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Diagnostic accuracy of qualitative elastography in comparison to conventional USG and FNAC correlation in diagnosis of thyroid nodules and evaluation of usefulness of elastography in diagnosis of thyroid nodules

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Abstract

Thyroid nodules are a common disease in general population with female predominance. HRUS has significantly increased detection and morphological characterization of thyroid nodules. Risk of malignancy is better predicted with the use of TIRADS system. Despite this, HRUS is not accurate and needs further refinement by use of newer modalities. Elastography is a good option to improve diagnostic accuracy of thyroid nodules. Various studies have supported its use and others have shown no added benefit. Our aim is to review the literature and study on accuracy of Elastography in diagnosis of thyroid nodules in comparison to conventional USG and its usefulness in diagnostic evaluation of thyroid nodules.

Keywords: Elastography, Sonograpraphic, USC, HRUS,

Introduction

Thyroid gland is the largest endocrine gland in human body. Being superficially located, thyroid gland is easily amenable to clinical examination and USG. USG has revolutionized diagnosis of diffuse thyroid gland disease and thyroid nodules and is useful in differentiating solid from cystic lesions besides assessing their vascularity, margins and calcifications.

USG is the best imaging method for diagnosis of thyroid disease. It is a noninvasive technique with no risk of radiation exposure. It is inexpensive and can be performed as a bedside procedure. Ultrasound of neck is done with extended neck position and by a high resolution linear frequency probe (5-15MHz). Thyroid gland is made of two lobes and isthmus and is located in anterior neck adjacent to the thyroid cartilage. Thyroid gland should be scanned in transverse and longitudinal planes.

Thyroid nodules are common in general population and are estimated to be present in about 4-7% of general population[1,2]. However, malignant nodules are relatively uncommon, occurring in about 5-15% of all thyroid nodules[3]. Sonography is indispensible in the diagnosis of the thyroid nodules and characterises their nature, echogenicity, vascularity, margins and calcifications. Sonograpraphic features suggestive of malignancy include micro or macrocalcifications, marked hypoechogenicity, taller than wide shape and thick irregular or lobulated margins[4,5]. However, USG in not precise in differentiating between malignant and benign nodules with reported sensitivity and specificity ranging between 52-97% and 26.6-83% respectively as reported in various studies[6,7].

There has been significant improvement in correct diagnosis of thyroid lesions by incorporation of TIRADS system. TIRDS classification gives us the idea of malignant potential of a thyroid nodule and the need of further conservative or surgical management .Thyroid lesions can be assigned to one of the six TIRADS categories. TIRADS I signifies no abnormality, II are benign with no malignant potential, III are probably benign with malignant potential of <5%, IV are suspicious with malignant potential ranging from 5-80%. Category V are probably malignant with malignant potent of greater than 80% and TIRADS VI are histopathologically proven malignant nodules[8,9].

Elastography is a recently advanced technique that helps in further characterization of lesions assessable by the technique. Elastography is sonological counterpart of palpation of thyroid nodules. Stiffness of lesions and their elasticity can be determined by elastography. Malignant nodules are stiffer with ill-defined margins and hence show blue and green color on elastrography.

Broadly there are two elastrography techniques: strain elastography and shear wave elastography. Strain elastography is further divided in two types; qualitative and semi quantitative. In strain elastography, external compression forces are applied to cause deformation of the tissues to be scanned. Tissues with stiffer texture are deformed less as compared to less stiffer tissues which deform more and this information is received by transducer to generate color maps.

IN qualitative strain elastography(SE), lesions are characterized by the type and pattern of color mapping only with no true measurement of tissue stiffness. Classical benign nodules are less stiffer and are represented in elastogram as red or green and suspicious nodules are more stiffer and are represented in elastogram as blue[10,11]. Accordingly, nodules can be classified to four elastrography patterns as follows[12,13].

Pattern 1 : Elasticity in whole nodule

Pattern 2 : Elasticity in large part of the nodule, with inconstant appearance of inelastic areas.

Pattern 3 : Constant areas of inelastic areas at the periphery.

Pattern 4 : Uniformly inelastic lesion.

In semi quantitative strain elastography, strain ratio of region of interest is calculated by comparing the stiffness of the nodule with normal thyroid or muscle by placing ROI on thyroid nodule and normal thyroid thyroid. ROIs should be placed at same or similar tissue depths with a difference of less than 10mm[14].

In Shear Wave Elastography, an external acoustic radiation force push pulse is generated by probe itself which induces a shear wave inside tissue and the shear wave speed produced is directly proportional to stiffness of the tissue. It has got a quantitative nature in the context that it is superior to strain elastography (SE). SWE can be displayed in three different modes: Velocity mode, Stiffness mode and propagation mode. It is interpreted in terms of structural property of the tissues and the nodules have different histological tissue structure than normal thyroid gland and hence are differentiated. In Point SWE, a standard ROI of 5 × 5mm is placed in thyroid nodule excluding cystic and calcified areas; patient holds his breath and operator exerts minimal force with the probe[14,15,16,] and normal thyroid parenchyma should not be included in the ROI.

Ultrasound is an easily available tool in differentiating between benign and malignant thyroid nodules. 70% of thyroid nodules are solid where as 30% show some cystic changes within. Thyroid nodules with cystic areas are usually benign usually representing cystic degeneration in colloid nodules. Cystic nodules may show comet tail artifacts likely representing micro crystal within. Benign nodules include colloid nodules, hyperplastic nodules and follicular adenomas. They are well defined with wider than tall shape and usually show cystic areas within are hyper or isoechoic with a thin halo with no pathological calcifications within. On elastography, these nodules generally show pattern I and II colour mapping[17].

Malignant thyroid lesions have are hypoechoic/markedly hypoechoic with taller than wide shape, are generally solid and may contain microcalcifications with significant internal vascularity and show pattern III and IV on sonoelastography. These lesions include papillary carcinoma, follicular carcinoma, anaplastic and medullary carcinoma. Papillary carcinoma is the most common malignant tumours of thyroid comprising about 75-90% of all cases[18]. Features of papillary carcinoma include hypoechogenity and may show cystic degeneration with significant internal vascularity and microcalcifications with early cervical nodal metastasis[19,20] Follicular carcinoma shows solid echopattern with irregular margins , a thick irregular halo and chaotic internal vascularity[21,22]. Sonographic appearance of medullary carcinoma includes hypoechoic solid mass with calcifications that tend to be more coarser than the calcifications of papillary carcinoma[23]. Anaplastic carcinoma is characterized by its infiltrative nature and is usually seen as hypoechoic large mass with infiltration into surrounding tissues causing encasement of carotid vessels, airways and neck muscles.

Materials and methods

Current study was performed in Government Medical College Srinagar for a period of one year from December 2018 to November 2019. Our study is a prospective study in which patients suspected of thyroid nodules on clinical examination were taken for sonoelastography of thyroid followed by histopathological examination. Findings on sonoelastography were correlated with histopathological findings.

Inclusion criteria

- Patients with palpable lumps on clinical examination.
- Patients with thyroid nodules on HRUS.

Exclusion criteria

- Patients with diagnosed cases of thyroid malignancy.
- Patients with postoperative cases of thyroid malignancy.
- Patients who don’t give consent for histopathological tests.

Examination method

Patients with thyroid lumps, referred to Department of Radiology were subjected to High Resolution Ultra-sonographic examination (Grey scale and elastography) and followed by Fine needle aspiration cytology under USG guidance after informed consent. Machine used was GE LOGIC S8 with linear probe having frequency range 7-12 MHz.

Technique of USG neck

Thyroid being a superficial structure; its anatomy and pathology can be demonstrated with remarkable clarity by high frequency transducer probe. Patients were evaluated in supine position with neck extended. Patients with thyroid nodules were examined by B mode ,evaluated for size, shape, location, margins , echopattern, calcifications and internal vascularity and then elastography mode was activated which displayed real-time SE image with a scale based on the relative strain (or stiffness) of the tissues.

Technique of FNAC of Thyroid nodule

After an informed consent, part was cleaned and draped. Needle was held in one hand and high frequency transducer in the other and needle introduced through skin into the thyroid nodule under USG guidance. Needle used was 23G attached to a 10cc disposable syringe. Material was aspirated by gentle suction and two slides were prepared and put in a jar containing absolute alcohol for fixation. Slides were sent for histopathological examination and findings were documented.

Observation and Results

We performed our study in Government Medical College Srinagar. Our study group comprised of 120 patients after proper selection criteria. In our study group, females were the predominant sex group with 96 females (80%) and 24 males (20%).

There were 66 patients (55%) in 18-40 years age group; 30 patients (25%) in age group of 40-50 years and 24 patients (20%) in age group greater 50 years.

In our study, 93 nodules came as benign and 27 nodules were malignant. Benign nodules were found in 77.5% cases and malignant nodules were found in 22.5% of cases.

Of the malignant nodules, 18 were papillary carcinoma (66.7%); 5 were follicular carcinoma (18.5%), one nodule was medullary carcinoma (3.7%) and one nodule came as squamous cell carcinoma(3.7%). Of benign nodules, 60 were colloid nodules (64.5%)), 27 were hyperplastic nodules (29%) and 6 were follicular adenomas (6.5%)).

On TIRADS, 30 nodules were category 1 and all came as benign nodules on histopathology; 33 nodules were category 2 and came as benign nodules; 24 nodules were category 3 but 6 nodules were malignant on histopathology; 21 nodules were category 4 and 9 of them were benign on histopathology; and 12 nodules were category 5 and all of them were malignant on histopathology.

TIRADS 4 And 5 Nodules On USG	FNAC Suggesting Malignant Nodule			
		Positive	Negative	
	Positive	21	9	30
	Negative	6	84	90
	Total	27	93	120

In our study group sensitivity of TIRADS in the diagnosis of malignant thyroid nodules in comparison to histopathology was 77.8%; specificity was 90.3%, ; PPV was 70%; NPV was 93%; and Accuracy was 87.6% with significant P value (<0.05).

Findings on elastography were compared with histopathological findings. Elastography pattern 1 was found in 39 patients and all came as benign on histopathology. Elastography pattern 2 was found in 51 patients of whom 6 nodules were malignant on histopathology. Elastography pattern 3 was seen in 18 patients, of which 3 nodules were found to be benign on histopathology; and elastography pattern 4 was found in 12 patients and all of the nodules were malignant on histopathology.

Elastography pattern 3 and 4 nodules	Number of patients with FNAC malignant nodules			
		Positive	Negative	Total
	Positive	24	6	30
	Negative	3	87	90
	Total	27	93	120

Sensitivity of Elastography for diagnosis of malignant nodules as compared to histopathology was 88.9%, specificity was 93.5%, PPV was 80%, NPV was 96.7%; and Accuracy was 92.5% with significant P value (<0.005).

Discussion

We studied about 120 nodules in our study group. In our study, females comprised about 80% and males about 20%. These findings were similar to **Reddy V et al**[24] who found thyroid nodules predominent in female population group (84%) in a study on 50 patients. About 55% of patients were in the age group of 18-40 years in our study. Our findings were consistent with the study done by **Gautam H.K et al**[25] who studied on 60 patients and found that 60% of cases were in the age group of 21-30 years.

In our, study 93 nodules were benign(77.5%) and 27 (22.5%) were malignant and hence benign nodules were about 3 times more common than malignant nodules Our study was comparable to a study by **Chen et al**[26] who found that 23.5% were malignant nodules and the rest were suggestive of benign etiology. Of the benign nodules in our study group, colloid nodules were the most common (64.5%), followed by hyperplastic (29%) and follicular adenomas (6.5%). These findings were comparable to the study performed by **Arun C et al**[27] where 60% of the benign nodules were found to be of colloid type.

There were about 27 malignant nodules in our study group (22.5%), among which 18 nodules papillary (66.7%) were, 5 were follicular (18.5%), one each were medullary and squamous cell carcinoma. A study conducted by **Jinu CK et al**[28] **s**howed comparable results where 7 out of 11 malignant lesions were papillary carcinoma (63.3%) and 2 were follicular carcinomas (18.2%). Sensitivity, specificity, PPV, NPV and Accuracy of gray scale USG in comparison to FNAC were 77.8%, 90.3%, 70%, 93% and 87.6% respectively. Our findings were in consistent with a study performed by **F Basolo et al**[29] who found sensitivity, specificity and accuracy of 70%, 91% and 95% respectively.

Sensitivity, specificity, PPV, NPV and Accuracy of elastography in comparison to FNAC for diagnosis of malignant thyroid nodules were 88.9%, 93.5%, 80%, 96.7% and 92.5% respectively. Our findings were in accordance to a study conducted by **Monika Garg et al**[30] where they found sensitivity, specificity and accuracy of 87.8%, 100% and 96.5% respectively.

On comparison, diagnostic accuracy between elastography and gray scale, we found higher sensitivity (88.9% vs 77.8%), specificity (93.5% vs 90.3%), PPV (80% vs 70%), NPV (96.7% vs 93%) and Accuracy (92.5% vs 87.6%) of elastography in comparison to gray scale USG for diagnosis of malignant thyroid lesions.

There are conflicting results among various studies performed for comparison between Elastography and conventional USG with some studies favouring Elastography over conventional USG as a superior modality and some showing no advantage of using Elastography. **Yang et al**[31] in their study on 150 nodules in 123 patients found higher sensitivity and specificity of strain elastography in diagnosis of thyroid nodules and stiffness parameters are useful in differentiation between benign and malignant thyroid nodules. Similarly, a study performed by **Bojuna at al**[32] in their meta-anlysis of 8 studies consisting of 639 nodules found that RTE is able to differentiate malignancy accurately as compared with FNAC. **Volander C et al**[33] in their study have found that elastography is accurate in diagnosis of thyroid nodules. Our findings were supported by a study conducted by **Nesreen Mohey**[34] on 46 patients where all 31 patients with benign nodules had elastography pattern of 1-3 and 14 out of 15 with carcinoma as final diagnosis had elastography pattern of 4-5 (sensitivity=93.3%, specificity=100% and accuracy =97.8%). Similarly, a study performed by **Veyrieres JB et al**[35] in a study on 148 patients found excellent sensitivity and specificity of SWE with cutoff value of 66KPascals and concluded that combined conventional USG and SWE further increases accuracy in diagnosis of thyroid nodules. Another study performed by **P Ewelina et al**[36] supported our findings on 393 nodules whereby they found SWE was superior to any other conventional markers in predicting the malignancy.

Various studies were not in accordance to our findings. A study conducted by **Hee Jung Moon et al**[37] concluded that elastography as well as combination of elastography and gray scale US showed inferior performance in the differentiation of malignant and benign thyroid nodules compared with gray scale ultrasound.

Many studies showed that combined conventional and SWE have better accuracy either diagnostic modality alone. A study performed by **Shweel M et al**[38] on 66 thyroid nodules found that the combined use of USE and HRS for differentiation of benign and malignant thyroid nodules resulted in higher diagnostic performances and a significant statistical differences as compared to HRUS or USE alone. Similarly, a study performed by **Trimboli P et al**[39] supported the combined use of SWE and HRS in diagnosis of thyroid lesions in comparison to either modality alone.

SWE has its limitations and shows calcifications and fibrosis having higher stiffness, thereby misleading them as malignant lesions. However, judicious use of combined SWE and HRS increases the accuracy by comparing colour maps with morphological features.

Conclusion

The findings in our study support the use of elastography in diagnosis of thyroid nodules and showed high diagnostic accuracy of US elastography than HRUS. However the combined use of SWE and HRUS improves the accuracy further but needs further studies to confirm utility of combined modalities in diagnosis of thyroid nodules.

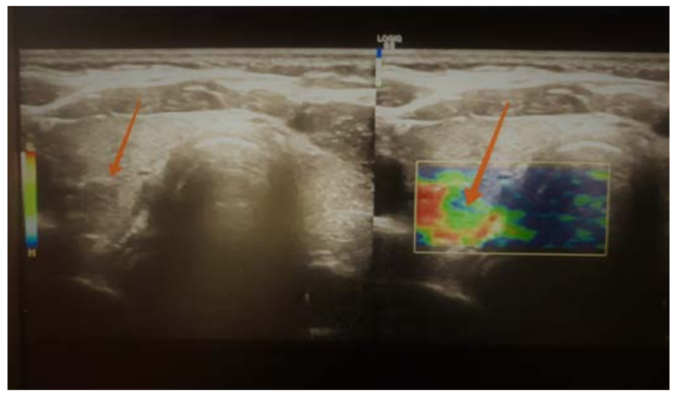

Figure 1: Mixed echogenicity solid cystic with predominant hypoechoic pattern well defined nodule in right lobe of thyroid (TIRADS 3) showing type 1 elastography pattern. FNAC showed features of benign thyroid nodule.

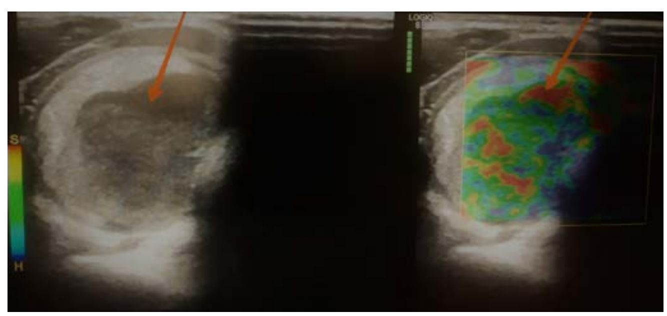

Figure 2: A well-defined lobulated predominantly hyperechoic solid cystic nodule on gray scale USG in right lobe of thyroid gland (TIRADS 4) showing type 2 pattern on elastography came as colloid nodule on histopathology report.

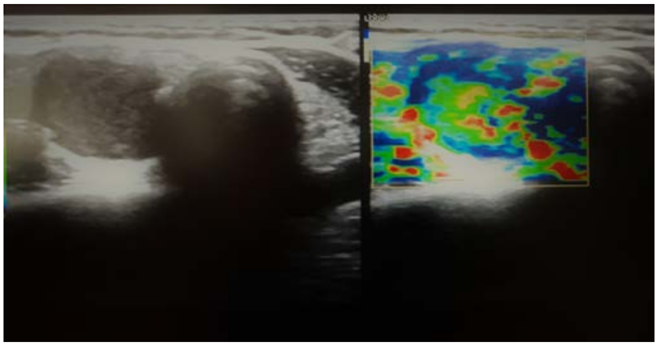

Figure 3: Gray scale USG showing predominantly isoechoic solid nodule, wider than taller with well defined margins in right lobe of thyroid (TIRADS 3) showing type 3 pattern on elastography. Histopathology features were consistent with a benign nodule.

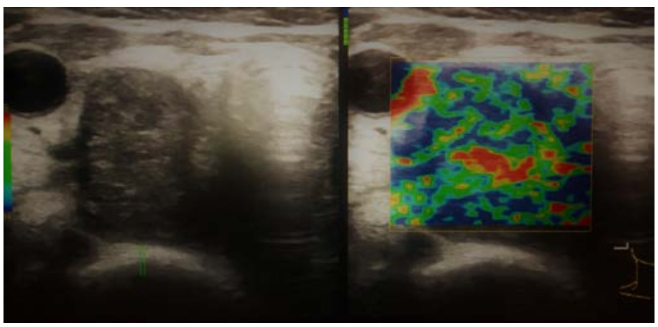

Figure 4: A mixed echogenicity solid taller than wider nodule with microcalcifications in right lobe of thyroid (TIRDS 5) with type 3 pattern on elastography and showed features of papillary on histopathology

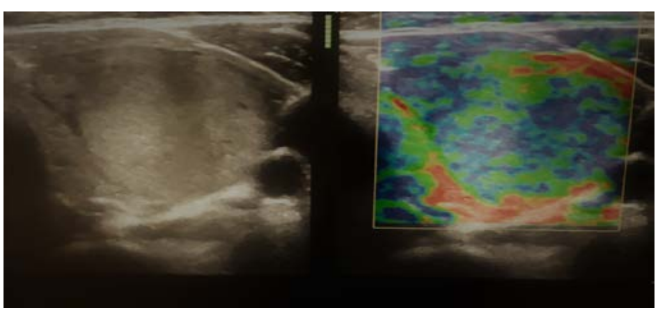

Figure 5: A hyperechoic nodule with capsular breach on medial aspect wider than taller with no microcalcifications in left lobe of thyroid (TIRADS 3) showing type 3 pattern on elastography. Histopathology of resected specimen showed features suggestive of follicular carcinoma.

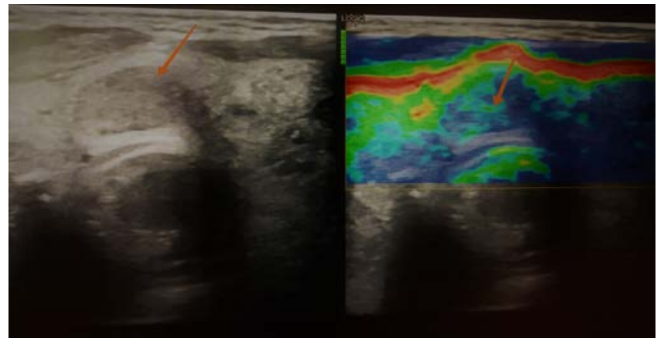

Figure 6: Gray scale USG revealed a well-defined solid, hyperechoic nodule, wider than taller with no internal calcifications in isthmus of thyroid gland (TIRADS 3) and show type 3 pattern on elastography. On FNAC it revealed features of follicular adenoma.

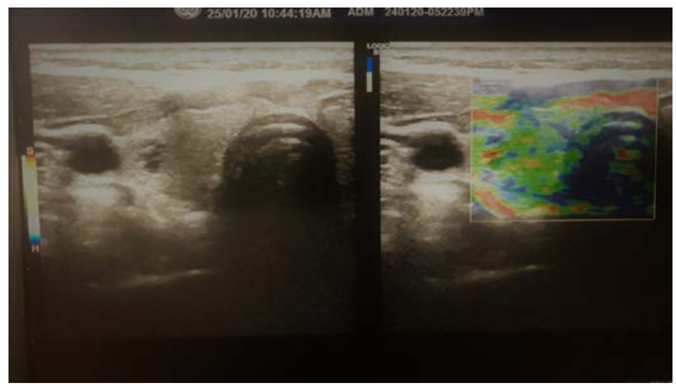

Figure 7: Gray scale USG shows solid cystic lesion with hyperechoic solid component, wider than taller with no internal calcifications in right lobe of thyroid (TIRADS 2) with type 2 pattern on elastography. FNAC features were consistent with benign thyroid nodule.

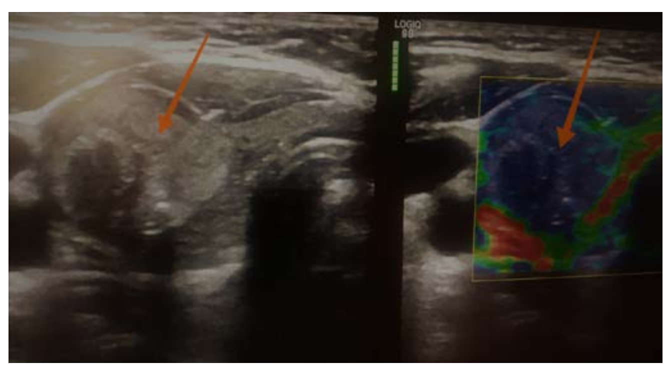

Figure 8. A mixed echogenicity lesion, wider than taller lesion with internal calcifications on convention USG in right lobe of thyroid (TIRADS 4) showed type 4

pattern on elastography. Histopathology features were consistent with papillary carcinoma.

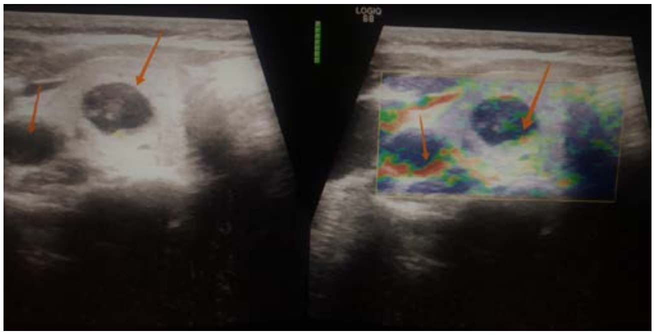

Figure 9: Gray scale USG shows two hypoechoic solid nodules wider than taller with no internal calcifications in right lobe of thyroid (TIRADS 4) with type 4 pattern on elastography. Histopathology revealed features suggestive of multifocal papillary carcinomas.

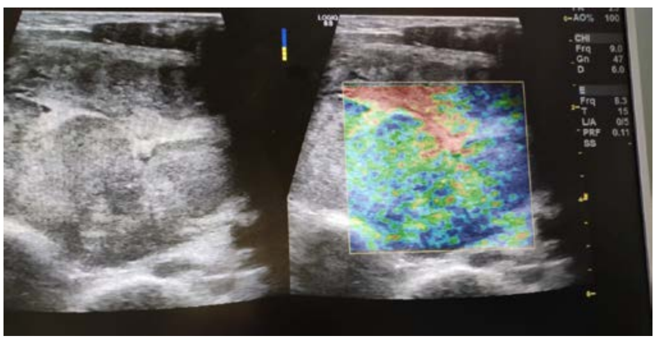

Figure 10: Gray scale USG shows a large predominantly hypoechoic solid lesion with extrathroidal invasion noted in right lobe of thyroid (TIRADS 5) with type 3 elastography pattern. Histopathology features were consistent with squamous cell carcinoma.

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