Combined Use of the Strain Ratio and Elastography Score Can Help Surgeons in Choosing which Thyroid Nodule Needs Surgery

Mahmoud Abdelbaky Mahmoud,[1] MD; Tarek Ismail Ahmed Ouf,[1] MD; Heba Tharwat Abdelaziz,[2] MD; Ahmed Hassan Soliman,[3] MD; Ayman Magdy Botrous Ghaly,[1] MD
[1]Department of General Surgery, Faculty of Medicine, Ain Shams University, Egypt
[2]Department of General Surgery, Faculty of Medicine, Al Azhar University, Egypt
[3]Department of Radiology, Faculty of Medicine, Ain Shams University, Egypt

Introduction: After Thyroidectomy, only 5%–15%of specimens are malignant. Most of procedures carried out of concern for cancer. Although FNAC recommended, it is invasiveness, expense and nondiagnostic outcomes.

Aim of work: The aim of study was to investigate whether the simultaneous use of the strain ratio, elasticity score together in the differential diagnosis of thyroid nodules can help surgeons deciding which thyroid nodule can left for follow up and which needs to remove.

Patients and methods: In all, 154 individuals 180 nodules were included. For symptomatic nodules with an elastography score of 1 or higher, as well as for nodules with a score of 2 or higher, all patients had complete thyroidectomy. The reference was the specimen histopathology final diagnosis. The examination of the receiver operating curve was used to calculate the values for the strain ratio and elasticity score.

Results: We had 35 malignant nodules and the elasticity score and strain ratio had a statistically significant ($p < 0.001$) success rate in predicting thyroid malignancy. Both had acceptable accuracy when employed independently, yet the elasticity score's accuracy was found to be higher than the strain ratio's, however the difference not statistically significant. When combined, they were 93.5% specific in identifying the right diagnosis.

Conclusion: More reliable findings obtained when the strain ratio and elasticity score are used for differential diagnosis of thyroid nodules. For suspected thyroid nodules, combining the two techniques might be a viable choice, helping surgeon avoids doing thyroidectomy.

Key words: Elastography, nodule, thyroid.

Introduction

In regions where there is a documented iodine deficit, thyroid nodular disease is frequently identified. Only 4%–7% of adult population thyroid nodules may be found by palpation. The incidence of asymptomatic thyroid nodule diagnosis has grown due to the increasing use of ultrasonography (US) neck imaging. As a result, there have been more benign thyroid nodules removed. Thyroid nodules detected by ultrasound investigations are common in the community; up to 67% of cases are benign, with just 5–12% of cases turning out to be malignant.[1]

Although a significant number of instances with high resolution ultrasonography indicate malignancy, there are still limitations in accurately diagnosing patients. The size of the nodule (In three dimensions), its location, and a description of its sonographic features—such as its composition (Solid, cystic proportion, or spongiform), echogenicity, margins, presence and type of calcifications, shape if it is taller than wide, and its pattern of vascularity—should all be clearly communicated using standard US reporting criteria.[2] Malignancies in thyroid nodules, which account for 5%–15% of cases, must be found using additional imaging modalities. Selecting worrisome nodules is therefore critical to prevent needless surgery. A novel method for estimating the viscoelastic characteristics of thyroid nodules was originally published in 2005 for thyroid lesions: thyroid elastography.[3] Determining whether these nodules are benign or cancerous without doing surgery is a significant difficulty. Fine needle aspiration is now the gold standard for the diagnosis of thyroid nodules. To rule out or diagnose cancer, however, about 15–20% of the findings are not diagnostic histologically, necessitating an operation. An invasive technique, the Fine Needle Aspiration Biopsy (FNAB) has a 90% diagnostic sensitivity for thyroid cancer. For nodules with noticeable ultrasonographic characteristics, it is necessary.[4]

The most common and conventional approach of detecting thyroid lesions is palpation, which is a subjective technique since nodules that are suspected of being malignant typically feel harder than others.[5] Imaging with ultrasound elastography is a novel noninvasive technique. Its foundation is an approximation of the tissue's mechanical characteristics. Data show that in the majority of thyroid carcinomas, reduced flexibility in comparison to the surrounding healthy tissue is indicative of malignancy.[3] Guidelines for the use of US and elastography methods in thyroid illnesses have been established by the World Federation for Ultrasound in Medicine and Biology (WFUMB).

In the same session as conventional ultrasound imaging, strain elastography (SE) offers a low-cost imaging methodology and a noninvasive, real-time tool for characterizing tissue stiffness without the need for a contrast agent.[6] Benign thyroid

DOI: 10.21608/asjs.2024.325481.1163

nodules are typically roughly 1.7 times stiffer than surrounding normal thyroid tissue, but malignant thyroid nodules are often about five times stiffer. The nodule stiffness may be measured relative to the surrounding thyroid parenchyma using the color scale this study produced and the elastic coefficients.[7] There are two ways to measure the diagnostic efficacy of SE: the strain ratio (SR), a semi-quantitative assessment utilizing numerical data,[8] and the elasticity score (ES), which uses qualitative assessment through color coding.

Only the solid component should be evaluated when a nodule exhibits both cystic and solid components,[9] since the cystic component could not yield any data or artifacts.[10] Because there may not be enough surrounding reference thyroid tissue in individuals with big nodules, it might be challenging to quantify the strain ratio (SR) using a neighboring muscle.[11] The most important component of sufficient SE is operator experience. It is very specific and sensitive in identifying thyroid nodule malignancy as well as lateral cervical lymph node malignancy.[12]

Aim of work: The aim of this study was to evaluate the effectiveness of using these two techniques together rather than separately in guiding surgeons which thyroid nodule needs surgical interference and which can be left for follow up to avoid unnecessary interventions.

Patients and methods

This prospective study was conducted in Ain Shams University Hospitals and El Azhar University Hospital for girls. The study was approved by the local ethics committee of both sides. Only patients provided a written informed consent were included in the study. For patients under 18 years of age, informed consent was provided by their parents. A total of 180 nodules from 154 patients were examined after applying the inclusion and exclusion criteria. The only inclusion criterion was simply the presence of single or multiple nodules with no history of the thyroid operation. Pure cystic lesions, insufficient normal tissue surrounding the measured nodule, rough calcification in the nodules and autoimmune thyroiditis were all exclusion criteria as well as patients with asymptomatic nodules with ElastographyScore 1 (F1) were excluded and left for follow up. All patients had a FNAB from the nodule.A total thyroidectomy was done to all patients with lymph node dissection in few selected cases. The final result of the specimen histopathology diagnosis after total thyroidectomy was used as the guiding reference.

Imaging methods

Strain elastography and B-mode high resolution ultrasonography were both used. Asteria et al. (13) created a categorization system that uses four scales to measure tissue stiffness inside a lesion, which forms the basis of the ES assessment **(Fig. 1).** Softer lesions are indicated by lower elastography scores (green color) and stiffer lesions are indicated by higher elastography scores (blue color) in this assessment approach. Soft nodules receive a score of 1 (F1); nodules with an intermediate degree of stiffness receive values of 2 and 3 (F2&F3); stiff lesions receive a score of 4 (F4). The likelihood of cancer increases as the nodule becomes harder and less elastic. One way to compute a strain ratio (SR) is to divide the strain of the nodule by the strain of the softest portion of the surrounding normal thyroid tissue.

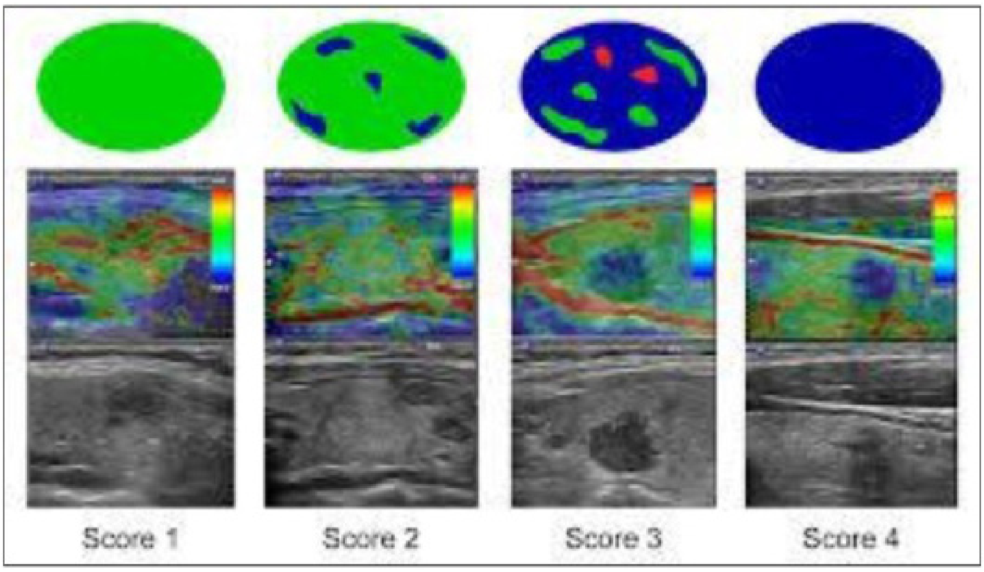

Fig 1: Strain elastographic scores by Asteria et al. A score of 1 indicated elasticity in the entire examined area. Ascore of 2 indicated elasticity in a large part of the examined area. A score of 3 indicated stiffness in a large part of the examined area. A score of 4 indicated a nodule without elasticity.

Statistical analysis

A student's t-test was utilized to compare the means of the two independent groups, and a Shapiro Wilk test was employed to determine whether or not a sample matches a normal distribution. The lowest and maximum values, together with the mean and standard deviation, were used to convey descriptive statistics. A Fisher Exact test was used for comparisons and a Chi-Square test was utilized to analyze the variables in the categories. Based on the histopathological findings, the cut-off point for the Strain Ratio and Elastography Score was established using the Receiver Operating Characteristic (ROC) analysis. Plotting the obtained sensitivities against the matching false positive rates allows one to create the curve by changing the cut point that is used to identify which values of the observed variable will be considered abnormal.The Medcalc system was utilized for the analysis of data. The area under the curve (AUC) was the statistical measure used for descriptive analysis. The Kappa statistic was used to determine the cut points for the SR and ES in order to evaluate their conformance. For all analyses, a statistically significant threshold of 0.05 was used.

Results

Included in the study were 180 nodules from 154 patients (109 females and 45 men; mean age: 49.13 ± 15.20 years; range: 17---68 years). The nodules ranged in size from 9 to 42 mm, with a mean size of 24.17 ± 12.21 mm. regarding age and gender, there were no statistically significant differences between the groups with benign and malignant histology. There was no statistically significant nodule size **(Table 1).**

Tables 2,3 show that the strain ratio and elastography score values were extremely significant in preoperatively discriminating benign from malignant histopathological thyroid nodules ($p < 0.001$). When diagnosing Bethesda Scores (BS) II, V, and VI, FNAB again demonstrated a high relevance **(Table 4).**

Regarding the differentiation of malignancy, the strain ratio cut-off point was found to be >3.71 ($p < 0.001$). The cut-off point for the elastography score (ES) was found to be ≥3 ($p < 0.001$). The two assessments were found to be statistically significant ($p < 0.001$) and statistically compatible with one another when utilized independently. When the ES and SR were combined, when employed independently, the sensitivity of accurately diagnosing thyroid cancer in the investigated nodules increased to 93.5%, compared to 86.77. **(Table 5).**

Table 1: Demographic results

	Benign (mean±SD) (Min-Max)	Malignant (mean±SD) (Min-Max)	Total (mean±SD) (Min-Max)	P value
age	46.25±11.38 (19---68)	41.59±16.72 (17---59)	49.13 ± 15.20 (17---68)	0.382
Sex				
male			45	0.448
female			109	
Nodule size	19.27±6.48 (13---42)	16.33±7.11 (9---26)	24.17 ± 12.21 mm (9---42 mm)	0.681

Table 2: Elastography Score in detection of malignant nodules

	Benign N. (% of benign)	Malignant N. (% of Malignant)	total	P value
Elastography score 1-2	126 (86.9%)	4 (11.42%)	130	<0.001
Elastography score 3-4	19 (13.1%)	31 (88.58%)	50	
Total, n. (%)	145 (100%)	35 (100%)	180	

Table 3: Strain Ratio in detection of malignant nodules

	Benign N. (% of benign)	Malignant N. (% of Malignant)	total	P value
Strain ratio ≥3.71	4 (2.75%)	32 (91.43%)	36	<0.001
Strain ratio <3.71	141 (97.25%)	3 (8.57%)	144	
Total, n. (%)	145 (100%)	35 (100%)	180	

Table 4: Fine Needle Aspiration Biopsy in detection of malignant nodules

Bethesda Score		Number (%)	Malignant final	P value
I	inconclusive	11(6.1%)	2	
II	Benign	36 (20)	1	<0.001
III	AUS/FLUS	72 (40%)	9	
IV	FN/SFN	48 (26.8%)	10	
V	SM	8 (4.4)	8	<0.001
VI	Malignant	5 (2.7)	5	<0.001
total		180	35	

AUS: Atypia of undetermined significance.
FLUS: Follicular lesion of undetermined significance.
FN: Follicular neoplasm.
SFN: Suspicious for follicular neoplasm.
SM: Suspicious for malignancy.

Table 5: Elastography Score together with Strain Ratio in detection of malignant nodules

	Strain ratio <3.71	Strain ratio ≥3.71	total	P value
Elastography score 1-2	128 (1 Malignant)	2 (1 Malignant)	130	<0.001
Elastography score 3-4	16 (2 Malignant)	34 (32 Malignant)	50	
Total, n. (%)	144	36	180	

Discussion

The major objective of their examination is to ascertain preoperatively whether a thyroid nodule is benign or malignant in order to minimize the number of unnecessary FNAC and operations carried out. There are no reliable molecular investigations or clinical characteristics to distinguish benign from malignant nodules. The recommended course of action for a nodule with indeterminate cytology is surgical removal.[14]

US examination is a suitable first approach for thyroid nodule assessment; nevertheless, its accuracy in differentiating benign from malignant thyroid nodules is not very high. Parameters that are highly suggestive for malignancy include irregular edges, a taller than wide form, calcifications, hypoechogenicity, and a solid composition.[15] Since the thyroid gland is a superficial organ, its outward deformation may be easily detected, making it a good candidate for ultrasound elastography, which is also applicable to cervical lymph nodes.[16]

Using standard ultrasound probes, strain elastography (SE) is a noninvasive, ultrasound-based technique that assesses tissue stiffness qualitatively and semiquantitatively. The Elastography Score (ES) and Strain Ratio (SR), which are employed as diagnostic measures for SE, can be derived.[17] In this work, we assessed the degree of elasticity of thyroid nodules using both the ES and SR techniques. A lesion is deemed to have a higher malignancy rate when its SR value is more than 1, indicating that the target lesion is more rigid than the reference tissue. Benign soft tissue lesions are thought to be softer than malignant lesions but stiffer than normal tissue, hence, the ES and SR values of benign thyroid nodules are lower than their malignant counterparts.[18]

According to some study, SR can increase overall diagnostic confidence and is more effective than the ES grading system at identifying malignancy in the nodules. In their investigation, Ma et al. discovered that the SR performed better in terms of diagnosis than the ES.[19] In their meta-analysis, Razavi and colleagues also confirmed this finding, showing that the SR was a more accurate indicator of thyroid nodule malignancy.[20] When OrhanGörgülü and his colleagues adopted a cutoff point of 3.59.[21] in a recent investigation, the sensitivities and specificities of the SR values were 100% and 84.5%, respectively.Their investigation revealed that strain ratios greater than 3.59 and elasticity ratings ranging from 3-to-4 are more suggestive of malignant nodules than benign ones. Our research revealed that the cutoff value for SR is marginally higher than theirs (>3.71), which had a strong significant value. Additionally, SR has a greater sensitivity than ES in predicting thyroid nodule malignancy. In a research by Magri, the threshold of SR for malignancy was calculated to be 2.9.[22] Some suggested a higher threshold of 3.85 to identify thyroid nodules that were malignant.[23]

The ES had encouraging outcomes in many additional investigations, demonstrating a high degree of precision in distinguishing benign from malignant thyroid nodules.[24] For nodules with non-diagnostic cytological features, Sun et al.'s meta-analysis,[17] revealed a greater sensitivity for ES but a higher specificity for SR and a lower specificity for ES. Additionally, we discovered that SR had a higher specificity than ES, although both had limited sensitivity.

The findings of OrhanGörgülü and colleagues demonstrated that ES and SR are highly useful in accurately and specifically identifying thyroid nodules that are malignant. Compared to the use of SR alone, the combination of the two approaches significantly improved the prediction of malignancy for solid thyroid nodules and increased the percentage of right diagnoses to 93.1%.[21] When SR and ES were combined, there was a 93.5% accuracy rate in correctly diagnosing thyroid cancer among the nodules that were analyzed.

More than half of the ambiguous lesions, which account for 10–25% of all cytological data and are the primary diagnostic limitation of FNAC, turned out to be histologically benign.[25] In accordance with the second edition of the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), the following is the risk of malignancy (ROM) resulting from indeterminate cytology Third, 10%–30% of cases are atypia of unknown significance or follicular lesion of undetermined significance (AUS/FLUS); Fourth, 25%–40% of cases are follicular neoplasms (FN) or suspect for a FN; and Fifth, 50%–75% of cases are suspicious for malignancy (SM).[26] FNA biopsy is advised as a standard diagnostic procedure for thyroid nodules that seem worrisome, despite concerns about its accuracy.[27] Research indicates that the FNA biopsy has a sensitivity range of 54–90% and a specificity range of 60–98%.[17] FNABs are not a suitable examination for all thyroid nodules since benign findings occur often in a significant percentage of thyroid nodules. Furthermore FNAB is not appropriate for every patient because to the high incidence of thyroid nodules, the invasive nature of the procedure, and its high expense. It is also inappropriate for use on a broad patient population due to a high rate of false positive US findings in nodules of 5 mm or smaller and the fact that it frequently provides inadequate cytology in FNAB.[28] Many investigations have shown that the necessity for FNAB in individuals with thyroid nodules has decreased to between 53 and 60.8%.[29] According to our research, the specificity of FNAB alone for distinguishing benign from malignant tumors was 91.4%; however, when SR and ES were combined, this discrimination rate increased to 93.1%.

Conclusion

In our investigation, we discovered that strain elastography, which assessed SR and ES together, had a significant relevance in differentiating between benign and malignant thyroid nodules. It was somewhat accurate. As an option beside FNAB, we advise using this non-invasive fast-resulting technique to treat thyroid nodules without the need for needless surgery. We suggest that by employing this research approach, surgeons may very confidently predict the disease in thyroid nodules based on strain elastography.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Gharib H, Papini E, Paschke R: Thyroid nodules: A review of current guidelines, practices, and prospects. *Eur J Endocrinol.* 2008; 1(59): 493--505.

2. Dietrich CF, Bojunga J. Ultrasound of the thyroid. *Z Gastroenterol.* 2015; 53: 208–225.

3. Gharib H, Papini E, Paschke R, Duick DS, Valcavi R, Hegedus L, Vitti P: AACE/AME/ETA task force on thyroid nodules 2010 American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules. *EndocrPract.* 2010; 16(Suppl 3): 468-475.

4. Lee YH, Baek JH, Jung SL, Kwak JY, Kim JH, Shin JH: Ultrasound guided fine needle aspiration of thyroid nodules: A consensus statement by the Korean society of thyroid radiology. *Korean J Radiol.* 2015; 1(6): 391-401.

5. Tan GH, Gharib H, Reading CC: Solitary thyroid nodule: Comparison between palpation and ultrasonography. *Arch Intern Med.* 1995; 1 55(241): 8-23.

6. David Cosogrove, Richard Barr, Joergojunga, Vito Cantisani, Maria Cristina, Chammas, MangiriDighe, udhirVinayak, Jun-Mei Xu, Ghristoph F. Dietrich. WFUMB Guidelines and recommendations on the clinical use of Ultrasound Elastography: Part 4 THYROID.

7. Aniqua S, Umme K, Sundas Y, Misbah D, Saba A, Riffat M: Diagnostic accuracy of strain ultrasound elastography in thyroid lesions compared to fine needle aspiration cytology. *Cureus.* 2022; 14(7): e271-e285.

8. Lim DJ, Luo S, Kim MH, Ko SH, Kim Y: Interobserver agreement and intraobserver reproducibility in thyroid ultrasound elastography. *AJR Am J Roentgenol.* 2012; 1(98): 896-901.

9. Liu BX, Xie XY, Liang JY, Zheng YL, Huang GL, Zhou LY, Wang Z, Xu M, Lu MD: Shear wave elastography versus real-time elastography on evaluation thyroid nodules: A preliminary study. *EurJRadiol.* 2014; 83: 1 135–143.

10. Oliver C, Vaillant-Lombard J, Albarel F, Berbis J, Veyrieres JB, Sebag F, Petit P: What is the contribution of elastography to thyroid nodules evaluation? *Ann Endocrinol (Paris).* 2011; 72: 120–124.

11. Aydin R, Elmali M, Polat AV, Danaci M, Akpolat I: Comparison of muscle-to-nodule and parenchyma-to-nodule strain ratios in the differentiation of benign and malignant thyroid nodules: Which one should we use? *Eur J Radiol.* 2014; 83: e131–e136.

12. Cantisani V, Grazhdani H, Ricci P, Mortele K, Di Segni M, et al: Q-Elastosonography of solid thyroid nodules: Assessment of diagnostic effificacy and interobserver variability in a large patient cohort. *EurRadiol.* 2014; 24: 143–150.

13. Asteria C, Giovanardi A, Pizzocaro A, Cozzaglio L, Morabito A, Somalvico F, et al: US-elastography in the differential diagnosis of benign and malignant thyroid nodules. *Thyroid.* 2008; 18: 523-531.

14. Gharib H, Papini E, Paschke R, Duick DS, Valcavi R, Hegedus L, Vitti P: AACE/AME/ETA Task Force on Thyroid Nodules 2010 American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules. *EndocrPract.* 2010; 16(Suppl 3): 468-475.

15. Choi SH, Kim EK, Kim SJ, Kwak JY: Thyroid ultrasonography: Pitfalls and techniques. *Korean J Radiol.* 2014; 1 (5): 267-276.

16. Hahn SY, Shin JH, Ko EY, Bae JM, Choi JS, Park KW: Complementary role of elastography using carotid artery pulsation in the ultrasonographic assessment of thyroid nodules: A prospective study. *Korean J Radiol.* 2018; 1(9): 992-999.

17. Sun J, Cai J, Wang X: Real-time ultrasound elastography for differentiation of benign and malignant thyroid nodules: A meta-analysis. *J Ultrasound Med.* 2014; 33: 495-502.

18. Kagoya R, Monobe H, Tojima H: Utility of elastography for differential diagnosis of benign and malignant thyroid nodules. *Otolaryngol Head Neck Surg.* 2010; 143: 230-234.

19. Ma HJ, Yang JC, Leng ZP, Chang Y, Kang H, Teng LH: Preoperative prediction of papillary thyroid microcarcinoma via multiparameter ultrasound. *ActaRadiol.* 2017; 58: 1303-1311.

20. Razavi SA, Hadduck TA, Sadigh G, Dwamena BA. Comparative effectiveness of elastographic and B-mode ultrasound criteria for diagnostic discrimination of thyroid nodules: A meta-analysis. *AJR Am J Roentgenol.* 2013; 200: 1317-1326.

21. Orhan G, Feride FG, Ayse SK: Can the unnecessary operations for suspected thyroid nodules be avoided by the combined use of the strain ratio and elastography score? *Brazilian Journal of Otorhinolaryngology.* 2021; 87(3): 338-345.

22. Magri F, Chytiris S, Capelli V, Gaiti M, Zerbini F, Carrara R: Comparison of elastographic strain index and thyroid fine-needle aspiration cytology in 631 thyroid nodules. *Journal of Clinical Endocrinology and Metabolism.* 2013; 98(12): 4790-4797.

23. Wang H, Brylka D, Sun LN, Lin YQ, Sui GQ, Gao J: Comparison of strain ratio with elastography score system in differentiating malignant from benign thyroid nodules. *Clinical Imaging.* 2013; 37(1): 50-55.

24. Lippolis PV, Tognini S, Materazzi G, Polini A, Mancini R, Ambrosini CE, Dardano A: Is elastography actually useful in the presurgicalselection of thyroid nodules with indeterminate cytology? *J ClinEndocrinolMetab.* 2011; 96: E1826–E1830.

25. Tian W, Hao S, Gao B, et al: Comparing the diagnostic accuracy of RTE and SWE in differentiating malignant thyroid nodules from benign ones: A Meta-Analysis. *Cell PhysiolBiochem.* 2016; 39: 2451–2463.

26. Xie X, Yu Y: Effect of the location and size of thyroid nodules on the diagnostic performance of ultrasound elastography: A retrospective analysis. *Clinics (Sao Paulo).* 2020; 75: e1720.

27. Okasha HH, Mansor M, Sheriba N, et al: Role of elastography strain ratio and TIRADS score in predicting malignant thyroid nodule. *Arch EndocrinolMetab.* 2021; 64: 735-7342.

28. Mazzaferri EL, Sipos J: Should all patients with subcentimeter thyroid nodules undergo fine-needle aspiration biopsy and preoperative neck ultrasonography to define the extent of tumor invasion? *Thyroid.* 2008; 18: 597-602.

29. Luo S, Kim EH, Dighe M, Kim Y: Screening of thyroid nodules by ultrasound elastography using diastolic strain variation. *Conf Proc IEEE Eng Med Biol Soc*. 2009; 2009: 4420-4423.