Thyroid Nodules: Comparison Between Ultrasound Elastography and FNAC

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Thyroid Nodules: Comparison Between Ultrasound Elastography and FNAC
Abdallah Ahmed Mohamed Abo zeid 1aM.B.B.Ch; Abdallah Mohamed Elkheshen 1MD and Ahmed Mohamed Eldeeb 1MD.

ABSTRACT
Background: Thyroid nodules are found in around 3%–7% of the population by palpation, 20%–76% by ultrasonography, and about 50% by autopsy. Due to advancements in medical imaging, the number of thyroid nodules discovered has increased. Thyroid nodules, regardless of size, are found to have a 5% risk of cancer, according to researches.

Aim of The Work: This prospective study was performed on 50 thyroid nodules in 50 adult patients of both sexes.

Patients and Methods: This prospective study was performed on 50 thyroid nodules in 50 adult patients of both sexes, referred to Sayed Galal University Hospital from internal medicine, endocrinology, surgery and oncology clinics between March 2021 to January 2022.

Results: USE is a reliable noninvasive diagnostic method for assessing dominant thyroid nodules, according to this study. On qualitative elastography, the benign histology of soft nodules may be predicted with a high degree of confidence. In the case of hard lesions, the likelihood of a malignant discovery is extremely high.

Conclusion: To summarise, elastography is an unquestionably beneficial technical advancement in thyroid nodule imaging, but it, like any other imaging modality, has its limitations.

Keywords: Thyroid Nodules; Ultrasound Elastography; FNAC.

INTRODUCTION
Thyroid nodules are found in around 3%–7% of the general population by palpation, 20%–76% by ultrasonography, and approximately 50% by autopsy. Because of advancements in medical imaging, the number of thyroid nodules discovered has increased.

Thyroid nodules, regardless of size, have a 5% risk of cancer, according to studies.

The prevalence rises in a linear relationship with age, ionizing radiation exposure, and iodine deficiency.

Ultrasound has many techniques which help in characterization of thyroid nodule. The most used conventional imaging techniques are B-mode US and color doppler US and one of the most recent techniques is US elastography.

B (basic) Ultrasonographic (US) examination has a number of advantages, including the detection of non-palpable nodules, estimate of nodule size to goiter volume, discrimination between solid and liquid lesions, and fine needle aspiration guiding.

Micro calcification, significant hypoechogenecity, and the absence of a hypo echoic halo around the nodule on B-Mode US have all been linked to an elevated risk of cancer in previous studies.

Clinical evaluation is also highly significant in the assessment of thyroid nodules. A firm or hard consistency is connected with a higher risk of malignancy, according to a recent agreement.

Elastography is a technique for imaging and evaluating the stiffness of tissues.

Elastography is made to enhance palpation testing results and verify the results of palpation.

The essential premise of US-Elastography is that compression of the studied tissue causes a strain that is smaller in hard tissues than in soft tissues. The degree of distortion of the US beam upon the introduction of an external force is measured and used to score the results of this procedure.

For successful clinical elastographic imaging, two conditions must be met: the ability to apply a quasi-static deformation and the ability to ultrasonically scan the tissue being deformed.

Elastography is divided into two categories. The first is strain elastography (quasistatic elastography), and the second is shear wave Elastography. Strain elastography compares the before and after effect of tissue compression while shear wave generate vibrations which travel through the tissue and its velocity is measured.

Elastography can be used to evaluate if a nodule is benign or cancerous by measuring its rigidity.
The benefit of elastography allow the patient to have a diagnosis which can eliminate the need for unnecessary surgery or biopsy. Fine needle cytology obtained by experienced hand and cytologist has a high accuracy rate in detecting malignant nodules. FNA results are classified as negative(benign),positive(malignant) and suspicious for cancer. In general false positive results are less than 1% and30% to 50% of aspirates read as suspicious for cancer will prove to be cancer at surgery. This work aimed to evaluate the thyroid nodules by ultrasound elastography in comparison to FNAC.

PATIENTS AND METHODS
Between March 2021 and January 2022, 50 thyroid nodules in 50 adult patients of both sexes were referred to sayed galal university hospital from internal medicine, endocrinology, surgery, and cancer clinics.

Inclusion criteria: Elastography was performed on the largest suitable nodule in cases of multinodular goiter (M.N.G.) and the only nodule in case of solitary thyroid nodule, taking care to ensure that the nodule to be examined fulfilled the following criteria: adequate amount of adjacent normal thyroid tissue was available for comparison, size of the nodule was more than 5mm and predominantly solid nodule with no or small cystic areas.

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

Patient preparation: The patient did not need to prepare for the exam. All patients gave their informed written consent, and our department and ethics review committee both authorised the study.

Machine:TOSHIPA APLIO 500, linear high frequency transducer.

Technique and image acquisition: For all patients, B-mode imaging was used to start the US scan then followed by Elastography. The resulting elastographic image was superimposed on the B-mode image on the screen as a colour coded image. Fine needle aspiration cytology was obtained from all thyroid nodules in all cases, and the results of cytology were recorded to compare with Elastography results. Blue denoted stiff tissue, red denoted soft tissue, and green or orange denoted intermediate stiffness.

Image analysis: Elastograms of nodules were qualitatively evaluated using a stepwise scoring system based on the predominant colour in the nodule as demonstrated by Rago et al, with a score of 1 indicating elasticity that is entirely soft in the nodule, 2 indicating mostly soft in the nodule, 3 indicating peripherally soft, 4 indicating entirely hard in the nodule (no elasticity), and 5 indicating hard in the nodule (no elasticity).

Tissue based diagnosis: Final diagnosis of nature of the thyroid nodules was made based upon US guided fine needle aspiration cytology (FNAC).

RESULTS
In this study, 50 thyroid nodules from 50 patients were evaluated. A total of 40 patients were found to have benign nodules. Malignant nodules were seen in ten of the individuals.(papillary carcinoma, n=6; follicular carcinoma, n=1,anaplastic carcinoma n=2,and lymphoma n=1).

<table>
<thead>
<tr>
<th>Studied patients (N = 50)</th>
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<tbody>
<tr>
<td>Elastography score</td>
</tr>
<tr>
<td>Score 1</td>
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<tr>
<td>Score 2</td>
</tr>
<tr>
<td>Score 3</td>
</tr>
<tr>
<td>Score 4</td>
</tr>
<tr>
<td>Benign</td>
</tr>
<tr>
<td>Malignant</td>
</tr>
<tr>
<td>E ratio</td>
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<tr>
<td>Mean ±SD</td>
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<td>Min - Max</td>
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Table 1: Description of Elastography score and E ratio of all studied patients.

<table>
<thead>
<tr>
<th>Studied patients (N = 50)</th>
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<tbody>
<tr>
<td>FNAC histopathology results</td>
</tr>
<tr>
<td>Bethesda II</td>
</tr>
<tr>
<td>Bethesda III</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
</tr>
<tr>
<td>Lymphoma</td>
</tr>
<tr>
<td>Papillary thyroid carcinoma</td>
</tr>
<tr>
<td>anaplastic thyroid carcinoma</td>
</tr>
<tr>
<td>Benign</td>
</tr>
<tr>
<td>Malignant</td>
</tr>
</tbody>
</table>

Table 2: Description of FNAC histopathology results of all studied patients.
Because of their high incidence in the community, thyroid nodules pose a diagnostic problem for clinicians. Although ultrasonography (US) is quite good at detecting thyroid nodules, it is not yet accurate enough to clearly discriminate between benign and cancerous nodules. Thyroid cancers have a firmer consistency than benign thyroid nodules, hence Ultrasound elastography (USE) was developed to increase US accuracy and limit the need for thyroid biopsies. USE is built on the idea that, under compression, tissues with softer components deform more easily than those with tougher ones; estimating tissue stiffness by comparing the stiffness of benign and malignant tumours to the stiffness of the normal parenchyma around them. Two sorts of elasticity evaluations can be obtained using this technique: (i) color-coded visual scoring within the nodule; (ii) semi-quantitative elasticity index or strain ratio measurement.¹⁴

The results of our study revealed that qualitative elastography grades were capable of distinguishing between benign and malignant thyroid nodules where higher elastography grades (ESGs) were more frequent in malignant nodules as opposed to benign nodules which consistently displayed lower elastography grades. In this study, a cutoff elastography grade of >3 could distinguish malignant thyroid nodules from benign nodules with a sensitivity, specificity, PPV, NPV of 70%, 100%, 100%, 76.9% respectively. Results of this study were compatible with many previous studies when a 5 point scoring system was used. ESGs were much greater in malignant nodules, according to Esfahanian et al.¹⁵ and the best point for distinguishing between benign and malignant thyroid nodules was 2 with sensitivity and specificity of 61 percent and 78 percent, respectively, 86 nodules in 66 patients were investigated by Astarita et al.¹⁶ They found that a cut-off point between 2 and 3 was the best for distinguishing benign from malignant thyroid nodules, with sensitivity and specificity of 94 and 81 percent, respectively. Rago et al.¹³ used a 5-point scoring system and ESGs 4–5 were found to be significantly predictive of malignancy, with a sensitivity and specificity of 97 and 100%, respectively. Concordant results were also reported by Gietka-Czernel et al.¹⁷ Friedrich-Rust et al.¹⁸ Wang et al.¹⁹ and Shao et al.²⁰. It is important to note that despite the consistent pattern of results described by these studies the calculated sensitivities, specificities, PPVs and NPVs differed considerably among the different studies including this study. This variation in values could be explained by differences in the inclusion criteria and the sample sizes used in different studies.

In spite of these promising results, overlap exists between the ESGs of benign and malignant nodules in individual cases. While no benign nodules displayed an ESG more than 3 in this study, 30 % of the malignant nodules displayed an elastography grade of 3. Likewise, all of the above-referenced studies showed that with intermediate ESGs of 2 and 3 and occasionally 4, misclassification of benign and malignant nodules may be unavoidable in individual cases. In some studies, the overlap was so great that it led the authors to question the value of USE. Kagoya et al.²¹ reported that only 9 of 21 thyroid nodules with ESGs of 3-4 were malignant ; similar results were reported by Lippolis et al.²² While grades 3 and 4 of the elastography scan may be used as predictive indicators for malignancy, their sensitivity and specificity were reduced. Moon et al.²³ and Zhang et al.²⁴ suggested that USE was not as useful as previously supposed, with diagnostic performance inferior to conventional ultrasonography in distinguishing benign from malignant thyroid nodules.

Several factors influence the diagnostic performance of USE and can explain the reasons behind the encountered false results, the most important of which is the histopathological type of the thyroid nodule. The most prevalent type of thyroid cancer, papillary thyroid carcinoma, is characterized by complex papillae with fibrovascular core, which are generally associated with psammoma bodies and fibrosis, making them with hard consistency (20). In this study, only 1 out of a total of 6 papillary carcinomas was one of the 3 malignant lesions which displayed an ESG of 3. Although uncommon, papillary carcinomas misdiagnosed as benign lesions on the basis of USE were also reported by several studies including those by Sebag et al.,²⁵ Bojunga et al.²⁶ Moon et al.²⁷ and Shao et al.²⁸ The existence of microcystic areas of degeneration and different histological variants of papillary carcinoma, some of which are softer than others may explain these confounding findings.²⁴

One case of follicular carcinoma seen in this study demonstrated an ESG of 4. Though our sample size was small and not conclusive, follicular carcinomas could be easily diagnosed as benign nodules as opposed to papillary carcinomas which are more frequently hard lesions. these findings were highlighted by Shao et al.²⁰ Bojunga et al.²⁶ and Hong et al.²⁷. Follicular carcinoma and benign follicular adenoma have similar physical anatomy and cellular patterns; both are made up of

<table>
<thead>
<tr>
<th>Elastography score</th>
<th>Benign (N = 40)</th>
<th>malignant (N = 10)</th>
<th>Stat. test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score 1</td>
<td>2</td>
<td>5%</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Score 2</td>
<td>27</td>
<td>67.5%</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Score 3</td>
<td>11</td>
<td>27.5%</td>
<td>3</td>
<td>30%</td>
</tr>
<tr>
<td>Score 4</td>
<td>0</td>
<td>0%</td>
<td>7</td>
<td>70%</td>
</tr>
</tbody>
</table>

X²: Chi-square test. HS: p-value < 0.001 is considered highly significant.
microscopic micro follicles with varying quantities of colloid. Only when a capsular or vascular invasion was identified on histological examination could follicular cancer be distinguished from benign follicular adenoma and hence, it would be expected that their elasticity patterns won't differ much from their benign counterparts, making them more susceptible to misdiagnosis as benign lesions. Nevertheless, some follicular carcinomas display increased cellular content which makes them stiff enough to be correctly diagnosed by Elastography. One case of the follicular carcinomas displayed an ESG of 4 in our study.

Finally, though not enough encountered in this study, thyroid lymphoma, medullary carcinoma and undifferentiated carcinoma were reported to demonstrate low stiffness and were misdiagnosed as benign lesions by USE, in our study two cases of anaplastic carcinoma display an ESG of 3.

Lastly, since elastograms of thyroid nodules give information on how elastic or stiff a thyroid nodule is in comparison to the surrounding tissue, the presence of a sufficient amount of healthy thyroid tissue is an essential prerequisite for accurate results. If the surrounding thyroid tissue was afflicted by a diffuse disease such as thyroiditis which would subsequently affect the elastic properties of the thyroid tissue, or in cases of insufficient healthy tissue as in cases of extensive MNG, elastograms of any superimposed nodules would be altered giving rise to potentially false and cofounding results. Fortunately, this was not an issue in this study as none of the cases of nodular goiter were extensive enough to hinder USE (due to our strict inclusion criteria) and the two cases of thyroiditis were correctly diagnosed as benign by USE, nevertheless, since it is a potential cause of false results, it is a point worth mentioning.

A final note to make regarding the diagnostic performance of the qualitative results of USE in this study is that Rago’s score 2 describes a mixed elastographic pattern with areas of green and blue, yet it does make a distinction based upon the amount of blue or green areas in the mixed pattern. This means that as long as a mixed pattern is seen, harder lesions with predominantly blue areas and softer lesions with predominantly green areas were both given a score of 2 which might impair diagnostic accuracy. Thus, using a 6 point scoring system such as that described by Hong et al. where an additional grade of elasticity describing a nodule which is mostly stiff save for small spots of higher elasticity was added to the Rago criteria, may potentially allow more accurate segregation of benign and malignant nodules.

CONCLUSION
To summarise, elastography is an unquestionably beneficial technical development in thyroid nodule imaging, but it, like any other imaging methods, has its limitations. To circumvent these limitations, it should always be done by an experienced practitioner who is aware of the possible difficulties, and the results should always be evaluated in conjunction with B-mode sonography findings.

Conflict of interest : none

REFERENCES


