criterion: > 37.7, sensitivity 61.8%, specificity 67%) [9].

In conclusion, our colleagues state that this is the largest study to have applied the concurrent evaluation of multiple ultrasound parameters of the thyroid gland in patients with hypothyroidism and the first to have used thyroid artery measurements to evaluate the therapeutic efficacy. Lymphocytic infiltration in autoimmune thyroiditis affects tissue echogenicity and causes a diffuse increase in parenchymal vascularization. In the natural history of the disease, as hypofunction gets severer, elasticity, volume of the gland and blood flow are reduced, indicating a fibrotic degeneration process. Effective monitoring and evaluation of LT4 supplementation are crucial to anticipate relapse of hypothyroidism. The monitoring is mainly based on thyroid hormone measurements since clinical symptoms may be absent in borderline TSH increases. However, in cases where blood tests are difficult to obtain, a color Doppler ultrasound can be used as an alternative tool in estimating responses to therapy and distinguishing those patients who should be further evaluated by hormonal examinations [9].

In the work of Soltani K. et al. [10] the authors note that the diagnostic role of Doppler ultrasonography regarding HT is not fully established. Our colleagues examined intraparenchymal RI as a Doppler parameter, thyroidal vascularity and other Gray-Scale findings in adults with HT in order to evaluate the clinical feasibility of RI in the diagnosis of this disease. This study is designed based on the cross-sectional analysis of sonographic findings in newly diagnosed patients with HT. The target population was selected from patients referred to the radiology department of Modarres Hospital from the endocrinology clinics of Modarres and Loghman Hospitals between 2013 and 2014. Subclinical hypothyroid patients were identified based on the clinical assessment of an endocrinologist. Exact laboratory data (TSH, FT4) were not available. Newly diagnosed patients without any history of receiving treatment for HT, who were either euthyroid or sub-clinically hypothyroid at the time of sonography, were included. Forty-eight females recently diagnosed with HT aging between 20 and 50. All the participants underwent Gray-scale (determining gland size, volume, and echogenicity) and color Doppler (evaluating vascularity and calculating RI of each lobe in 2 points) sonography by 1 radiology resident using a Medison X8 sonography device with a 7 MHz probe. Thyromegaly in females was defined as thyroid gland volume exceeding 15 mL. Gray-scale findings were classified into 4 grades (1–4) using the classification system introduced by Sostre and Reyes (Sostre S., Reyes M.M., 1991). Color Doppler findings were divided into 4 patterns (0–III) based on a visual scale provided by Schulz et al., 2003. The settings of the ultrasound equipment (gain and PRF) were calibrated such that aliasing of the carotid artery and jugular vein could not be seen. The RI (minimum PRF and maximum gain) of both upper and lower poles of each thyroid lobe were calculated by the ultrasound device using the formula below and the mean RI measured from both lobes was considered as the total RI of the thyroid gland. In addition, 45 controls aged between 20 and 70 years with normal thyroid laboratory results and without any prior history of thyroid disease were examined sonographically and the RI of those participants whose Gray-scale results proved to be normal was measured in 3 different points in each lobe. The mean RI of each participant from each of these 2 groups was calculated and compared to the mean RI of the control group.

Based on the definition provided by the World Health Organization, out of every 48 patients with HT, 30 (62.5%) had a normal thyroid gland volume (thyroid gland volume < 15mL) and 18 had thyromegaly (thyroid gland volume > 15mL). Based on the Gray-scale grading, 13 patients (27.08%) were classified as grade 1, 12 patients (25.00%) as grade 2, 18 patients (37.50%) as grade 3, and 5 patients (10.42%) as grade 4. The parenchymal vascularity of the thyroid gland (color Doppler appearance) presented as pattern 0 in 22 patients (45.83%), pattern I in 15 patients (31.25%), pattern II in 6 patients (12.5%), and pattern III in in 5 patients (10.42%). The RI ranged between 0.50 and 0.70 in the patient group and 0.47 and 0.70 in the control group. The average RI in the patient group was 0.5733 ± 0.05012and 0.5453 ± 0.05061 in the control group. Independent t-testing of the average RI showed a statistically significant difference between the patient and control groups (P = 0.009). The highest average RI was seen in Grade 1 (0.5808 ± 0.04173) and the lowest in Grade 4 (0.5500 ± 0.03808). One-way ANOVA of the average RI between different Gray-scale grading groups showed no statistically significant difference (P = 0.352). Furthermore, participants with grade 1 Gray-scale findings were considered as part of the normal or near-normal group and those with grades 2, 3, and 4 as part of the substantial Gray-scale changes group. The average RI of the normal or near-normal group was 0.5808 ± 0.04173 and 0.5706 ± 0.05319 in the substantial Gray-scale changes group. Independent t-testing showed no statistically significant difference in average RI when comparing the normal or near-normal with the substantial Gray-scale changes group (P = 0.537). The highest RI was seen in pattern 0 of color Doppler findings (0.5845 ± 0.04828) and the lowest in pattern II (0.5300 ± 0.04817). ANOVA results showed no statistically significant difference in average RI among different groups of color Doppler findings (P = 0.109). Results of Kruskal–Wallis test followed by pairwise comparisons showed a statistically significant relationship in terms of average RI between the grade 1 patient group and control group (P = 0.010) and between the grade 3 patient group and control group (P = 0.015). But the same comparison showed no statistically significant relationship between the grade 2 patient group and control group (P = .406) and between the grade 4 patient group and control group (P = 0.752). Results of Kruskal–Wallis test followed by pairwise comparisons showed a statistically significant relationship in terms of average RI between the pattern 0 patient group and control group (P = 0.003) and between the pattern I patient group and control group (P = 0.034). But the same comparison showed no statistically significant relationship between the pattern II patient group and control group (P = .418) and between the pattern III patient group and control group (P = 0.381). Summarizing the study, the authors state that the results of this study show that, regardless of gray-scale views and color Doppler patterns, the intraparenchymal RI of patients diagnosed with HT was higher compared to normal controls and, thus, this sonographic parameter may be a useful yet noninvasive modality in the diagnosis of HT [10].

It is impossible to ignore technological developments and the increasingly active development of thyroid ultrasound examination using artificial intelligence (AI).

In the clinical trial by Edström A.B. et al. [11] it was examined how the articifial intelligence (AI)-based diagnostics system S-Detect (this is a built-in AI feature in ultrasound machines that helps the doctor analyze the detected formations) for Thyroid influences the ultrasound diagnostic work-up of thyroid ultrasound performed by different ultrasound users in clinical practice and how different ultrasound users influences the diagnostic accuracy of S-Detect. The researchers conducted a clinical trial with 20 participants, including medical students, ultrasound novice physicians, and ultrasound experienced physicians. Five patients with thyroid nodules (one malignant and four benign) volunteered to undergo a thyroid ultrasound scan performed by all 20 participants using the same ultrasound systems with S-Detect installed. Participants performed a focused thyroid ultrasound on each patient case and made a nodule classification according to the European Thyroid Imaging Reporting And Data System (EU-TIRADS) [12]. They then performed a S-Detect analysis of the same nodule and were asked to re-evaluate their EU-TIRADS reporting. From the EU-TIRADS assessments by participants, authors derived a biopsy recommendation outcome of whether FNAB was recommended.

In this clinical trial, our colleagues observed that using S-Detect did not improve the thyroid diagnostic work-up of thyroid nodules among novice and intermediate ultrasound operators. Furthermore, they observed that the operator had a strong impact on the AI-generated ultrasound diagnosis, with a variation in diagnostic accuracy ranging from 40 to 100%, even though the same patients and ultrasound machines were used in the trial. A strength of this study is the controlled experimental setup, including participants with different ultrasound experiences who used S-Detect on the same ultrasound equipment and patient cases. In this way, we could measure the impact of the ultrasound operator's influence on the diagnostic accuracy of AI-assisted thyroid nodule diagnosis and how AI influenced the operator's assessments. Another strength is that we had a cytological/histological diagnosis on all the patients, and three experts were used to define the reference standard for the ultrasound characteristics. The authors believe that for AI-assisted ultrasound diagnosis to be successfully implemented in clinical settings, the technology should be developed with a clear purpose as a tool for the clinician in mind. Future research should focus more on how AI-assisted tools are affected by the image quality obtained by the ultrasound operator and how they affect the diagnostic process, including time use and patient outcomes. In conclusion, they observed that using S-Detect did not enhance the diagnostic accuracy of thyroid nodule evaluation among novice and intermediate ultrasound operators. The operator significantly influenced the AI-generated ultrasound diagnosis, with diagnostic accuracy ranging from 40 to 100%, despite the same patients and ultrasound machines used. While AI systems like S-Detect have the potential to improve the diagnostic work-up of thyroid nodules, more research is needed to ensure how it should be used in the diagnostic process to save time and improve final patient outcomes [11].

A fundamental study concerning multimodal imaging of solid thyroid lesions was conducted by Jung E.M. et al. [13]. Goal of the study was the assessment of AI-assisted diagnosis of solid thyroid foci with multimodal modern ultrasound imaging. 50 patients (26–81 years, 54.7±13.1 years) were included in the study. Multimodal ultrasound imaging by means of B-mode with linear probe (4–12 MHz) with option of automated documentation of findings by means of AI, with supplementary ultra-microangiography (UMA) was used. Macrovascularisation was assessed by dynamic contrast ultrasonography (CEUS) with parametric evaluation and perfusion analysis, and microvascularization was assessed by combined strain and shear wave elastography on a novel high-performance ultrasound system (Resona R9/Mindray) by an experienced examiner with independent reading. The evaluation was performed according to TI-RADS III-V. Inclusion criterion was preparation for immediate surgery by indication through interdisciplinary case conferences with endocrinologic, nuclear medicine, and surgical evaluation. All examinations with CEUS were performed after written consent. The evaluation of the examinations was performed retrospectively with the approval of the local ethics committee. The examinations were requested after preliminary examinations by special outpatient clinics with the question of the assessment of solid thyroid lesions that had been noticed in out-of-town preliminary examinations. An evaluation according to TI-RADS III-V had to be performed and it had to be decided to what extent a histological clarification was necessary or whether a follow-up should be performed. All examinations were performed by an experienced investigator (more than 3000 examinations per year, over more than 20 years) using a linear multifrequency probe (L 4–12 MHz) on high-performance ultrasound equipment with digital image documentation. This allowed independent subsequent evaluation by experienced readers. According to the predefined scheme of an AI image evaluation program, both thyroid lobes were measured in longitudinal and transverse axis with length, depth and width, the volume was calculated, the echogenicity was evaluated as homogeneous, discrete inhomogeneous or inhomogeneous and the echo pattern was judged as echo-complex or echo-normal. The ultrasound elastography techniques available in parallel mode as strain or shear wave elastography were used to assess compaction of thyroid tissue and solid foci. The pulsatile region of a carotid artery was bypassed as much as possible to avoid artifacts. Image quality could be assessed automatically, optimally with 5 green stars. False colors informed about homogeneous or inhomogeneous compaction. Measured values over individually adjusted ROI could be recorded in m/s or kPA, with values > 2.5 m/s or > 30 kPA considered suspicious for possible malignant lesions.

Detectable solid lesions were also measured by AI in three planes, and the rim contour was bypassed for volumetric detection. Then, marginal contour had to be assessed as regular, lobulated or irregular, rim as complete or incomplete, or absent, growth axis, parallel or directed in depth, shape as oval or roundish, and possible macro- or microcalcifications and entered into a predetermined scheme. After localization of the suspicious lesion, the evaluation according to TI-RADS III-V was then color-coded in a final scheme with topogram. This then also considers a possible tumor vascularization, as irregular malignancy-suspicious, or as regular marginal benign. UMA was used to assess the vascularization of tumor foci in as much detail as possible with velocity ranges < 10 cm/s. Vascular patterns were recorded dynamically in short cine loops up to 10 s. This also captured possible conspicuous lymph nodes with regular benign vascularization from the hilus or malignancy-typical from the margin. Macrovascularization of thyroid lobes and foci was classified as normal, enhanced, or decreased, and that of foci as regular or irregular. Color-coded duplex sonography, flow with glazing flow, and UMA were used for this purpose. The criterion for benign findings was a regular vascular pattern, especially a marginal vascularization, for example in adenomas. Irregular vascularization was considered suspicious for malignancy. This was then additionally investigated with CEUS to determine the extent to which irregular arterial hypervascularization with delayed wash out occurs, which is evaluated as a malignancy criterion. CEUS after bolus administration of 1 to 1.5 ml of sulphuhexafluoride microbubbles with 10 ml of saline solution cubital, if possible, was used to assess dynamic microvascularization of the suspicious solid lesions. When possible, cine loops of incipient arterial vascularization after 10 to 15 s up to one minute were then evaluated parametrically and by time intensity curve using the High-End Devices internal perfusion program. ROI were individually matched, in the center, at the edge of the lesion to be assessed compared with surrounding thyroid tissue. Parametric color maps were fitted to the corresponding perfusion parameters such as time to peak, peak, mean transit time, wash in area under the curve (wash in AUC) and tabulated at the end [13].

50 cases (26–81 years, mean age: 43±7 years) were examined with multimodal imaging consisting of B-mode, UMA, elastography and CEUS with parametric and perfusion analysis with good to very good image quality in all cases, according to the internal evaluation mode especially in the shear wave elastography technique with clearly>85% or 5 green stars. The volume of the thyroid lobes on both sides averaged 39 ml±5 ml (27 to 69 ml). All echo-poor, irregularly vascularized, inhomogeneously indurated lesion>1 cm were identified as highly suspicious for malignancy with early wash out kinetics and were also confirmed surgically. The 13 cases of histologically confirmed thyroid carcinoma (8 papillary, 2 medullary, 2 microfollicular, 1 anaplastic carcinoma) with a mean size of 15 mm±6 mm (9–21 mm) were correctly evaluated by TI-RADS IV based on irregular shape, induration>2.5 m/s or>30kPA and appositional wash-out kinetics using CEUS (TI-RADS V). Tumor lymph nodes could be correctly detected preoperatively only in one case of medullary carcinoma according to the surgical findings, based on irregular vascularization with UMA in roundish shape with cortex>4 mm with a transverse diameter up to 11 mm. In 25 cases of inhomogeneous nodular goiter, evaluation with TI-RADS III was performed in 31 cases, evaluation with TI-RADS IV was performed in 4 cases with incomplete marginal contour, partial marginal vascularization with UMA and partial wash out with indurations up to 2.5 m/s or 30 kPA, and surgical excision was performed for nodular goiter. In 12 cases of adenomas with diameters of 1.7 to 3.5 cm, mean 26 cm±0.5 cm, nodular goiter resulted in proportionately regressive nodular changes. Only in 7/12 cases a typical echo-poor rim and a typical rim vascularization were found. In 5 cases, the rim was incomplete. CEUS also showed a partial central wash out in these cases with but preserved marginal vascularization and elastography revealed partial induration up to 2.5 m/s or 30 kPA an assessment with TI-RADS III or IV rating. Using the AI tool, the 20 of 25 goiter nodes were evaluated as TI-RADS III, 7 of 12 adenomas, 5 goiter nodes and 5 adenomas as TI-RADS IV, 5 of 13 carcinomas as TI-RADS IV and 8 of 13 carcinomas as TI-RADS V. Microcalcification as a definite malignancy criterion was automatically detected in 5 of 13 malignancies, an echo-poor irregular echo structure in all cases, and in intracystic tumors in 2 cases. The shape was irregular in all cases, proportionately lobulated, but oriented in depth in only 8 of 13 cases. Of the 25 struma nodules evaluated as possibly also malignant, partial necrosis and inhomogeneous microvascularization with also induration on elastography occurred in all cases. For 37 patients both classifications were identical. From the 12 cases, histologically classified as TI-RADS V, 11 were also classified as TI-RADS V by the AI-based diagnosis. Of the 13 remaining cases in which there were discrepancies between the two methods, 12 were histologically confirmed grade 3 carcinoma. Using AI-based diagnostic they were classified at least one grade higher by AI (n=12, including 2 two grades higher) and in one case a histologically confirmed as TI-RADS V case one grade lower. During the course of the work, the authors established the new multimodal ultrasound modalities offer the possibility of early detection of malignant foci. Multicenter evaluation is needed to evaluate the possibility of additional AI in terms of differentiation from TI-RADS III to TI-RADS V [13].

In conclusion, it is worth noting that modern thyroid ultrasound diagnostics is a high-tech, multi-level system for assessing structural and functional changes in the organ, providing high clinical information value in identifying thyroid lesions, including solitary or multinodular thyroid nodules, inflammatory processes, and tumors. B-mode diagnostic ultrasound remains the primary method, allowing for the assessment of size, contours, echogenicity, echostructure, and calcifications, as well as precise ROI selection for subsequent quantitative analysis.

In thyroid cancer diagnostics, ultrasound risk stratification based on the TI-RADS standardizes descriptions and defines indications for fine needle aspiration biopsy, improving the clinical validity of invasive interventions. The additional use of Color Doppler ultrasound and microcirculation imaging technologies, including UMA and ultra-microvascular imaging technology, enables detailed analysis of the vascular pattern of nodular lesions. Evaluation of hemodynamic parameters such as PRF, PSV, EDV, PI, and RI expands the possibilities for differentiating between benign and malignant processes.

Elastography significantly contributes to increased diagnostic specificity, including the quantitative elastography ratio, which reflects tissue mechanical properties and the degree of fibrosis. This method is particularly informative in chronic inflammatory diseases such as autoimmune thyroiditis, including the most common form, HT, as well as in conditions accompanied by hypothyroidism. A comprehensive assessment of ultrasound features, combined with laboratory values for thyroid-stimulating hormone and free thyroxin, provides a comprehensive picture of the functional state of the thyroid gland.

A promising approach is CEUS, which allows for the analysis of the perfusion characteristics of lesions. The concept of multimodal imaging, consisting of B-mode, UMA, elastography, and CEUS, significantly improves diagnostic accuracy by integrating morphological, vascular, and biomechanical parameters.

The implementation of computer-assisted diagnosis (CAD) systems and artificial intelligence algorithms enables automated image processing, objectivization of ROI assessment, and reduction of operator dependence. The use of intelligent technologies contributes to the improvement of positive predictive value (PPV) and negative predictive value (NPV), increasing the reliability of risk stratification and clinical decisions.

Thus, the integration of B-mode, Doppler techniques, microangiographic technologies, elastography, contrast-enhanced ultrasound, and digital analysis algorithms forms the modern standard for comprehensive thyroid ultrasound examination. Ultrasound diagnostic techniques for various thyroid pathologies in general, and thyroid cancer in particular, are an important link in the specialty of "Radiology." Their high information content, sensitivity, and specificity often allow for an accurate diagnosis without resorting to more complex examination methods, which often carry a fairly high risk of complications and/or radiation exposure, and make it possible to conduct targeted, specialized treatment for these patients.

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