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ОРИГИНАЛЬНАЯ СТАТЬЯ

ROLE OF ULTRASOUND ELASTOGRAPHY IN CLASSIFICATION OF THYROID NODULE IN COMPARISON WITH HISTOPATHOLOGY

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Thyroid nodules are distinct lesions and are very easy differentiation from the surrounding thyroid tissues because of their unique characters. A new developmental medical imaging as ultrasound elastography capable to assess the elasticity and stiffness of thyroid nodules.

Purpose. The study aimed to determine the roles of ultrasound elastography in classification of thyroid lesions in patients with thyroid nodules and to compare between ultrasound elastography findings of thyroid nodules in relation to the histopathology.

Materials and methods. A prospective study with total of 30 patients with neck lumps were included during a period from 26th July 2023 to 29th May 2024. Sample composed from 10 males (33.3%) and 20 females (66.7%), who referred to Department of Radiology in private clinic. Participants data, including age, sex and histopathology report were included. All cases underwent FNA of the suspicious nodules, under US guidance. All nodules subjected to B-mode US-Eg (SAMSUNG, MEDISON, KOREA) followed by Doppler. ES scoring was color coded was used.

Results. In this study, the mean age was 46.1±8.61 yrs (median =48 yrs). The mean (median) thyroid nodule size was 14.53±5.59 mm (14.5 mm). Most of nodular masses was solid (22; 73.3%). The majority of lesion had iso-echoic echogenicity (21; 70%). Non-homogeneous lesion noticed in 24 patients (80%). Irregular margin was seen in ten patients (33.3%). The mean (median) volume of nodule detected was 8.39±4.72 cm3 (9 cm3). The results of ES are: Score 1# and 2# recorded in 12 patients which all appeared as benign nodules. Score 4# and 5# recorded in eight cases all appeared as malignant nodules with a high statistical difference (P<0.0001). The results of Strain ratio are the ratio (<1.55) recorded in 17 cases (56.7%) (9 benign and 8 malignant) and ratio (>1.55) recorded in 13 cases (43.3%) (12 benign and 1 malignant), with high statistical difference (P=0.022). As a results, 21 of 30 nodules (70%) appeared as benign and 9 nodules (30%) were malignant. In regard to histopathological diagnosis, benign nodules were documented in 17(56.7%) patients, while malignant nodules were seen nine cases (30%). In addition, four cases appeared as intermediate pattern. The highest sensitivity calculated among Elastography score, Micro-calcifications, volume, Echogenicity and Irregular margin as 92.4%, 91.1%, 88.9%, 85.6% and 80.2%, respectively. The highest specificity calculated among Elastography score, and Echogenicity as 90.8% and 85.7%, respectively. The more accurate test was Elastography score (89.8%). The greater AUC seen in Elastography score (0.976).

Discussion. Dissimilarly, Abdallah et al. reported 40 patients with benign nodules and 10 cases with malignant nodules, moreover, they recorded score 1 and 2 in 29 cases, score 3 in 14 patients and score 4 in seven cases with ratio of 2.5, these due to different in equipment used, large sample size, and early methods of diagnosis. Yang and co-authors, analyzed 265 nodules by US. They found 212 nodules measured >1 cm (patients=178), mean size (2.32 mm), 163 solid, 117 hypoechoic, 138 homogeneous, 106 micro-calcifications, 222 irregular margin, 53 Halo sign and volume (9.51 cm3), which extensively different from our finding because of large number of cases and long-time conducted for study.

Conclusion. Suspicious malignant thyroid nodule characters by solid, iso-echoic echogenicity, non-homogeneous, micro-calcifications, and irregular margin. Elastography Score 1# and 2# recorded for benign nodules. Elastography Score 4# and 5# recorded for malignant nodules. Strain ratio are the ratio (<1.55) recorded for benign and malignant and ratio (>1.55) recorded benign nodules. The highest sensitivity and specificity for distinguish thyroid malignancy calculated in Elastography score 92.4% and 90.8%, respectively. The accuracy of Elastography score is 89.8% with greater AUC (0.976). This study revealed that qualitative Elastography data are able of differentiation between malignant and benign thyroid nodules. The greater elastography score are more reprehensive to malignant lesions versus benign lesions (lower Elastography).

Keywords: ultrasound elastography, thyroid nodules, elastography score, strain ratio, papillary thyroid carcinoma.

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РОЛЬ УЛЬТРАЗВУКОВОЙ ЭЛАСТОГРАФИИ В КЛАССИФИКАЦИИ УЗЛОВ ЩИТОВИДНОЙ ЖЕЛЕЗЫ В СРАВНЕНИИ С ГИСТОПАТОЛОГИЧЕСКИМ ИССЛЕДОВАНИЕМ

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Узлы щитовидной железы являются четко выраженными образованиями и очень легко дифференцируются от окружающих тканей щитовидной железы из-за их уникальных характеристик. Новый развивающийся метод визуализации такой, как ультразвуковая эластография, способен оценивать эластичность и жесткость узлов щитовидной железы.

Цель исследования. Определить роль ультразвуковой эластографии в классификации узлов щитовидной железы и сравнить результаты ультразвуковой эластографии узлов щитовидной железы с гистопатологическим исследованием.

Материалы и методы. В проспективное исследование было включено 30 пациентов с уплотнениями на шее в период с 26 июля 2023 года по 29 мая 2024 года. Выборка состояла из 10 мужчин (33,3%) и 20 женщин (66,7%), которые обратились в отделение лучевой диагностики частной клиники. Были включены данные пациентов, включая возраст, пол и отчет о гистопатологическом исследовании. Во всех случаях была проведена тонкоигольная аспирационная биопсия подозрительных узлов под контролем УЗИ. Все узлы были подвергнуты УЗИ в В-режиме (SAMSUNG, MEDISON, КОРЕЯ) с последующей допплерографией. Использовалась цветовая шкала оценки эластографии.

Результаты. В этом исследовании средний возраст составил 46,1±8,61 лет (медиана=48 лет). Средний (медианный) размер узла щитовидной железы составил 14,53±5,59 мм (14,5 мм). Большинство узловых масс были солидными (22; 73,3%). Большинство узлов имели изоэхогенную структуру (21; 70%). Неоднородная структура узлов была отмечена у 24 пациентов (80%). Неровные края наблюдались у десяти пациентов (33,3%). Средний (медианный) объем обнаруженного узла составил 8,39±4,72 см3 (9 см3). Результаты эластографии следующие: оценка 1# и 2# зарегистрирована у 12 пациентов, все они выглядели как доброкачественные узлы. Оценка 4# и 5# зарегистрирована в 8 случаях, все они выглядели как злокачественные узлы с высокой статистической разницей (P < 0,0001). Результаты коэффициента деформации – это соотношение (<1,55), зарегистрированное в 17 случаях (56,7%) (9 доброкачественных и 8 злокачественных) и соотношение (>1,55), зарегистрированное в 13 случаях (43,3%) (12 доброкачественных и 1 злокачественный), с высокой статистической разницей (P=0,022). В результате 21 из 30 узлов (70%) оказались доброкачественными, а 9 узлов (30%) были злокачественными. Что касается гистопатологической диагностики, доброкачественные узлы были зарегистрированы у 17 пациентов (56,7%), в то время как злокачественные узлы наблюдались в девяти случаях (30%). Кроме того, четыре случая квалифицировались как промежуточный результат. Самая высокая чувствительность, рассчитанная среди баллов эластографии, микрокальцификаций, объема, эхогенности и неровного края составила 92,4%, 91,1%, 88,9%, 85,6% и 80,2% соответственно. Самая высокая специфичность, рассчитанная среди оценок эластографии и эхогенности, составила 90,8% и 85,7% соответственно. Более точным тестом была оценка эластографии (89,8%). Большая AUC наблюдалась в оценке эластографии (0,976).

Обсуждение. В отличие от этого, авторы Абдалла и др. сообщили о 40 пациентах с доброкачественными узлами и 10 случаях со злокачественными узлами, более того, они зарегистрировали оценку 1 и 2 в 29 случаях, оценку 3 у 14 пациентов, оценку 4 в 7 случаях с соотношением 2,5, что связано с разным используемым оборудованием, большим размером выборки и ранними методами диагностики. Янг и соавторы проанализировали 265 узлов с помощью УЗИ. Они обнаружили 212 узлов размером >1 см (пациентов = 178), средний размер (2,32 мм), 163 солидных, 117 гипоэхогенных, 138 однородных, 106 с микрокальцификатами, 222 с неровными краями, 53 с симптомом «ободка» и объема (9,51 см3), что значительно отличается от наших результатов из-за большого количества случаев и длительности проведения исследования.

Заключение. Подозрительные злокачественные признаки узлов щитовидной железы были выявлены по солидной, изоэхогенной, негомогенной структуре, микрокальцификации и неровному краю. Эластографические баллы 1# и 2# регистрировались для доброкачественных узлов. Эластографические баллы 4# и 5# регистрировались для злокачественных узлов. Коэффициент деформации – это отношение (<1,55), регистрируемое для доброкачественных и злокачественных, и отношение (>1,55), регистрируемое для доброкачественных узлов. Самая высокая чувствительность и специфичность для различия злокачественности щитовидной железы рассчитывалась по шкале эластографии (92,4% и 90,8% соответственно). Точность шкалы эластографии составила 89,8% с большей AUC (0,976). Это исследование показало, что качественные данные эластографии способны различать злокачественные и доброкачественные узлы щитовидной железы. Более высокие баллы эластографии больше характерны для злокачественных поражений по сравнению с доброкачественными (более низкие показатели эластографии).

Ключевые слова: ультразвуковая эластография, узлы щитовидной железы, оценка эластографии, коэффициент деформации, папиллярная карцинома щитовидной железы.

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Thyroid nodules are distinct lesions situated within the thyroid gland, and their unique characteristics often allow for easy differentiation from the surrounding thyroid tissue [1]. The natural progression of benign nodules is not well understood, but it is likely that most palpable nodules tend to decrease in size of 38% potentially disappear entirely. A primary concerning associated with thyroid lesions is potential for malignant pattern [2]. A small percentage of thyroid nodule eventually turns out to be malignant, approximately 5% [3]. The prevalence of thyroid nodules is widespread, with approximately 4–7% of the population palpably detecting them and as many as 19–67% being identified through more sensitive ultrasound imaging [4]. Nodules that exhibit characteristics like firmness, immobility, or rapid growth necessitate prompt evaluation as they may indicate a higher likelihood of malignancy [5].

Thyroid gland US is simple and inexpensive, doesn't involving exposure to ionizing radiations and provide valuable data. It is mainstay of diagnostic image of thyroid gland: superficial side of gland mean that its shape, size, fine structures, and vascularity can be demonstrating through high-frequency probes (lineararray-transducer) with excellent, axial and lateral image resolution. B-scan, color Doppler imaging provide useful data about thyroid perfusion, that is useful in differential diagnosis of inflammatory diseases and thyroid nodules [6, 7].

US play a crucial role in diagnosing thyroid nodules, with various radiographic features providing valuable insights. In fact, it is recommended that all cases with a nodular thyroid undergoing US assessment. An ultrasound examination should focus on several key features, including the size of nodules, its echogenicity and composition, presentation of additional nodules and any sonographic appearances suggestive of cancer. While no single ultrasound feature has high sensitivity and positive predictive value for thyroid cancer, certain characteristics, when occurring in the combination, are associated with a greater risk of malignant lesions [8]. Lonely, nodular size is not predictive of cancer, and risks for malignancy in a thyroid nodules are shown to be a same regardless of size on US. Furthermore, while ultrasound is valuable for detecting nodules, it also has its own constraints. Distinguishing between benign and malignant nodules based solely on ultrasound features is challenging due to difficulties in interpreting margin delineation, nodule consistency, and reflectivity, influenced by technical aspects of the ultrasound equipment [9].

One of the significant features that is assessed by ultrasound is calcification, often correlated with malignant lesions [10]. Microcalcifications, characterized by punctate echogenic foci with no posterior shadows, are highly specific for malignancy, especially in PTC cases. In addition, coarse calcifications and peripheral rim calcification, although seen in both malignant and benign nodules, may suggest the presence of papillary or medullary thyroid carcinoma [11]. Nodules can appear hypo-echoic, iso-echoic and hyper-echoic related to normal gland. Hypo-echoic solid nodules are commonly found in PTC and nearly all MTC. Iso-echoic and hyper-echoic solid nodules, though less common, may still exhibit malignant potential. Moreover, a substantial cystic component generally indicates a benign condition, although it is noteworthy that a considerable percentage of papillary carcinomas may exhibit a cystic component. In contrast, the presence of a halo around a well-defined hypo-echoic or iso-echoic nodule is typically associated with a follicular-adenoma. However, it is important to note that this halo is absent in over 50% of benign nodules. Additionally, up to 24% of PTC may present with a halo, whether complete or incomplete [12]. Moreover, thyroid colloid nodules have the characteristic appearance of comet-tail artifact [13].

Additional features contributing to the suspicion of malignancy include irregular margins, taller-than-wide nodules, and invasion of local structures. Moreover, shadowing all-over the edges of nodules (edge refraction shadow) are associated with PTC [12, 14]. Conversely, sonographic features favoring benign nodules include a large cystic component, hyper-echoic solid appearance, comet-tail artifact, and a spongi-form appearance [15]. Ultrasound is also effective in detecting cervical lymphadenopathy, with specific features indicating a higher risk for malignancy, such as a hetero-geneous echotexture, calcifications, absence of hilus, rounded appearance, cystic changes, and increased color Doppler flow. Notably, there is no strict threshold for lymph node biopsy, however, it is advised for lymph nodes exhibiting suspicious features, even in absence of a malignant-appearing thyroid nodules [16].

A relatively new development in medical imaging called ultrasound elastography assesses the elasticity or stiffness of tissues, including thyroid nodules. It operates on the premise that malignant tissues tend to be stiffer than benign ones [17]. There are primarily two types: shear-wave elastography, measuring the speed of shear waves through the tissue, and strain elastography, measuring tissue displacement under an applied force [18]. Its introduction as a diagnostic tool for thyroid nodules provide a non-invasive method to distinguish between benign and potentially malignant nodules. Elastography surpass traditional US in evaluating thyroid nodules in several aspects [19]. Despite the advantages of elastography, histopathology remains the gold standard for thyroid nodule diagnosis, involving the examination of tissue taken from a biopsy under a microscope. Histopathology provides a comprehensive cellular-level view necessary for a conclusive diagnosis [20]. However, this approach carries the risk of sampling errors and is invasive [21]. Elastography offers a rapid, easy, and non-invasive method for evaluating nodules, but its results should be cautiously interpreted in conjunction with other imaging and clinical findings [19]. Although histopathology is invasive, it delivers a conclusive diagnosis [20]. Hazem et al. concluded that SWE is an effective non-invasive method helpful in the discrimination of malignant and benign thyroid nodules [22].

Several studies demonstrated promising results for the use of sono-elastography combined or not combined with conventional-US [23-25]. In SWE, tissues elasticity can be measured directly by the Young's modulus to estimate thyroid tissue stiffness in kilopascals (kPa) [26]. In 2016, guidelines for SWE were published by Cosgrove et al. [27]. The SWE influenced by the arterial pulsation, cystic components and calcification in the nodules [28]. Lymphocytic infiltration and fibrosis may result in the changes in stiffness pattern [29]. In 2022, Petersen et al. indicated that a combination of SWE and TIRADS seeming to be superior for a risk stratification of thyroid lesions than each method alone [30]. A strain ratio is generated in real – time by the device or offline by dividing the strain of normal thyroid parenchyma by that of the nodule. It is important that the two region of interest at the same tissue depths, with different less than 10mm, in order to obtviate the effects of strain decay. Strain ratio measure how much stiffer the lesion is than normal thyroid [31].

Purpose.

To determine the roles of ultrasound elastography in classification of thyroid lesions in patients with thyroid nodules and to compared between US elastography findings of thyroid nodules in relation to the histopathology.

Materials and Methods.

Study design and setting.

A prospective study with total of 30 patients with neck lumps were included in this study during a period from 26th July 2023 to 29th May 2024. Sample composed from 10 males (33.3%) and 20 females (66.7%), they referral to Department of Radiology in private clinic.

Data collection.

Participants data, including age, sex and histopathology report (Bethesda II, Bethesda III, Follicular carcinoma, Lymphoma, Papillary thyroid carcinoma, Medullary carcinoma, Anaplastic thyroid carcinoma, Adenoma and Hürthle tumor). We selected patients who underwent thyroidectomy due to certain reasons, such as highly suspicious malignancy, thyrotoxic and compression symptoms, who were subjected to pathological section examination and use a result as a gold standard.

Inclusion criteria.

In cases of multi-nodular goiter (M.N.G.) Elastography was performed on the largest suitable nodule and the only nodule in case of solitary thyroid nodule, taking care to ensure that the nodule to be examined fulfilled the following criteria: adequate amount of adjacent normal thyroid tissue was available for comparison, size of the nodule was more than 5mm ,suspicious nodule according to American Thyroid Association Management Guidelines [Thyroid nodule] (69), the US properties included: hypoechogenicity, micro-calcifications; raise nodular vascularity; infiltrative margin and taller>wide on transverse view, and predominantly solid nodule with no or small cystic areas.

Exclusion criteria.

Nodules with a cystic component >15 percent of the nodule volume, a Large nodules represent >75 percent of the thyroid lobe volume, peripheral egg-shell calcification or significant intra-lesional coarse calcifications nodules were all avoided.

Ultrasound and ultrasound elastography examinations.

We did examination to all patients. A 2–14 MHz was the frequency that all cases were examined the transducer (Shenzhen Mindray Bio-Medical Electronics Co., Ltd., China) of US was put on the neck with a gel, the neck was hyperextended and the chin was raised, techniques done by the same senior. All nodules subjected to B-mode US (SAMSUNG, MEDISON, KOREA, 620LM3HW100004H) followed by color Doppler (TOSHIPA-APLIO, Japan). The parameters of nodules were collected: Nodule size (cm), Nodule nature (solid, cystic, mixed), Echogenicity (isoechoic, hyper, hypo), Homogeneity (Homogeneous and nonhomogeneous), presence of microcalcifications, Irregular margin, Halo sign and volume (cm3). Real-time elastography measurements were performed after conventional US examination using the same probe. as for conventional B-mode US. Patients were lying in the same position. With US probe a light external compression was applied to the anterior neck above the nodule to fix its position and to prevent lateral movement. The region of interest was set to include the evaluated nodule and the surrounding thyroid and subcutaneous tissue, as this technique of elastography measures relative stiffness.

US elastogram was superimposed over the B-mode image and the stiffness of the tissue was colour-coded between red and green (softest) to blue (hardest) upon fivepoint scale according to the classification of Ahn et al., Yerli et al. and Rago et al. [32-34] (Fig. 1):

- 1 Elasticity in whole nodule
- 2 Elasticity in a large part of the nodule.
- 3 Elasticity only at the peripheral part of the nodule.
- 4 No elasticity in the nodule.
- 5 No elasticity in the nodule and in the posterior shadowing.

Strain ratio was measured as the operator traced the outline of the lesion in the two-dimensional figure. Then, the area adjacent to the target lesion, which was at the same depth as the lesion, was selected as a reference. The SR was automatically calculated by the software.

Ethical considerations.

Written informed consent was obtained from the cases for participating in this research. The study was approved by The Medical Ethical

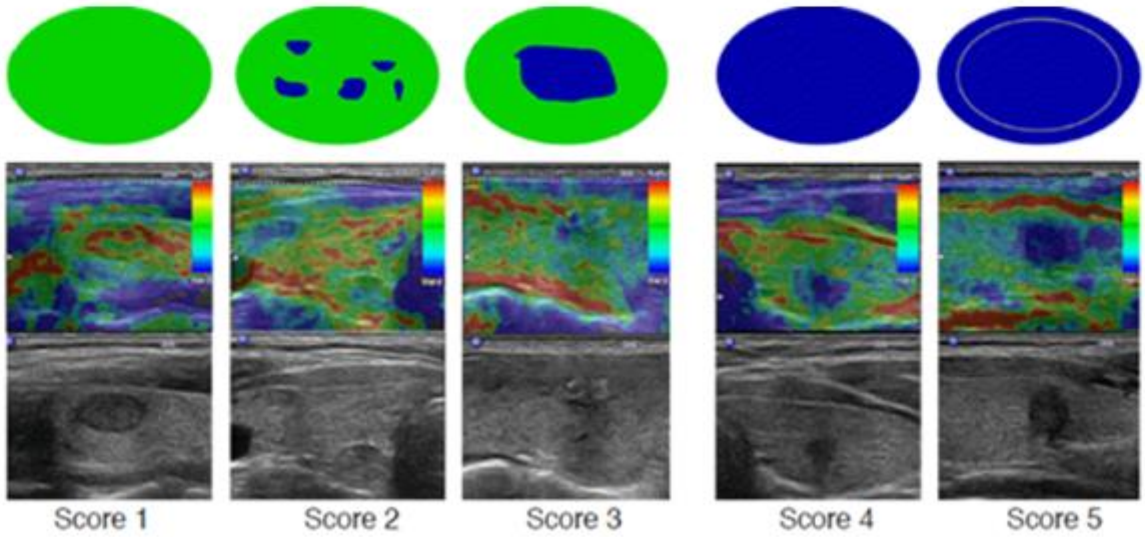

Fig. 1 (Рис. 1)

Fig. 1. Scheme.

Thyroid nodule elastographic scoring system [34].

Рис. 1. Схема.

Эластографическая система оценки узлов щитовидной железы [34].

Table №1. Demographic data distribution (n=30).

Variables		No. of patient	%
Age (years)	20-30	2	6.7
	31-40	6	20.0
	41-50	14	46.7
	51-60	7	23.3
	>60	1	3.3
Gender	Male	10	33.3
	Female	20	66.7

Committee of College of Medicine, Babylon University (5053 in 26-07-2023).

Statistical analysis.

Statistical package for social science (SPSS version 24.0, Chicago, US, IBM Inc.) was used. Data were described as number and percentage for qualitative data and (mean, median and SD) calculation for quantitative data. Monte Carlo test was used to compare two groups. Diagnostic accuracy was evaluated with ROC curve analysis. The area under curve (AUC) for the diagnostic test was used. The accuracy, sensitivity, and specificity were calculated. A one-sided P value of <0.05 was considered statistically significant.

Results.

Demographic data.

In this study, 30 patients with neck lumps were enrolled. The mean age of patients was 46.1±8.61 yrs ranged from 28 yrs to 61 yrs (median=48 yrs). The common recorded age group was (41-50 yrs) in 14 (46.7%), followed by those aged (51-60 yrs), (n=7, 23.3%). In relation to gender, 20 (66.7%) were females, and 10 (33.3%) were males (Table №1).

US data.

The mean (median) nodule size was 14.53±5.59 mm (14.5 mm). The largest dimensional of nodule was between (11-20 mm) in 18 cases (60%). Most of nodular masses was solid (22; 73.3%) whereas cystic lesions reported in 8 cases (26.7%). The majority of lesion had isoechoic echogenicity (21; 70%). The hypo-echoic found in seven cases and hyper-echoic in two cases. Regarding homogeneity, non-homogeneous lesion noticed in 24 cases (80%) of patients while homogeneous nodule seen in six cases. Micro-calcifications presented in nine cases (30%), however, 21 (70%) didn't showed this. Irregular margin was seen in ten patients (33.3%) while it was absent in 20 patients (66.7%). The mean (median) volume of nodule

Table №2. US parameters (n=30).

Parameters		No. of patient	%
Nodule size (mm) mean±SD (median)= 14.53±5.59 (14.5)	1-10	9	30.0
	11-20	18	60.0
	>20	3	10.0
Nodule nature	Cystic	8	26.7
	Solid	22	73.3
Echogenicity	Hypo	7	23.3
	Hyper	2	6.7
	isoechoic	21	70.0
Homogeneity	Non	24	80.0
	Homogeneous	6	20.0
Micro-calcifications	No	21	70.0
	Yes	9	30.0
Irregular margin	Absent	20	66.7
	Present	10	33.3
Volume (cm3) mean±SD (median)= 8.39±4.72 (9)	≤1.0	2	6.7
	1.1-5.0	8	26.7
	5.1-10.0	10	33.3
	>10.0	10	33.3

detected was 8.39±4.72 cm3 (9 cm3), as shown in Table №2.

Elastography score and Strain ratio.

Table 3 listed the results of ES. Score 1# recorded in five cases (16.7%) which all appeared as benign nodules. Score 2# recorded in seven patients (23.3%) which all appeared as benign nodules. Score 3# recorded in ten cases (33.3%) (9 benign and 1 malignant). Score 4# recorded in two cases (6.7%) all appeared as malignant nodules. Score 5# recorded in six cases (20%) all appeared as malignant nodules, with a high statistical difference (Monte Carlo= 25.71, P<0.0001) as showed in (fig. 2, 3).

Table №4 listed the results of Strain ratio. The mean ratio was 1.673 (median= 1.4). the interquartile range was (1.55). Ratio (<1.55) recorded in 17 (56.7%) cases (9 benign and 8 malignant). Ratio (>1.55) recorded in 13 cases (43.3%) (12 benign and 1 malignant). These findings presented with high statistical difference (Monte Carlo= 5.43, P=0.022).

The diagnosis by Eg was listed in Table 5. 21 of 30 nodules (70%) appeared as benign and 9 nodules (30%) were malignant.

Histopathological data.

In regard to histopathological diagnosis as showed in Table №6, benign nodules were documented in 17 patients (56.7%), while malignant nodules were seen nine cases (30%). In addition, four cases appeared as intermediate pattern. Finally, 14 cases (46.7) showed Bethesda II class by FNA. Six cases belonged to Bethesda III. Seven cases proved to be papillary thyroid carcinoma (PTC). One case was Lipoma. One case was Medullary carcinoma (MTC) and other was Anaplastic thyroid carcinoma (ATC).

Receiver operating characteristic (ROC) curves and accuracy rates of Elastography.

The diagnostic accuracy was determined by using the area under a receiver operating characteristic (ROC) curve beside accuracy rates to identify malignant from benign thyroid nodules. The highest sensitivity calculated among Elastography score, Micro-calcifications, volume, Echogenicity and Irregular margin as 92.4%, 91.1%, 88.9%, 85.6% and 80.2%, respectively. Whereas the least sensitive value was Homogeneity (50%). The highest specificity calculated among Elastography score, and Echogenicity as 90.8% and 85.7%, respectively. Whereas the least specific value was Homogeneity (50%). The more accurate test was Elastography score (89.8%) and the lowest accurate value was Homogeneity (45.2%) as shown in Table №7.

The greater AUC seen in Elastography score (0.976), while the least specific value was Homogeneity (0.357).

All other parameters illustrated as Nodule size, Nodule nature, Echogenicity, Homogeneity, Micro-calcifications, Irregular margin, Volume

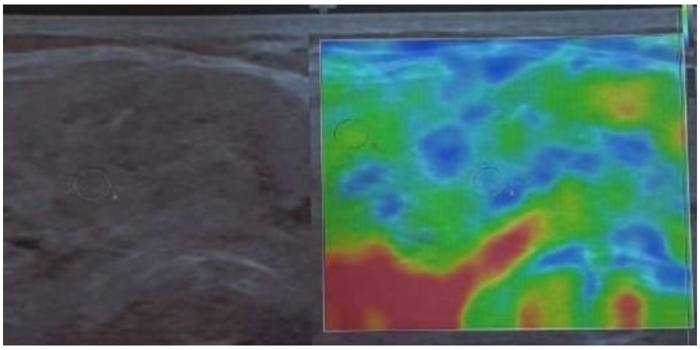

Fig. 2 (Рис. 2)

Fig. 2. Echogram, thyroid gland.

50-years-old female with thyroid nodules (10 in number, largest diameter 20x13x9 mm), solid isoechoic non homogeneous, with irregular margin. Elastography score 5 and strain ratio >1.55 (Histopathology: Papillary thyroid carcinoma).

Рис. 2. Эхограмма, щитовидная железа.

Женщина, 50 лет, с узлами щитовидной железы (по количеству – 10, наибольший размерами 20x13x9 мм), солидные изоэхогенные, негомогенные по структуре, с неровными краями. Эластографический балл соответствует 5 и коэффициент деформации >1,55 (гистопатология: папиллярная карцинома щитовидной железы).

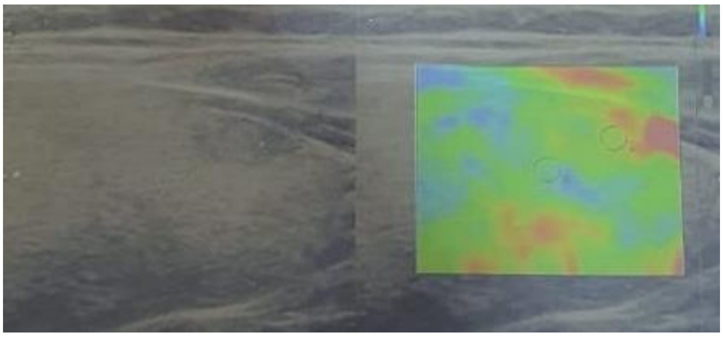

Fig. 3 (Рис. 3)

Fig. 3. Echogram, thyroid gland.

52-years-old female with thyroid nodules (13 in number), solid isoechoic homogeneous, with regular margin. Elastography score 3 and strain ratio <1.55 (Histopathology: Bethesda II).

Рис. 3. Эхограмма, щитовидная железа.

Женщина, 52 года, с узлами щитовидной железы (по количеству – 13), плотными изоэхогенными, однородными, с ровными краями. Эластографический балл соответствует 3 и коэффициент деформации <1,55 (Гистопатология: Bethesda II).

Table №.3 Elastography score (ES).

Score	Benign	Malignant
	No. (%)	
1	5 (16.7)	-
2	7 (23.3)	-
3	9 (30)	1 (3.3)
4	-	2 (6.7)
5	-	6 (20)

Monte Carlo= 25.71, df=4, P<0.0001

Table №.4 Strain ratio.

Ratio	Benign	Malignant
	No. (%)	
≤1.55	9 (30)	8 (26.7)
>1.55	12 (40)	1 (3.3)
Monte Carlo= 5.43, df=1, P=0.022		

Table №.5 The diagnosis by elastography.

Lesion	No. of patient	%
Benign	21	70.0
Malignant	9	30.0

Table №.6 Histopathological FNA reports data (n=30).

Diagnosis		No.	%
Diagnosis	Benign	17	56.7
	Malignant	9	30.0
	Intermediate	4	13.3
Histopathological FNA reports	Lipoma	1	3.3
	Bethesda II	14	46.7
	Bethesda III	6	20.0
	PTC	7	23.3
	ATC	1	3.3
	MTC	1	3.3

Table №.7 Accuracy rates of Elastography.

Findings	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
	%					
Nodule size	66.7	88.9	77.8	71.4	52.4	0.558
Nodule nature	77.8	74.1	66.4	47.6	51.7	0.532
Echogenicity	85.6	85.7	76.2	55.6	70	0.776
Homogeneity	50	50	28.6	66.7	45.2	0.357
Micro-calcifications	91.1	55.6	81.2	50	77.8	0.683
Irregular margin	80.2	80.4	66.8	44.4	72.8	0.579
Volume	88.9	77.8	61.9	57.1	81	0.672
Elastography score	92.4	90.8	88.9	66.7	89.8	0.976
Strain ratio	75.5	81.1	77.5	44.5	65	0.72

and Strain ratio.

Discussion.

In the present study, 30 patients with neck lumps were enrolled, all cases underwent Elastography examination. The mean age of patients was 46.1±8.61 yrs (28-61 yrs), with 20 males (66.7%), and 10 females (33.3%). Dislike Abdallah et al. whom enrolled 50 Egyptian patients of both gender with thyroid nodules [35]. Large cohort conducted by Yang et al., by studied 205 cases (aged 25-65 yrs) [36]. Same sample of patients was collected by Habib et al., included 25 females and 5 males (aged between 23-67 yrs) [37].

Regarding Eg findings in this study, the mean (median) nodule size was 14.53±5.59 mm (14.5 mm). Most of nodular masses was solid (22; 73.3%). The majority of lesion had isoechoic echogenicity (21; 70%). Non-homogeneous lesion noticed in 24 patients (80%). Micro-calcifications were absent in 21 cases (70%). Irregular margin was absent in 20 patients (66.7%). The mean (median) volume of nodule detected was 8.39±4.72 cm3 (9 cm3). The results of ES are: Score 1# and 2# recorded in 12 patients which all appeared as benign nodules. Score 3# recorded in ten cases (33.3%) (9 benign and 1 malignant). Score 4# and 5# recorded in eight cases all appeared as malignant nodules. These findings presented with high statistical difference (P<0.0001). The results of Strain ratio are the ratio (<1.55) recorded in 17 cases (56.7%) (9 benign and 8 malignant) and ratio (>1.55) recorded in 13(43.3%) cases (12 benign and 1 malignant). These findings presented with high statistical difference (P=0.022). As a results, 21 of 30 nodules (70%) appeared as benign and 9 nodules (30%) were malignant. Dissimilarly, Abdallah et al. reported 40 patients with benign nodules and 10 cases with malignant nodules, moreover, they recorded score 1 and 2 in 29 cases, score 3 in 14 patients and score 4 in seven cases with ratio of 2.5, these due to different in equipment used, large sample size, and early methods of diagnosis [35].

Yang and co-authors, analyzed 265 nodules by US [36]. They found 212 nodules measured >1 cm (patients=178), mean size (2.32 mm), 163 solid, 117 hypoechoic, 138 homogeneous, 106 micro-calcifications, 222 irregular margin, 53 Halo sign and volume (9.51 cm3), which extensively different from our finding because of large number of cases and long-time conducted for study.

Histologically, benign nodules were documented in 17 patients (56.7%) in this study, while malignant nodules were seen nine cases (30%). In addition, four cases appeared as intermediate pattern. Finally, 14 cases (46.7) showed Bethesda II class by FNA. Six cases belonged to Bethesda III. Seven cases proved to be PTC. One case was Lipoma. One case was MTC and other was ATC. These consistent with Abdallah et al., recorded 32 cases of Bethesda II, 8 cases of Bethesda III, 6 cases of PTC, two cases of ATC, one case lymphoma, and one case follicular TC [35]. However, Xang et al., found 35 benign nodules, 88 intermediate nodules and 78 malignant (suspicious) nodules [36]. This could be explained by different in locality, years of experiences of examiners, multi-team working and more than two radiologists reader.

Habib and colleagues revealed that absent halo sign in thyroid nodules had a higher malignancy frequency, than those without (P<0.001), which not present in our findings [37]. Also, they reported none score 1 of ES, 16 cases (44.4%) with score 2, 11 nodules (30.6%) with score 3, 8 nodules (22.2%) with score 4 and one nodule (3.8%) had a score 5. In score 2, all were benign. In score 3, 6 nodules were benign and 5 nodules were malignant. In score 4, 7 nodules were malignant and only one was benign. In score 5, the nodule was malignant. Strain ratio in benign nodules was 1.72± 0.35, while malignant nodules was 3.12 ±0.84 (p< 0.001).

Habib et al., estimated 91% sensitivity and 72% specificity with accuracy of 91% for ES [37]. Also, ROC analyses determined the optimal cutoff strain ratio to be 1.6 for the separation of benign and malignant thyroid nodules, with AUC of 0.86. In strain ratio, sensitivity and specificity were 89% and 70% respectively. The PPV and NPV were 78% and 90% respectively and accuracy rate was 86%. The same data measured in the present study, highest sensitivity calculated among Elastography score 92.4%, whereas the least sensitive value was Homogeneity (50%). The highest specificity calculated among Elastography score as 90.8%, whereas the least specific value was nodule No. (38.1%). The more accurate test was Elastography score (89.8%). As a result, this study revealed that qualitative ES data are able of differentiation among malignant and benign thyroid nodules. The greater elastography score are more reprehensive to malignant nodules opposed to benign lesions (lower ES). In regard to Esfahanian et al. the best point for differentiation among malignant and benign thyroid lesions was two (61% sensitivity and 78% specificity) [38]. Asteria et al. studied 66 patients (86 nodules), found that a cut-off point was 2 and 3 was the best (94% sensitivity and 81% specificity) [39]. Rago et al. found that 5-score and ES 4-5 were significantly predictive to malignant thyroid nodules (97% sensitivity and 100% specificity) [40]. Beside, these all previous studies which concordant and reported the same information, but with different variations of calculated sensitivities, specificities, and accuracies [41]. This could be explained by differences in the inclusion criteria and the sizes of sample used.

Abdallah et al., concluded that elastography have unquestionably advantages technical development in thyroid nodules imaging and must be done by an experienced radiologist who is aware of the possible limitations, difficulties, and the data should always be determined in combination with B-mode US-sonography results [35].

Previously, the prospective studies by Magri et al., Trimboli et al. and Cakir et al. are showed a results in accordance with this study, but Unlütürk et al. showed different results [42-45]. Strain US-Eg may be a good alternative to FNA histo-cytology for the distinguishing diagnosis of thyroid lesions [36]. Furthermore, strain US-Eg, US and histo-pathological investigation of specimens of surgery had substantial, moderate and perfect agreements, respectively [35, 36].

Yang et al., concluded that the conventional-US couldn't distinguish benign from malignant lesions, however, dislike that for US and FNA cytology, the inter-observer variability for strain US-Eg revealed substantial agreement [36]. Strain-US-Eg for highly and moderately suspicious nodules accelerated the diagnosis of mild suspicious nodules, nor benign nodules. Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer indicated that FNAC is the more accurate and cost effective way for differentiating thyroid nodules, with some limitation are that (10-15%) of specimens are non-diagnostic, and (10-20%) are indeterminate [34, 46].

US findings predictive of malignant thyroid nodules including the hypo-echogenicity, presence of irregular margins, micro-calcifications, raised vascularity and absent halo sign [33, 34]. In the present study, absence of halo sign was the strongest factor independently indicated malignant thyroid nodules, followed by presence of micro-calcifications and irregular margin.

There are two kinds of elastography strain and shear wave, which are used in this study. Also, same equipment used by Habib et al., and they used multivariate logistic regression analysis for selecting elastographic features which independently related to thyroid malignancy [37]. They reported that ES were significantly greater in malignant than in benign nodules ($p<0.0001$), with high sensitivity, specificity, PPV and NPV, which are accordance with our data. Yet, a disagreement with Jun-Mei Xu et al., Moon et al., and Vorlander et al., who mentioned that US-Eg imaging was not statistical significantly related with thyroid cancer [47-49].

Kagoya et al., concluded that a strain ratio (strain index) greater than 1.5 is a predictor of thyroid cancer and exhibit 90%sensitivity and 50%specificity, which is in concordance with our results, that revealed a strain ratio more than 1.6, to be an independent predictor of thyroid cancer, with sensitivity and specificity of 89% and 70%, respectively [50]. Many factors can influence the information of Eg, include nodules character (micro-calcifications and cystic contents), the radiologist experience, and motions artifacts (carotid artery pulsation) [51].

Habib et al., concluded that US-Eg is an easy, non-invasive and rapid technique which in routine done in neck US (including thyroid) scans to choose patients for FNAC, drop the unnecessary biopsies number and consequent decline the risks and money cost [37].

Conclusions.

Suspicious malignant thyroid nodule characters by solid, iso-echoic echogenicity, non- homogeneous, micro-calcifications, and irregular margin. Elastography Score 1# and 2# recorded for benign nodules. Elastography Score 3# for indolent nodules. Elastography Score 4# and 5# recorded for malignant nodules. Strain ratio are the ratio (<1.55) recorded for benign and malignant and ratio (>1.55) recorded benign nodules. The highest sensitivity and specificity for distinguish thyroid malignancy calculated in Elastography score (92.4% and 90.8%), respectively. The accuracy of Elastography score is (89.8%) with greater AUC (0.976). This study revealed that qualitative ES data are able of differentiation between benign and malignant thyroid nodules. The higher elastography score are more reprehensive to malignant nodules opposed to benign lesions (lower ES).

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