Original Article

Ultrasound Elastography is a Useful Adjunct to Conventional Ultrasonography and Needle Aspiration in Preoperative Prediction of Malignancy in Thyroid Nodules: A Northern India Perspective

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Abstract

Introduction: Data on ultrasound elastography (USE) are scant from India. This study aimed to compare the sensitivity and specificity of USE with thyroid ultrasonography (USG) and fine-needle aspiration (FNA) as preoperative predictor of malignancy, using postoperative histopathology as gold standard. **Materials and Methods:** Consecutive patients with thyroid swelling/goiter underwent thyroid USG followed by USE. Patients with pure cystic nodules or eggshell calcification were excluded. Patients with nodules >10 mm with one or more high-risk USG features underwent FNA. Patients with no USG high-risk features, benign score on USE, and benign FNA were conservatively followed. All other patients underwent thyroidectomy. **Results:** 246 consecutive patients underwent USG. Data from 97 patients (117 nodules) were analyzed. Median age of patients was 43 years with 85.4% females. All patients with USE score-1 had benign USG and FNA characteristics. Of 86 nodules having USE score-2, 18.6% nodules were hypoechoic and 16.28% had microcalcification. Hypoechogenicity and microcalcifications were observed in 66.67% nodules with USE score-3. All nodules with USE score-4 and 5 were hypoechoic and had microcalcifications. Histopathology was benign in 84 and malignant in 33 patients. Occurrence of malignancy in USE scores 1–5 was 0, 4.65, 100, 90.5, and 100%, respectively. All eight nodules with diagnosis of follicular adenoma had preoperative USE score-2. The sensitivity of preoperative USG, USE, and FNA in picking up malignancy was 66.67, 87.88, and 69.70%, respectively. Specificity of USG, USE, and FNA in detecting thyroid malignancy was 88.10, 100, and 97.6%, respectively. False positivity rates for USG, USE, and FNA in diagnosing thyroid malignancy was 11.9, 0, and 2.4%, respectively. The overall diagnostic accuracy of USG, USE, and FNA cytology in this study was 82.05, 96.58, and 89.74%, respectively. **Conclusion:** USE may be better than USG for preoperative detection of malignancy in thyroid nodules.

Keywords: Elastography, malignancy, needle aspiration, nodule, thyroid, nodule, ultrasonography

Introduction

Population-based studies have documented the prevalence of clinically palpable thyroid nodules in 5–7% in the general population, which increases to 20–76% when thyroid ultrasonography (USG) is used for diagnosis.[1] However, <5% of nodules thus detected (palpable or incidentalomas) proved to have malignancy in autopsy series.[2] USG is a commonly used imaging modality in the evaluation of goiter.[3] Few reports have suggested lack of adequate knowledge, excessive and irrational use of USG in clinical practice.[3,4] However, no USG feature has both high sensitivity and high specificity in detecting malignancy in thyroid nodules.[2] Fine-needle aspiration cytology (FNAC), in conjunction with high-resolution thyroid ultrasound are the two most commonly used investigations in the evaluation of thyroid nodules. FNAC has a sensitivity

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of 65–98% and specificity of 72–100% in detecting thyroid neoplasms.[2] However, the inability of FNAC to comment on the tissue architecture makes it difficult to diagnose follicular neoplasms and certain other benign lesions of thyroid, which can mimic malignancy.[5] Thyroid elastography is increasingly being used in the evaluation of thyroid nodules and has been documented to be useful in differentiating benign from malignant thyroid nodules.[6,7] Elastography works on the principle of detecting decreased elasticity (increased stiffness) of tissue. Malignant tumors, in general, have firmer stroma due to increased presence of collagen and myofibroblasts. Hence decreased elasticity of any tissue in general is treated with a suspicion of malignancy.[8] Advantage of elastography over FNAC is that it is a noninvasive test. Data are scant comparing elastography with FNAC in the evaluation of thyroid nodules, especially from India. Hence the aim of this study was to compare the sensitivity and specificity of ultrasound elastography (USE) with fine-needle aspiration (FNA) and thyroid USG as preoperative predictor of malignancy, using postoperative histopathology as the gold standard.

Table 1: TIRADS of thyroid nodule

TIRADS 1: Normal thyroid gland
TIRADS 2: Benign lesions (0% risk of malignancy)
Avascular anechoic lesion with echogenic specks (colloid type I)
Vascular heteroechoic nonexpansile, nonencapsulated nodules with peripheral halo (colloid type II)
Isoechoic or heteroechoic, nonencapsulated, expansile vascular nodules (colloid type III)
TIRADS 3: Probably benign lesions
None of the suspicious malignant sonographic features (vide infra). These lesions are mostly benign with <5% risk of malignancy
TIRADS 4: Suspicious lesions (subclassified as 4a, 4b, and later 4c, 4 with increasing risk of malignancy)
Solid nodule with marked stiffness on elastography; Markedly hypoechoic nodule; Microlobulations or irregular margins; Microcalcifications; Taller-than-wider shape
TIRADS 4a: One suspicious feature (5-10% risk of malignancy)
TIRADS 4b: Two suspicious features (10-80% risk of malignancy)
TIRADS 4c: Three/four suspicious features (10-80% risk of malignancy)
TIRADS 5: Probably malignant lesions (more than 80% risk of malignancy)
All five suspicious features (>80% risk of malignancy)
TIRADS 6: Biopsy proven malignancy

Materials and Methods

Consecutive patients attending the outpatient department of two tertiary care centers in Delhi with complaints of thyroid swelling/goiter were considered. The considered patients underwent detailed clinical evaluation. Patients with prior diagnosis of thyroid neoplasms, thyroid surgery, radioiodine therapy, or any severe comorbid states were excluded. The study protocol was explained to all the considered patients and only those who gave informed written consent were included. The study duration was January 2016 to October 2017. The Institutional Ethics Committee of both the hospitals approved the study.

All included patients underwent biochemical evaluation of thyroid function and thyroid USG. Patients detected to have pure cystic thyroid nodules (anechoic nodules without solid components), or nodules with eggshell calcification were excluded from the study. Thyroid image reporting and data system (TIRADS) scoring was done for risk stratification of thyroid nodules [Table 1].[9,10] Thyroid nodules with TIRADS score of 2 and above were taken for FNA after thyroid USE.[2,11]

USG and USE were done on Siemens ACUSON S2000 machine with high-frequency transducer of 7.5–12 MHz. The ultrasound probe was placed on the fully extended neck and the usual ultrasonographic study was carried out. Then the examined nodule was pressed with a stable light pressure, and a box was highlighted by the operator that included the nodule to be evaluated as well as sufficient surrounding thyroid tissue. The principle of elastography is to acquire two ultrasonic images (before and after tissue compression by the probe) and track tissue displacement by assessing the propagation of the imaging beam. Care was taken to ensure that the level of pressure is maintained constant throughout the examination. Dedicated software was used which provided an accurate measurement of tissue distortion. The elasticity software includes a scale for pressure monitoring.[11]

B-mode images and elasticity images were displayed simultaneously side-by-side on the same screen to aid in lesion identification. For each lesion examined, multiple frames of elasticity images, which were acquired during compression and relaxation by continuously moving the probe, were stored in the cine-buffer memory of the scanner. We then selected the best-fit B-mode USG elastogram image pairs for examination. The elasticity image was matched with an elasticity color scale displayed on the computer monitor. Color images were constructed automatically with the same image processing settings throughout the study. To classify elasticity images, we evaluated the color pattern in the nodule. On the basis of the overall pattern, each image was given a score of five elasticity scores (1–5) using the Rago's Criteria [Table 2 and Figure 1].[11]

FNAC was performed using 22–23G disposable needles fitted to 5 ml plastic syringes after positioning of the patient in supine neck extended state and cleaning of skin with povidone iodine solution. A maximum of four to five passes of the thyroid nodule was performed. The aspirated contents of the needle were expelled onto clean glass slides. At least four slides were made for each case and were immediately fixed in 95% ethyl alcohol at room temperature for about 15 min. The slides were stained with the modified Papanicolaou stain and examined with a light microscope by the cytopathologists. The adequacy of aspirates was defined according to the guidelines of the Papanicolaou Society.[12] Cytological specimens were evaluated blindly (without knowing the scores of elastography) and classified according to the recent Bethesda classification as follows: insufficient for diagnosis (these cases were excluded from the beginning of the

Table 2: Rago's criteria of scoring of thyroid nodules on elastography

USE score	Characteristics	Interpretation
1	Even strain or elasticity in the entire lesion (i.e., the entire lesion is evenly shaded in green as is the surrounding area) [Figure 1a]	Benign
2	Strain or elasticity in most of the lesion with some areas of no strain (i.e., a mosaic pattern of green and blue) [Figure 1b]	Benign
3	Strain or elasticity at the peripheral part of the lesion sparing the central part of the lesion (i.e., the peripheral part of the lesion is green and the central part of the lesion is blue) [Figure 1c]	Indeterminate
4	No strain or elasticity in the entire lesion (i.e., the entire lesion is blue but its surrounding area is not included) [Figure 1d]	Malignant
5	No strain or elasticity in the entire lesion or in the surrounding area (i.e., both the entire lesion and its surrounding area are blue) [Figure 1e]	Malignant

USE: Ultrasound elastography

Table 3: Bethesda classification of FNAC of thyroid nodule

Grade-I: Nondiagnostic or Unsatisfactory
Cyst fluid only
Virtually acellular specimen
Other (obscuring blood, clotting artifact, etc.)
Grade-II: Benign
Consistent with a benign follicular nodule
(includes adenomatoid nodule, colloid nodule, etc.)
Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context
Consistent with granulomatous (subacute) thyroiditis
Other
Grade-III: Atypia of undetermined significance or follicular lesion of undetermined significance
Grade-IV: Follicular neoplasm or suspicious for a follicular neoplasm
Specify if Hürthle cell (oncocytic) type
Grade-V: Suspicious for malignancy
Suspicious for papillary carcinoma
Suspicious for medullary carcinoma
Suspicious for metastatic carcinoma
Suspicious for lymphoma
Other
Grade-VI: Malignant
Papillary thyroid carcinoma
Poorly differentiated carcinoma
Medullary thyroid carcinoma
Undifferentiated (anaplastic) carcinoma
Squamous cell carcinoma with mixed features (specify)
Metastatic carcinoma
Non-Hodgkin lymphoma

work); benign; follicular lesion of undetermined significance; follicular neoplasm; suspicious for malignancy; and malignant sampling [Table 3].[13]

Patients with TIRADS score of 1–3, benign score on USE, and benign FNA report were conservatively followed up. All other patients underwent either hemithyroidectomy or near total thyroidectomy depending on the FNA diagnosis, after informed written consent of the patient. These included patients with indeterminate cytological results. Postsurgery

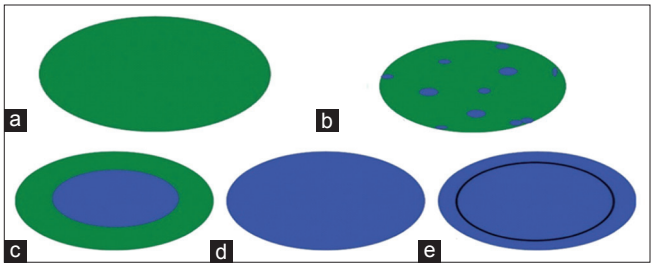

Figure 1: The applied standard elastography color scoring system according to Rago's criteria[8] (a) A score of 1 indicates even elasticity in the whole nodule; (b) A score of 2 indicates elasticity in a large part of the nodule; (c) A score of 3 indicates elasticity only at the peripheral part of the nodule; (d) A score of 4 indicates no elasticity in the nodule; (e) A score of 5 indicates no elasticity in the nodule or in the area showing posterior shadowing

histopathology diagnosis was taken as the gold standard (benign vs. malignancy), and the performance of USG, USE, and FNA as a preoperative predictor of malignancy in thyroid nodules was evaluated.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation, qualitative variables are expressed as frequencies/percentages and compared using Chi-square/Fisher's exact test. Calculation of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy was done for both FNAC and USE. A P value <0.05 is considered statistically significant. Statistical Package for the Social Sciences version 16.0 software was used for analysis.

With regards to FNA, the false-negative cases included those diagnosed as negative on FNA but confirmed as malignant upon surgical excision. Patients with reports of follicular neoplasm (indeterminate), suspicious for malignancy, and malignancy on FNA were considered to be "positive" for malignancy because they led to a recommendation for surgery. The false-positive category included those cases that were diagnosed as positive for neoplasm/malignancy on FNA, but subsequently confirmed to be benign on postoperative histopathology.

With regards to USE, it must be highlighted that the use of the term "positive" is for statistical purposes only as a preoperative predictor of malignancy. Statistically, USE scores 1 and 2, describing high elasticity (soft nodule), were strongly predictive of benignity with no need for surgical intervention, hence defined as "negative samples." Score 3 being indeterminate was considered to be "positive" for malignancy in our study. Scores 4 and 5 describing nodules with low elasticity were strongly predictive of malignancy, hence were also considered as "positive" for malignancy in our study.

Results

In this study, 246 consecutive patients underwent thyroid USG at the two centers (138 patients at Center-A and 108 patients at Center-B). Of these, 116 patients who fulfilled all the criteria were considered for our study, out of which data from 97 patients (117 thyroid nodules) who underwent the entire evaluation of thyroid nodules at the study centers, surgery, and had details of postoperative histopathology diagnosis available were analyzed. The flow of patients in this study has been elaborated in Figure 2.

The median [25–75th percentile] age of the patients evaluated in this study was 43 (31–52) years, with 85.4% (n = 100) being females. The median size of the thyroid nodules evaluated by USG, USE, and FNA in our patients was 14 [9–24] cm^2, having median length and height of 4 (3.4–6) cm and 3 (3–4) cm, respectively.

The USG and FNA features of the thyroid nodules evaluated in this study as per the TIRADS and USE score of the thyroid nodules have been elaborated in Table 4. All the nodules with USE score-1 had benign USG and FNA characteristics. Of the 86 thyroid nodules having USE score-2, 18.6% were hypoechoic and 16.28% had microcalcifications [Table 4]. Hypoechogenicity and microcalcifications were observed in 66.67% thyroid nodules with USE score-3 [Table 4]. All the thyroid nodules with USE score-4 and 5 were hypoechoic in nature and had microcalcifications. Irregular nodule margins and heterogenous nodules were predominantly seen in thyroid nodules with USE scores of 3–5 [Table 4]. With regards to TIRADS score, all the nodules with USE score-1 had TIRADS score-2 (benign). A large majority of USE score-2 nodules had TIRADS score-2 (benign; 77.90%) and TIRADS score-3 (benign; 19.76%). Only 2.32% nodules with USE score-2 had TIRADS score of 4 (suspicious of malignancy) [Table 4]. In contrast, 66.67, 100, and 100% of nodules with USE score-3, 4, and 5, respectively, had TIRADS score of 4 or 5 (high likelihood of malignancy) [Table 4].

Histopathology diagnosis was benign in 84 nodules and malignant in 33 nodules [Tables 5 and 6]. The sensitivity of preoperative thyroid USG, USE, and FNA in picking up thyroid malignancy was 66.67% (22/33), 87.88% (29/33), and 69.70% (23/33), respectively [Table 6]. The specificity of thyroid USG, USE, and FNA in detecting thyroid malignancy was 88.10, 100, and 97.6%, respectively. The false positivity rates for thyroid USG, USE, and FNA in diagnosing thyroid malignancy was 11.9, 0, and 2.4%, respectively [Table 6].

Review of the postoperative diagnosis revealed that the two nodules with USE score-1 had colloid nodules. Of the 86 nodules with USE score-2, 4 (4.65%) had thyroid malignancy and the remaining all had benign lesions [Table 5]. All the six nodules with USE score-3 (100%) had thyroid malignancy. Nineteen out of 21 nodules with USE score-4 (90.45%) thyroid lesion had thyroid malignancy. The two nodules with USE score-5 (100%) thyroid lesion also were diagnosed to have thyroid malignancy [Table 5].

All the eight nodules with diagnosis of follicular adenoma had preoperative USE score-2, hence achieving 100% diagnostic accuracy in terms of confirming the benign etiology. Of the four nodules with follicular carcinoma, two (50%) were correctly given an indeterminate/suspicion of

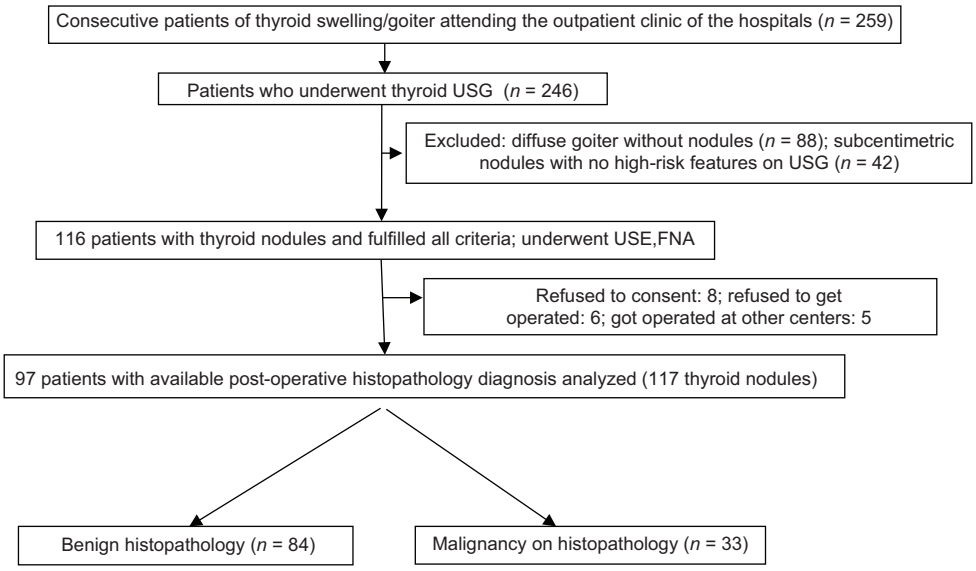

Figure 2: Flowchart elaborating the study protocol and flow of patients

Table 4: USG and FNA characteristics of thyroid nodules based on the USE score of thyroid nodules

Nodule parameters	USE score				
	Type-1 (*n*=2)	Type-2 (*n*=86)	Type-3 (*n*=6)	Type-4 (*n*=21)	Type-5 (*n*=2)
Irregular margins (USG)	-	4	6 (100%)	19 (90.48%)	2 (100%)
Heterogeneous (USG)	-	60 (69.77%)	6 (100%)	18 (85.71%)	2 (100%)
Echogenicity (USG)					
Hypoechoic	-	16 (18.6%)	4 (66.67%)	21 (100%)	2 (100%)
Isoechoic	2 (100%)	27 (31.4%)	2 (33.33%)	-	-
Hyperechoic	-	43 (50%)	0	-	-
Calcification (USG)					
No calcifications	2 (100%)	67 (77.91%)	2 (33.33%)	-	-
Microcalcifications	-	14 (16.28%)	4 (66.67%)	21 (100%)	2 (100%)
Coarse calcifications	-	5 (58.14%)	-	-	-
TIRADS-2	2 (100%)	67 (77.90%)	2 (33.33%)	-	-
TIRADS-3	-	17 (19.76%)	-	-	-
TIRADS-4	-	2 (2.32%)	3 (50%)	14 (66.67%)	1 (50%)
TIRADS-5	-	-	1 (16.67%)	7 (33.33%)	1 (50%)
Bethesda Grade-2	2 (100%)	82 (95.34%)	4 (66.67%)	4 (19.05%)	-
Bethesda Grade-3	-	2 (2.32%)	-	7 (33.33%)	-
Bethesda Grade-5	-	2 (2.32%)	2 (33.33%)	10 (47.62%)	2 (100%)

USG: ultrasonography; TIRADS: Thyroid image reporting and data system; because there were no patients in the TIRADS-1 group, it has not been mentioned in the table. *Because there were no patients in Bethesda Grade-1, 4, and 6, the same have not been included in the table. Bethesda grade was determined using slides obtained on FNA; USE scores 1 and 2, describing high elasticity (soft nodule) were strongly predictive of benignity with no need for surgical intervention, hence defined as "negative samples." Score 3 being indeterminate was considered to be "positive" for malignancy in our study. Scores 4 and 5 describing nodules with low elasticity were strongly predictive of malignancy, hence were also considered as "positive" for malignancy in our study

Table 5: Final histopathologic diagnosis of the thyroid nodules classified based on the initial thyroid USE score

Histopathology diagnosis	USE score				
	Type-1 (*n*=2)	Type-2 (*n*=86)	Type-3 (*n*=6)	Type-4 (*n*=21)	Type-5 (*n*=2)
Isolated colloid nodule/colloid MNG	2	62	-	-	-
Lymphocytic thyroiditis	-	10	-	-	-
Spindle cell tumor	-	-	-	2	-
Hurthle cell tumor	-	2	-	-	-
Follicular adenoma	-	8	-	-	-
Follicular carcinoma	-	2	2	-	-
Papillary carcinoma	-	2	4	16	2
Medullary carcinoma	-	-	-	2	
Anaplastic carcinoma	-	-	-	1	-

USG: ultrasonography; *MNG: multinodular goiter; USE scores 1 and 2, describing high elasticity (soft nodule), were strongly predictive of benignity with no need for surgical intervention, hence defined as "negative samples." Score 3 being indeterminate was considered to be "positive" for malignancy in our study. Scores 4 and 5 describing nodules with low elasticity were strongly predictive of malignancy, hence were also considered as "positive" for malignancy in our study.

malignancy (USE score 3) and two patients were incorrectly labeled as benign by USE (USE score-2). All the 24 nodules with a final histopathological diagnosis of papillary carcinoma 22 were correctly scored as malignant by USE (91.66%) [USE score 4/5 (suggestive of malignancy) in 18 and USE score-3 (indeterminate/suspicious of malignancy) in 4 patients]. Only two nodules were incorrectly given a USE score-2 (8.33%). Both of the two nodules with medullary carcinoma thyroid were correctly given an USE score-4 (malignancy). The single patient of anaplastic carcinoma was correctly diagnosed as malignancy by USE (USE score-4) [Table 4].

In our study, analysis of the preoperative Bethesda scores revealed that 92 were graded as benign (Grade-2), 16 were graded as malignancy (Grade-5), and 9 nodules were graded as indeterminate (Grade-3). All the 16 nodules with Grade-5 Bethesda score were diagnosed to have papillary carcinoma of thyroid on postoperative histopathologic evaluation. Of the 92 nodules graded as benign on FNA study, four finally were diagnosed to have papillary carcinoma, four had follicular carcinoma, and two had medullary carcinoma of thyroid. Of the nine nodules with Bethesda Grade-3 lesion (indeterminate; atypia of undetermined significance; or follicular lesion of undetermined significance), two were scored as benign by USE (USE score-2) and seven were scored as likely malignancy based on USE score of 4. The overall diagnostic accuracy of USG, USE, and FNAC in this study was

Table 6: Performance of USE and FNA in preoperative distinction of benign vs. malignant lesion as compared to the postoperative histopathologic diagnosis

Preoperative investigation	Histopathology diagnosis	
	True benign lesion ($n=84$)	True malignant lesion ($n=33$)
Conventional USG[#]		
S/O benign lesion	74	11
S/O malignancy	10	22
USE*		
S/O benign lesion	84	4
Indeterminate	0	6
S/O malignancy	0	23
Fine-needle aspiration		
Benign lesion	82	10
Atypia	2	7
Malignancy	0	16

[#]Conventional USG of thyroid nodule/lesion was suggestive of malignancy (S/O) if the lesion had TIRADS scores of 4-6; *TIRADS scores of 1-3 were considered to be benign; TIRADS: Thyroid image reporting and data system

82.05% (96/117), 96.58% (113/117), and 89.74% (105/117), respectively.

Discussion

The single most important objective of preoperative evaluation of thyroid nodules is to exactly determine which of the lesion is benign and to reduce the occurrence of thyroid surgeries which could have otherwise been avoided. FNAC has played an important role in obviating the need for thyroid surgeries.[13,14] Occurrence of malignancy in resected thyroid specimen increased from 14% in the pre-FNAC era to more than 50% in clinical practices where routine preoperative FNAC of thyroid lesions was done, highlighting the importance of thyroid FNAC in avoiding surgery for benign lesions.[13,14] However, the observation that 50% of the resected thyroid continued to have benign etiology highlighted that we need better tools for preoperative differentiation of benign from malignant lesions, thus further decreasing thyroid surgeries and associated morbidity.

The FNAC sensitivity and specificity data from our study (69.7 and 97.6%, respectively) is in accordance with previous published data, where FNAC thyroid has been reported to have a sensitivity ranging from 65 to 98%, specificity 72 to 100%, PPV 34 to 100%, and NPV from 83 to 100%.[13-15] Difference in the number, size and nature of thyroid nodules evaluated, variance in cytopathologist reporting, especially with regards to follicular lesions of undetermined significance can explain this variance in the ranges. The published guidelines of the Papanicolaou Society of Cytopathology suggested that a false-negative and a false-positive rate of <2 and <3%, respectively, should ideally be achieved with FNAC.[14,15] Additional advantages of FNAC include the option of measuring thyroglobulin and/or parathyroid hormone levels in the aspirate, which can help in differentiating thyroid from parathyroid lesions.[16,17] Limitations of FNAC include the difficulty in differentiating hyperplastic nodules from follicular neoplasm.[18] Diagnosis of follicular and Hurthle cell carcinoma requires demonstration of capsular and/or vascular invasion, which is not possible with FNAC.[19]

In our study, tissue stiffness was scored from 1 to 5 on the basis of subjective analysis of the elastogram, with 1 being the least stiffness and 5 being the maximum stiffness.[11] Our study highlights that USE scores of 1 and 2 (soft nodule) is highly predictive of benign lesion, and scores 3–5 are predictive of malignant lesion. Our results are comparable to another study were all the 49 patients with USE scores 1 and 2 had benign thyroid lesions.[11] Previous published literature on USE in the detection of neoplastic thyroid nodules revealed sensitivity ranges from 82 to 100%, specificity from 81 to 100%, PPV from 55 to 100%, and NPV from 93 to 100%.[6,7,11] Different machines used (gray-scale patterns or color-scale patterns) 4, 5, or 6-point scoring of USE thyroid tissue stiffness and method of case section may explain this difference.[11,20-22] However, what has been universally observed in all reports is that low elasticity (increased stiffness) on USE highly correlated with malignancy. Increased thyroid nodule stiffness is associated with increased nodule fibrosis and along with expression of Gal-3 and FN-1, which are poor prognostic features in thyroid malignancy.[23]

In our study, the overall diagnostic accuracy of USE was 96.58%, which was marginally higher than that reported in other studies (90–95%).[24-26] There are reports to suggest that USE is not suitable for the diagnosis of follicular carcinoma, as four of nine follicular carcinomas in the meta-analysis published by Bojunga *et al*.[25] were missed on USE. We had two cases of follicular carcinoma in our series that were incorrectly scored, highlighting the limitation of USE in this scenario. It is believed that most types of thyroid cancers have consistently increased stiffness and hence reliably picked up by thyroid elastography.[8] The exception to this rule is follicular thyroid cancer with modified elasticities, explaining the poorer performance of elastography in their detection.[8] Our study highlights that the sensitivity, specificity, PPV, NPV of USE are higher than that of FNAC. Only few reports had studied the relation between the thyroid FNAC and USE score.[24,26] In these works, FNAC was used as the reference standard for the diagnosis of benign nodules, but histopathological evaluations were performed when results suspicious for malignancy or malignant results were obtained on FNAC as well as in indeterminate lesions. In the series of 103 patients who have been studied with elastography evaluation of 106 thyroid nodules, Merino *et al*.[26] demonstrated a significant statistical association between elasticity score and cytological results, and malignant nodules could be excluded by elastography. There are reports to suggest that combined use of BRAF mutation analysis in FNAC with USE is superior to USE alone in the diagnosing malignant thyroid nodules.[27]

In the series of 142 nodules with indeterminate cytological results, only one of 103 nodules classified as negative on elastography had malignancy on histopathological correlation, whereas 9 out of 39 nodules with positive elastography were benign, highlighting the important role of USE in ruling out malignancy.[28] In another study on 32 nodules with indeterminate cytology, 25 had a benign follicular adenoma on histology and seven had carcinoma.[11] Positive scores were observed in six of seven (86%) patients with carcinoma and negative scores in all 25 patients with benign lesions.[11] Similar to our observations, a lower diagnostic accuracy of USE was reported for the detection of follicular thyroid carcinoma.[29] The results of this study reinforce the recent suggestion that thyroid nodules with benign feature, both on USG (no high risk features) and USE (score-1/2), can be safely conservatively followed up without serial FNAC.[30] Thyroid elastography is less operator dependent with regards to USG thyroid.[8] Hence reproducibility of elastography is better with regards to USG. Strength of this study included that a single operator expert in both USG and USE did the evaluation of the patients. Rago's criteria was used for quasi-static elastography scoring of thyroid nodules in this study. Although Rago's criteria have been extensively used in clinical research, there remains a subjective component in the elasticity scoring. Shear wave elastography, another variant of elastography, commonly used in breast evaluation, is a more quantitative form of elastography assessment.[8]

To conclude, this initial study from India provided encouraging data that elastography can be a useful adjunct to USG and FNAC in the evaluation of thyroid nodules. Its major strength entails the detection of benignity. Our study highlights that FNAC can safely be avoided in patients with soft thyroid nodules (USE scores 1 and 2) as they are highly predictive of benign etiology. Further studies from different centers of India are warranted before USE can be recommended in conjunction with USG for routine use in the management of thyroid nodules in India.

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Conflicts of interest

There are no conflicts of interest.

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