Preoperative Characterization of Thyroid Nodule with Cytological Reading of Follicular Neoplasm Using 99mTc-MIBI Scanning and Ultrasound Elastography

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Abstract:

Background and Aim: Non-invasive imaging techniques such as 99mTc-Sestamibi (MIBI) thyroid scanning and US Elastography are widely utilized in the evaluation of thyroid nodule. However, the outcomes of these diagnostic tests are inconsistent; the goal of our study was to compare the accuracy of US Elastography and 99mTc-MIBI in distinguishing between malignant and benign thyroid nodules in patients with a cytological diagnosis of follicular neoplasm.

Patients and Methods: Twenty-one patients with thyroid nodules underwent US-elastography by an experienced radiologist to obtain the Elastography score (ES) and the strain ratio (SR). 99mTc-Pertechnetate scintigraphy and dual phase MIBI SPECT/CT scanning were also done. Tracer uptake in MIBI images were visually graded as; no, faint, iso-, and intense uptake. Additionally, the pattern of tracer washout—decreased, unchanged, or increased uptake in the delayed images as compared to the early images was used. As the gold standard, radiologic follow-up and histopathology were utilized.

Results: The majority of nodules (16/21) were TI-RADS IV, while the remaining five were TI-RADS III. Elastography showed that the majority of benign nodules (87.5%, 14/16 patients) had a score of 3, with one nodule in each category for score 2 and score 4, while malignant nodules had two with a score of 3, two with a score 4, and one with a score 5, yielding 60% sensitivity, 93.8% specificity, and 85.7% accuracy (P=0.008).The mean SR value for the benign nodules was insignificantly lower than that of the malignant ones (3.1±1.9 versus 4.5±3.2, P= 0.236). With an AUC of 0.619 (95%- CI: 0.294-0.944 and P=.433), the optimal SR cutoff value for detecting malignancy was set at 0.82, yielding 100% sensitivity and 93.8% specificity. The number of malignant and benign nodules was found to be 5 and 16, respectively. Most nodules were hypo-functioning in nature. With a 100 % NPV, delayed MIBI image scoring outperformed the early one. Despite having the same sensitivity (80%), the washout pattern in delayed SPECT/CT scans had a significantly higher specificity, accuracy, NPV, and PPV (P=0.003) than that in the delayed planar ones (P=0.003).

Conclusion: In cases of thyroid nodules with a cytological diagnosis of follicular neoplasm; SR yields considerably higher sensitivity and specificity than the Elastography score. Additionally, the use of SPECT/CT strengthens the diagnostic accuracy of the late MIBI scans. The results of MIBI readings proved superior to those of Elastography scores.

Keywords: US Elastography, SR, Sestamibi, MIBI washout, semiquantitative parameters, thyroid

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Introduction:

Approximately 5% of females and 1% of males in iodine-deficient regions of the world have thyroid nodules, with rates as high as 68% in randomly selected individuals, making the thyroid nodule a common clinical issue. Thyroid nodules are a common condition, but just 5% of them are cancerous [1, 2].

Clinical examination, laboratory testing, ultrasonography, and radionuclide scanning are frequently used to evaluate thyroid nodule, with fine-needle aspiration cytology (FNAC) as a complementing technique in the event of worrisome lesions [3]. The primary imaging test for figuring out if thyroid nodules are benign or cancerous is ultrasonography (US) [4].

Because suspicious US characteristics can appear in both benign and neoplastic thyroid nodules, other US methods such as Elastography are currently being employed to increase diagnosis accuracy [5]. Elastography is a recently discovered non-invasive dynamic US method used to evaluate tissue stiffness by detecting the degree of deformation caused by an external force [6, 7]. Thyroid tissue's structure and elastic characteristics are altered in response to any clinical situation [8].

The primary use of FNAC, a rapid, affordable, and widely accessible diagnostic technique [9] is to determine which patients require surgical intervention, thereby lowering the frequency of unneeded thyroidectomies and their complications [10]. It has problems, though, because it can give false-positive and false-negative findings [11].

Thyroid scintigraphy using 123I or 99mTc-pertechnetate represents the rate of thyroid cell metabolism and absorption of the tracer, making it a well-established method for excluding cancer in hyperfunctioning (hot) nodules, While 99mTc-methoxyisobutylisonitrile (99mTc-MIBI) thyroid scintigraphy depicts active mitochondrial and cellular oxidative metabolism, It has been suggested that it attains a strong negative predictive value approaching 100% for distinguishing malignant from benign hypoactive (cold) thyroid nodule [3, 12-14].

Numerous trials have been conducted to determine the possible relevance of 99mTc-MIBI imaging in predicting or ruling out a malignancy in a hypoactive thyroid nodule, yet the findings are inconsistent [15, 16]. This study aimed to distinguish benign from malignant thyroid nodule by comparing the results of 99mTc-MIBI thyroid scintigraphy and thyroid US Elastography in individuals with the cytological diagnosis of follicular neoplasm.

Patients and Methods:

Ethics statement:

The study protocol was approved by the Institutional Review Board of faculty of Medicine, Assiut University and getting each patient's signed consent. All methods were performed in accordance with the relevant guidelines and regulations.

In this study, we prospectively evaluated 21 cases with a cytological reading of follicular neoplasm, euthyroid, hypo- or iso-functioning nodule on 99mTc-Pertechnetate thyroid scan, or a thyroid nodule >1 cm in its maximum dimension. Patients under the age of 18, those with a history of thyroid operation, uniform thyroid enlargement, and hypo- or hyperthyroidism, were all excluded from the study.

All cases were subjected to a complete medical history, clinical examination, TSH assay, thyroid US, radionuclide imaging (99mTc-pertechntate thyroid scan and 99mTc-MIBI scan), surgical excision, and histopathological examination.

Thyroid ultrasound

A GE Logiq F8 expert was used blindly for the evaluation of the thyroid gland by a professional radiologist. Patients were assessed in the supine position with a pillow under their shoulders to keep their necks straight. In our work, the thyroid gland was imaged using the brightness mode (B-mode), color-coded Doppler imaging (CCDI), power Doppler imaging (PDI), real-time elastography, and SR in both longitudinal and transverse planes.

Image interpretation

Comments on the thyroid nodule includes: echogenicity (hyperechoic, isoechoic, hypoechoic, marked hypoechoic, heterogeneous, cystic, or complex cystic), borders (regular or irregular), presence of calcification, and its type (egg shell, micro-calcification, or punctate). Other parameters of the nodules were recorded, including anteroposterior diameter/transverse ratio (taller-than-wide, ≥ 1 mm, and wider-than-tall, < 1 mm), presence of breakdown, or a surrounding halo.

The nodules were further stratified according to the European Thyroid Imaging Reporting and Data System (TIRADS): TIRADS-1 indicates a normal thyroid gland; TIRADS-2 indicates a thyroid gland with a simple or spongiform cyst, isolated macro-calcification, or a diffusely enlarged hypoechoic thyroid gland; TIRADS-3 indicates a nodule with isoechoic or hyperechoic characteristics but no high suspicious US signs; TIRADS-5 has at least one of the high-suspicious US criteria or adenopathy; TIRAD-4 has a mildly hypoechogenic nodule but no high suspicious US findings. Signs of high suspicion are irregular margins, irregular shape, micro-calcification, and marked hypo-echogenicity.

Nodules are categorized on a scale of 1 to 5 using the scale of Rago et al. [17]. Scores of 4 and 5 are categorized as suggestive for malignancy, while the first three scores are regarded as benign [18].

The SR method represented the semi-quantitative Elastography score. Two regions were chosen: area I, which represented the region of interest, while area II, represented the normal region, area II was then divided by area I. Area I was selected from any tissue with a uniform pattern of elasticity, but for those with heterogeneous patterns, it was selected to include all heterogeneous areas as much as possible. Additionally, multiple measures of SR were taken, and the median of these measures was recorded and considered for statistical analysis.

99mTc-pertechntate thyroid scintigraphy:

Using a dual-head SPECT/CT gamma camera (Siemens Healthcare, Symbia T, Erlangen, Germany), and after 15 minutes of intravenous injection of 74-111 MBq 99mTc-pertechnetate, anterior images of the neck were generated in the planar projection. A low energy high-resolution (LEHR) collimator and a 20 % energy window set over 140 keV were utilized. The acquisition parameters were; magnification: 1; 256 × 256 matrix size and frame count of 100 K.

99mTc-MIBI protocol:

Following intravenous injection (IV) of 99mTc – MIBI n a dose of 740 MBq (20 mci), planar and SPECT scans were obtained using the same gamma camera, approximately at 30 min (early images) and at 90-120 min (late images). Patients were scanned in the supine position. A total of 64 frames were obtained (25-seconds /frame) in a 360-degree non-circular arc with 128X128 matrix size. A low dose non-contrast CT was conducted after SPECT acquisition for attenuation correction and anatomical localization. The following CT parameters were utilized; tube current 80 mA, tube voltage 130kV, and 1 mm slice thickness. SPECT/CT scans were reconstructed and viewed in the trans-axial, coronal, and sagittal planes.

Image interpretation

Two nuclear medicine specialists with 14 and 18 years of experience visually reported tracer uptake at thyroid and MIBI scans while being blinded to the patient's clinical information and to one another in order to assess inter-reader agreement. Before a consensus reading was recorded, the two doctors discussed their divergent readings.

Tracer uptake was visually graded in the form of; no uptake, faint uptake, iso-intense uptake, and intense uptake. No and faint uptake were regarded as negative, whereas iso-intense and intense uptake were reported as positive. Additionally, the pattern of tracer washout on the late MIBI images as compared to the early images was reported in the form of; decreased, unchanged, or increased uptake.

Fine Needle Aspiration Cytology

A board certified experienced cytopathologist performed the cytologic diagnosis using the recent Bethesda system's cytological criteria [18]. The fine needle aspiration was done under ultrasonographic guidance using a 22 gauge needle with a 5-ml plastic syringe. Two to 3 passes were obtained from each nodule for conventional smear cytology. Aspirate was smeared onto uncharged slides and stained with May-Grunwald-Giemsa. The presence of six groups of the follicular cells, each containing at least ten cells, was deemed sufficient [19]. A different slide was created for Papanicolaou staining.

Surgical procedure

All routine laboratory work, neck U/S, US elastography, and an ENT examination of vocal cord mobility were part of the preoperative preparation. Patients had a traditional neck collar incision and a full evaluation of thyroid swelling. Then proper identification of both recurrent laryngeal nerves and external laryngeal nerves was also done, as well as identification and preservation of the parathyroid glands. Then either a hemi- or total thyroidectomy was performed according to the case and the specimen was put in a saline filled container to be sent for histopathology.

Reference standard

In most of the study population, we relied on the histopathological examination as the gold standard, apart from four patients for whom clinical and radiologic imaging follow up were considered the gold standard.

Statistical analysis:

Data were interpreted using SPSS 23.0 (Statistical Package for Social Sciences). Continuous parametric variables were expressed as means plus standard deviations. Median and interquartile ranges were displayed for nonparametric variables. To compare means and medians, we used the independent sample t-test and Mann–Whitney U test, respectively. Diagnostic accuracy, sensitivity, specificity, positive and negative predictive values (PPV and NPV) were calculated for 99mTc-MIBI and thyroid US Elastography. A receiver operating characteristic (ROC) analysis was performed to determine the ideal cutoff value above which the used parameters could recognize a malignant thyroid nodule. The Spearman's rank correlation analysis was used to assess the degree of correlation between quantitative variables, which was classified as low (0-0.25), moderate (0.25-0.75), or high (0.75–1.0). A regression analysis was carried out to evaluate the independent variables for neoplasia prediction. A P value less than .05 was considered significant.

Results:

Patients

Twenty-one patients with cytologically proven follicular neoplasm; (19 females, 2 males, and the mean age; 38.7 ± 13 years) were recruited in this prospective cohort. The nodules' sizes range from 2.0 to 6.8 cm, with a mean of 3.37 ± 1.2 cm. Patients with malignant nodules were younger than those with benign one (mean age; 35±12.5 for malignant nodules and 40±13.5 for benign ones, P=.468). 16 cases had a solitary thyroid nodule, compared to only five cases with multiple nodules. In the TC-99m-pertechnetate scan, 57.1% of the nodules were hypofunctioning, while 33.3% were isofunctioning (Table 1). The mean TSH level was 1.8 ± 1mIU (normal= 0.5–4.5 mIU).

Histopathological results

All patients were considered to have category IV (follicular neoplasm) according to the Bethesda system classification. Thyroid surgery was performed on 17 cases, while the remaining four cases refused surgical intervention and were monitored clinically and via US to reach the final outcome. Histopathology identified 12 and 5 benign and malignant nodules, respectively. Among the malignant nodules, one was poorly differentiated thyroid carcinoma, two were follicular variants of papillary carcinoma, and two were minimally invasive follicular carcinoma. The ultimate follow-up of patients who declined surgical intervention revealed the benign nature of the nodule.

US-Elastography findings

The majority of nodules (16/21) were TI-RADS IV (12 benign and 4 malignant), while the remaining 5 were TI-RADS III (4 benign and 1 malignant). More than half (52.4%) of the nodules were hard, including 8 benign and 3 malignant, while the remaining 47.6% were soft, including 8 benign and 2 malignant.

Regarding the Elastography scoring of the benign nodules, most of the nodules (14/16) had a score of 3, with scores of 2 and 4 having one nodule in each category, while for the malignant nodules, two of them had a score of 3, two had a score of 4, and one had a score of 5, giving a sensitivity of 60%, a specificity of 93.8%, accuracy of 85.7%, an NPV of 88.2%, and a PPV of 75% (P =.008).

There was no statistically significant difference between the benign and the malignant thyroid nodule sizes. (3.3±1 for the benign nodules compared to 3.7±1.9 for the malignant nodules, P= .697). The mean SR value for the benign nodules was insignificantly lower than those of the malignant ones (3.1±1.9. Vs. 4.5±3.2, P= .236).

In ROC analysis, the best SR cutoff value to predict malignancy in a thyroid nodule was 0.82, giving a sensitivity and a specificity of 100 % and 93.8 %, respectively, with an AUC of 0.619 (95 % CI: 0.294-0.944 and P =.433) (Figure 1).

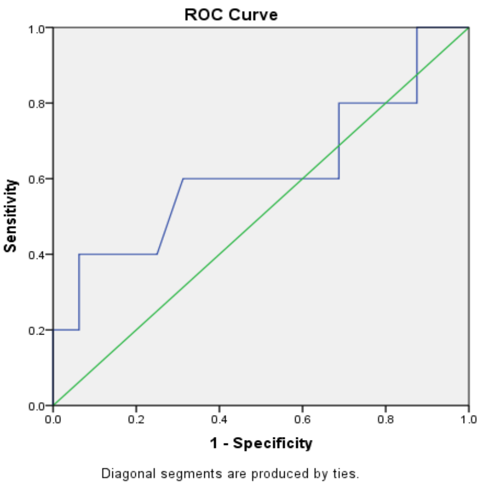

Figure 1: ROC analysis of SR in respect to histopathology of the thyroid nodule.

I-Qualitative analysis:

The two readers agreed on the reporting of 18 out of 19 99mTc thyroid scintigraphy, 21 early and 18 late planar MIBI scans, with an inter-reader kappa value of 0.910, 1.0, and 0.790, respectively (95% CI: 0.00-0.133 and p<.01 for all). The agreement value on SPECT/CT images was one (95% CI: 1.00-1.00, p<.01). The two readers reached a consensus reading for the final analysis after debating the images.

A-Visual interpretations of 99mTc-pertechnetate thyroid scan

Thyroid scintigraphy was performed in 19/21 of the study population; 12/19 had hypoactive nodules (10 with faint uptake and 2 with no uptake), while the remaining seven cases had iso-intense uptake. Pathology revealed that three of the hypoactive nodules were malignant, while six of the iso-intense nodules were benign.

B-visual interpretations of the early planar MIBI scans:

The majority of benign nodules (9/16) had intense, 1/16 had faint, and 6/16 had iso-intense uptake. While in the malignant nodules, one nodule had a faint uptake, two had iso-intense uptake, and two nodules had intense uptake.

C-Visual interpretations of the late planar MIBI scans:

Six of the benign nodules had intense, five had faint, and five had iso-intense uptake, while four of the malignant nodules had iso-intense uptake and only one had intense uptake (Figures 2,3,4 and 5). The visual tracer grading achieved high sensitivity in the thyroid scan, early and late MIBI scans but low specificity, especially in the early MIBI scan (Tables 2 and 3).

D-Visual interpretation of the tracer's washout pattern in late planar and SPECT/CT MIBI scans:

Complete tracer washout was deemed negative for malignancy, however, both constant and increased tracer uptake were regarded as worrisome for malignancy.

1-late planar MIBI scan: one malignant and 12 benign nodules exhibited complete washout, constant tracer uptake pattern was noted in three benign and four malignant nodules, while only one benign nodule showed an increased tracer uptake (tracer retention) pattern.

True negative and true positive reading findings were documented in 12 and 4 nodules, respectively, while false negative and false positive readings were encountered in one and 4 nodules, respectively, with 80 % sensitivity and 75% specificity, 76.2% accuracy, 50 % PPV, and 92.3 % NPV (P = 0.04).

2-Late SPECT/CT MIBI: the pattern of washout correctly identified and exclude malignancy in 4 and 13 nodules respectively, we found one false negative and 3 false positive nodules with 80 % sensitivity, 81.2% specificity, 92.7% NPV, 80% PPV, and 80.95% accuracy (P=.003).

Correlation between the age, TSH, nodule size, Elastography score and SR.

The SR was insignificantly low positively correlated with age, TSH, and Elastography score. Elastography score was insignificantly moderately positively correlated with TSH and nodule size. The nodule size was insignificantly positively correlated with SR, and Elastography score (r= 0.162 and 0.277, P= .236, and .495, respectively), while it was insignificantly negatively correlated with TSH (r=, -0.140, P=.555, Table 4).

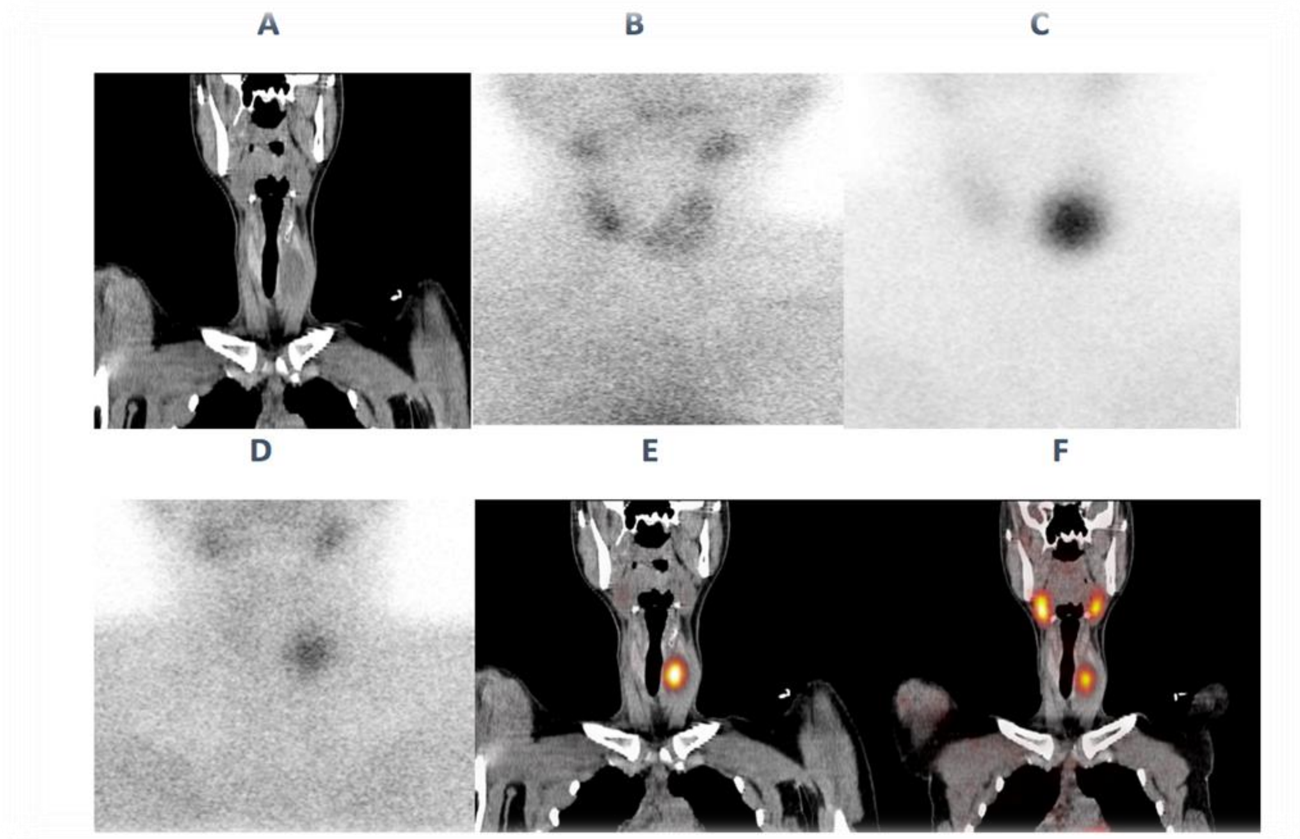

Figure 2: A 26-years old female patient with a hypodense left thyroid lobe nodule on CT image (A), (B)^{99m}Tc-pertechnetate thyroid scintigraphy demonstrating an isofunctioning left thyroid lobe nodule.^{99m}Tc-MIBI early (C), late (D) planar images, early (E) and late (F) SPECT/CT images: the tracer washout pattern is consistent with decreased uptake. Final pathology revealed a follicular adenoma.

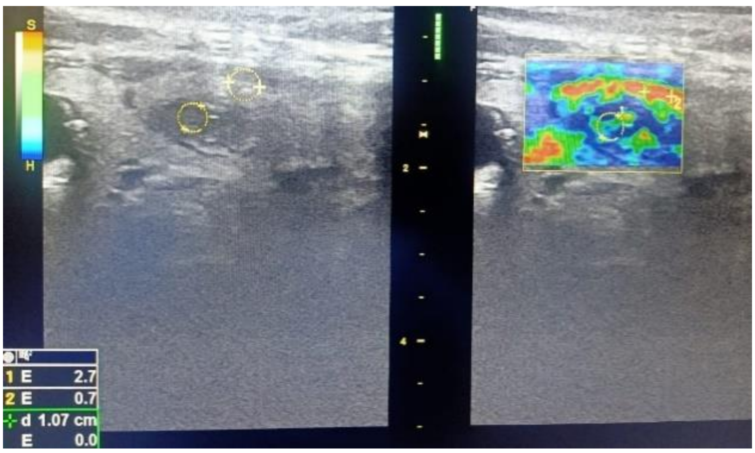

Figure 3: A well-defined hypoechoic left thyroid nodule (TIRADS-III) with elastography score 3 the ER=1.07Kpl

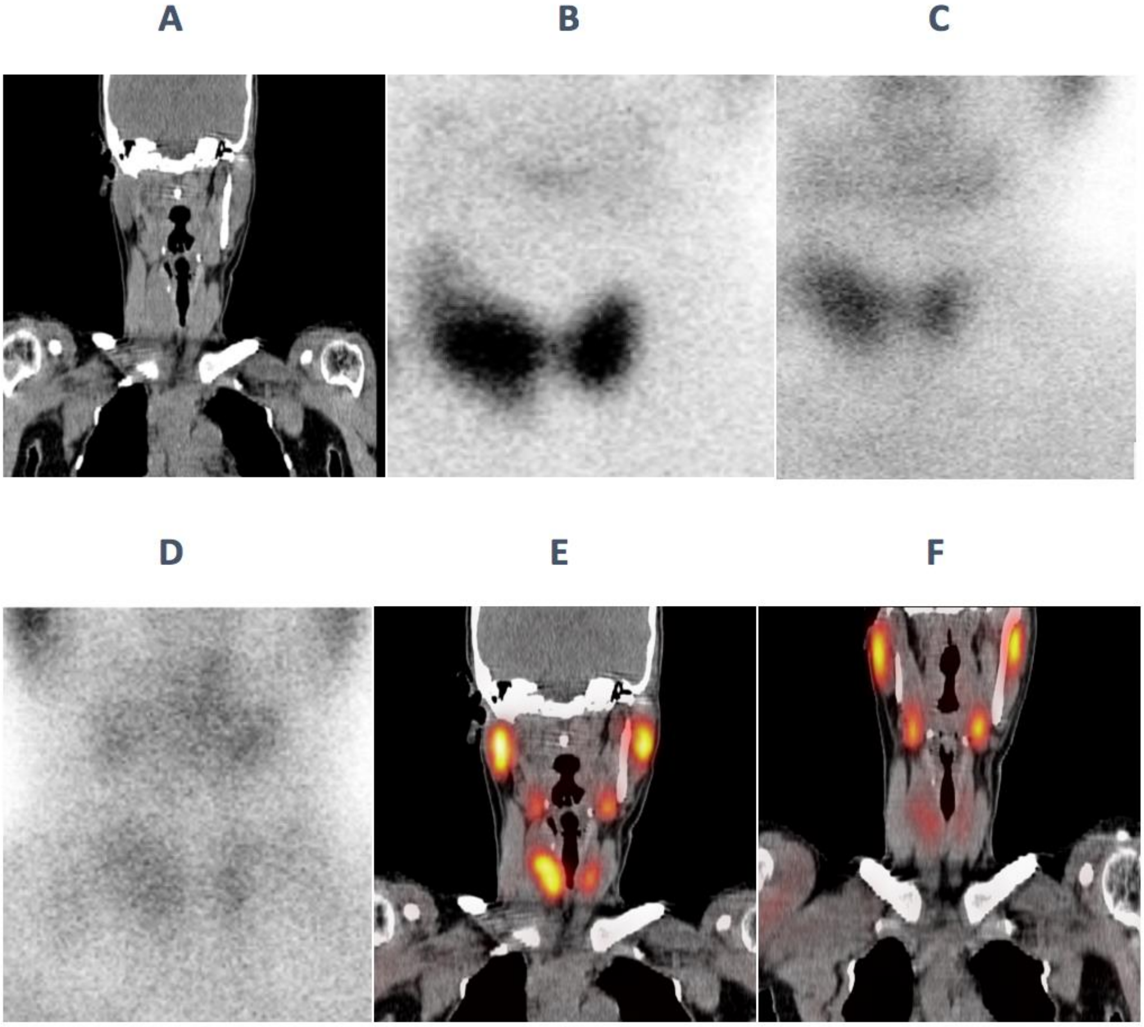

Figure (4): A 23-years old female patient with hypo-dense right thyroid lobe nodule on CT image (A). (B)^{99m}Tc-pertechnetate thyroid scintigraphy demonstrating an iso-functioning left lobe thyroid nodule. ^{99m}Tc-MIBI early (C), late (D) planar images, early (E) and late (F) SPECT/CT images: washout pattern is consistent with decreased uptake. The final histopathology report revealed minimally invasive follicular carcinoma.

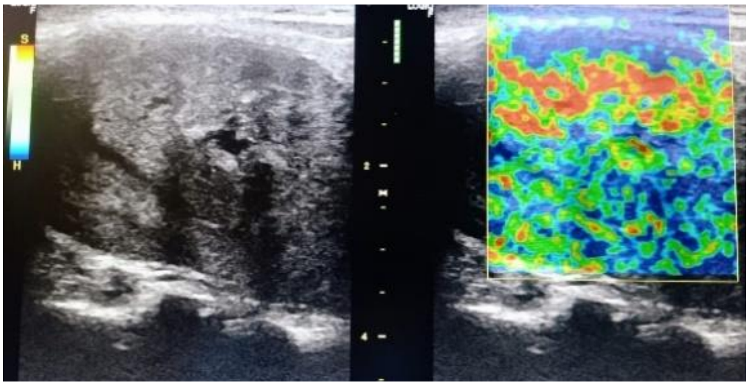

Figure 5: Large right iso- to hypoechoic thyroid nodule (TIRADS IV) with elastography score 3-4 and ER=2

Table 1: US characteristics of the thyroid nodules.

Variable	Final outcome		*P*-value
	Benign 16 (76.2%)	Malignant 5(23.8%)	
Echogenicity:			
• Hypoechoic	7(43.8%)	1(20%)	.065*
• Isoechoic	7(43.8%)	1(20%)	
• Hyperechoic	1 (6.2%)	0	
• Heterogeneous	1 (6.2%)	3(60%)	
Laterality:			
• Right	9(65.2%)	5(100%)	.070*
• Left	7(43.8%)	0	
Number:			
• Solitary	12(75%)	4(80%)	.819*
• Multiple	4(25%)	1(20%)	
Margin:			
• Well defined	10(62.5%)	3(60%)	.169*
• Ill-defined	0	1(20%)	
• Not assessed	6(37.5%)	1(20%)	
Shape:			
• Ovoid	4(25%)	2(40%)	.720*
• Wider than tall	1(6.2%)	0	
• Not assessed	11(68.8%)	3(60%)	
Calcification:			
• Positive	2(12.5%)	1(20%)	.676*
• Negative	14 (87.5%)	4(80%)	
Degeneration/cystic changes:			
• Present	6(37.5%)	2(40%)	.920*
• Absent	10(62.5%)	3(60%)	
US Elastography:			
• Hard	8(50%)	3(60%)	.696*
• Soft	8(50%)	2(20%)	
TIRADS:			
• III	4(25%)	1(20%)	.819*
• IV	12(75%)	4(80%)	
Elastography score:			
• Benign:			.008*
○ score 1	0	0	
○ score 2	1(6.2%)	0	
○ score 3	14(87.5%)	2(40%)	
• Malignant:			
○ score 4	1(6.2%)	2(40%)	
○ score 5	0	1(20%)	
Size of the nodule in cm.			
• Mean + SD	3.3+1	3.7+1.9	.697**
SR			
• Mean	3.1±1.9	4.5±3.2	.236**

*The Chi-square test, ** The Independent sample t-test.

Table 2: The pattern of tracer washout and the degree of uptake by the thyroid nodules.

Variable	Benign	Malignant	P-value
Tc-99m thyroid scan uptake:			
• No uptake	1(6.7%)	1(25%)	.581*
• Faint uptake	8(53.3%)	2(50%)	
• iso-intense uptake	6(40%)	1(25%)	
MIBI uptake:			
• Early:			.620*
○ No	0	0	
○ Faint	1(6.2%)	1(20%)	
○ Iso-intense	6(37.5%)	2(40%)	
○ intense	9(56.2%)	2(40%)	
• Late:			
○ No	0	0	.134*
○ Faint	5(31.2%)	0	
○ Iso-intense	5(31.2%)	4(80%)	
○ intense	6(37.5%)	1(20%)	
Pattern of washout			
• Complete washout	12(75%)	1(20%)	.040*
• Constant uptake	3(18.8%)	4(80%)	
• Increased uptake	1(6.2%)	0	

*Chi-square test.

Table 3: The diagnostic performance of the tracer washout pattern and the degree of tracer uptake.

Variable	Sensitivity	Specificity	P-value
Pattern of washout	80%	75%	.040
Degree of uptake on ^{99m}Tc- pertechntate scintigraphy	75%	40%	.581
Degree of uptake on Early MIBI scan	80%	6.2%	.620
Degree of uptake on Late MIBI scan	100%	31.2%	.134

Table 4: The correlation between TSH, patient’s age, the nodule size, SR, and Elastography score.

Variable	Age		TSH		Nodule size		Elastography score		SR	
	R	P	R	P	R	P	R	P	R	P-value
Age		0.633	-0.111	0.633	-0.264	0.616	-0.116	0.616	0.062	0.790
TSH	-0.111	0.260			-0.140	0.555	0.283	0.213	0.095	0.681
Nodule size	-0.264	0.616	-0.140	0.555			0.277	0.236	0.162	0.495
Elastography score	-0.11	0.632	0.283	0.213	0.277	0.236			0.407	0.067

Discussion:

Thyroid nodules are diagnosed using a multidisciplinary approach that includes laboratory tests, ultrasonography, and a thyroid scan to definitively exclude an autonomously functioning nodule that is regarded as benign [3].The 2015 American Thyroid Association (ATA) guidelines for the management of patients with thyroid nodules and differentiated thyroid carcinoma emphasized the importance of neck ultrasound in thyroid nodule management and suggested that a biopsy should be performed according to the sonographic features [21].

The FNAC test is a simple, low-cost way to diagnose cancer, and its use has significantly reduced the frequency of unnecessary thyroid operations [22]. The inability of FNAB to detect tumor vascular or capsule invasion is its most significant limitation in characterizing follicular neoplasms. Additionally, the diagnosis may be difficult in patients with follicular variants of papillary thyroid carcinoma, in whom the classic diagnostic cytological features for papillary carcinoma are absent, as well as in patients with a microfollicular goiter with a hypercellular pattern [4].

Elastography is a newly introduced non-invasive dynamic US methodology utilized to assess tissue stiffness by estimating the degree of distortion upon the application of an external force, depending on the fact that benign soft-tissue lesions are often softer than the malignant ones yet firmer than the normal tissue [6, 7]. In a meta-analysis, Elastography score was found to be valuable in the evaluation of the malignant potential of the nodule with 92% sensitivity and 90% specificity, in another meta-analysis, the mean sensitivity and specificity were 0.79 and 0.77 [23]. According to these figures, we found 60% sensitivity and 93.8% specificity (P =.008); varying degrees of sensitivities and specificities can be attributed to varying study populations, an unequal number of patients with malignant nodules in each study, and the lower sensitivity in our cohort may be attributed to our cohort's small sample size [24]. Consistent with the findings of Cantisani et al., we discovered that benign nodules had a significantly lower mean SR than malignant ones. We also observed that the SR showed an insignificant positive correlation with nodule size [24].

We found that the optimal SR cutoff point to predict malignancy in a thyroid nodule was ≥0.82 giving 100 % sensitivity and 93.8 % specificity. In contrast, Unluturk et al. found a higher cutoff value of 2.1 with lower sensitivity and specificity than ours (69% and 67%, respectively) [25], this may be explained by different operators and US devices.

Numerous variables can influence the elastography results, such as nodule characteristics (cystic components and calcifications), motion artifacts such as carotid artery pulsation, and operator knowledge [26,27]. Elastography can be used selectively in thyroid nodules without evidence of cystic changes or large calcifications to provide accurate results, and it should be carried out by a well-trained physician using the parameters provided by the elastographic machines.

Numerous publications have described the diagnostic role of MIBI-scintigraphy in evaluating thyroid nodules according to the degree of MIBI uptake by the nodule or the change in its uptake over the imaging time [28], the sensitivity and specificity of MIBI scintigraphy in identifying malignant thyroid nodules reached 85.1 -87% and 45.7- 78 % respectively [29, 30], keeping with these figures we found sensitivity of 80 % and specificity of 75% for planar imaging while SPECT/CT imaging had 80 %sensitivity and specificity of 81.2%.

In distinguishing isointense from increased or decreased MIBI uptake, SPECT/CT outperformed planar imaging. Thus, SPECT had a high NPV and could detect most carcinomas down to 1 cm in diameter [31]. It is critical to understand that MIBI has a high negative predictive value approaching 100% [28], whereas we found a relatively lower NPV of around 92.3% in our study, which may be attributed to the inclusion of iso-functioning as well as hypoactive nodules on the thyroid Scan.

MIBI scanning has a positive predictive value between 10% and 60% [23,24] which is higher than the 20% found by Theissen et al., and the 50% we found [30]. This wide range of values may be attributable to the varying prevalence of thyroid carcinomas in the study populations.

The increased MIBI uptake does not necessarily indicate malignancy; up to 23% of the nodules with positive MIBI uptake were ultimately identified as benign ones (false positives) [31]. In this work, we encountered 4 false positive readings on planar imaging in which the histopathology was typical follicular adenoma, which was similar to Foldes et al. [32]. By identifying washout in one nodule with iso-intense tracer uptake, SPECT/CT lowers the number of false positives to three cases.

Two cases with anaplastic/undifferentiated carcinoma were incorrectly interpreted as negative by Foldes et al and Kresnik et al., [32, 33], also a small number of patients with follicular and papillary thyroid carcinomas were incorrectly negatively interpreted by Sathekge et al. and Theissen et al. [30, 34]; In line with the previous literature, we found one case with minimally invasive follicular carcinoma whose planar and SPECT/CT results were reported as negative.

The false negative results in the literature were attributed to a number of factors including; small tumor size, image misinterpretation and cases of goiter with multiple pathologies; when the hypo-active nodule was in close proximity to an autonomous nodule, as well as false positive histological results when examining hypercellular or heterogeneous adenomas [16, 31].

MIBI over-accumulation is rarely found in degenerative nodules; accordingly, and in agreement with Mezosi et al., our false negative case can be clarified (a well-defined, and degenerated 2.5 cm nodule that was detected on the SPECT/CT) [35].

In this work, variable levels of activity were seen in the early and late MIBI images, when the nodules with iso- or intense uptake on the late images was considered malignant, the scan offered 100% sensitivity and 100% NPV in discriminating malignant from benign nodules, these results were matched with those of Riazi et al. [36].

Schenke et al. established an inter-observer reliability of 0.76 for planar and 0.80 for SPECT MIBI scanning [37], but we found higher figures: 0.78 for delayed planar and 1.0 for both early planar and SPECT, as well as a value of 0.90 for the thyroid scan. To the best of our knowledge, this is the first work to contrast the results of MIBI with US-elastography. The results of MIBI readings outperformed those of elastography scores.

Limitations of the current study:

Because this study was conducted during the coronavirus pandemic, the sample size was relatively small, and our study was limited to a single center. The current study, on the other hand, has the advantage of using planar as well as SPECT/CT imaging modalities and comparing the results to those of US elastography.

Conclusion:

In cases of thyroid nodules with a cytological diagnosis of follicular neoplasm; SR yields considerably higher sensitivity and specificity than the Elastography score. Additionally, the use of SPECT/CT strengthens the diagnostic accuracy of the late MIBI scans. The results of MIBI readings proved superior to those of elastography scores.

Ethical approval and consent to participate:

This study was approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Assiut University. All methods were performed in accordance with the relevant guidelines and regulations.

Conflict interest: The authors declare that they have no conflict of interest.

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AUTHOR CONTRIBUTIONS

All authors contributed to conceptualization, methodology, formal analysis, Writing original draft, review & editing. All authors approved the final manuscript for submission.

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