The role of qualified elastography ultrasound in assessment of malignant thyroid nodules

Tuong Thi Hong Hanh, Nguyen Huy Hoang *108 Military Central Hospital*

Summary

Objective: To study the stiffness characteristics of benign and malignant thyroid nodules on elastography ultrasound and the evaluation of elastography ultrasound in the diagnosis of thyroid cancer. *Subject and method:* This study included 535 patients with 557 thyroid nodules confirmed by histopathology, from September 2019 to August 2020. All patients were evaluated by elastography ultrasound, using US machine (GE Logiq S8, US) and ROI Qualified Elastography, the class the score of stiffness according to the Rago T.'s score (2007). *Result:* Of 557 thyroid nodules, 7 nodules with stiffness score 1 (1.3%), 78 nodules with stiffness of score 2 (14.0%), 197 nodules with stiffness of score 3 (35.4%), 170 nodules with stiffness of score 4 (40.3%), 105 nodules with stiffness of score 5 (18.8%). In the group's low stiffness (score 1, 2), the rate of benign thyroid nodules was higher than that of malignant's group with $p<0.05$. In contrast, in the group's high stiffness (score 4, 5), the rate of malignant thyroid nodules was higher than benign's group with $p<0.05$. In the group's medium stiffness (score 3), the difference between groups of benign and malignant thyroid nodules was not statistically significant ($p>0.05$). Diagnosis of a malignant thyroid nodules by elastography ultrasound had a sensitivity of 57.4% and a specificity of 91.3%. *Conclusion:* The stiffness of the malignant thyroid nodules was higher than that of thyroid nodules by elastography ultrasound; The diagnostic value of the malignant thyroid nodules had a sensitivity of 57.3% and a specificity of 91.3%.

Keywords: Elastography ultrasound, thyroid cancer.

1. Background

Thyroid cancer (breast cancer) accounts for about 90% of endocrine cancers and has been on an annual increase in recent years. According to the International Cancer Organization (UICC), in 2012 the incidence of breast cancer in women was 230,000 cases and for men was 70,000, the standard rate of cancer by age in women was 6.1/100,000 population and for men 1.9/100,000 (the incidence varies by region with women from 4.7 - 11.1/100,000 and men from 1.4 to 3.6/100,000 people). The number of deaths caused by cancer in 2012 was 27,000 cases in women, accounting for 0.6/100,000 people and in men 13,000 cases, accounting for 0.3/100,0000 people [1].

In Vietnam, according to the statistics of the Global Anti-Cancer Organization (UICC) in 2002, the age-standardized rate for women is 2.7/100,000 and for men it is 1.3/100,000. In Hanoi, in the period 2001 - 2004, according to UICC's statistics, the UICC ranked the 6th among common cancers in women with the age-standard frequency of women of 5.6/100,000 population in men is 1.8/100,000, the rate of disease women to men is 3/1.

Correspondence to: Tuong Thi Hong Hanh - Department of Diagnostic Function, 108 Military Central Hospital

Email: hanhbssa@gmail.com

Current conventional ultrasound for thyroid cancer has a relatively high sensitivity but relatively low specificity [2], the diagnosis depends on the assessment of the ultrasound, the judgment on the characteristics of benign and malignant thyroid nudules also has subjective factors depending on qualifications and experience. Elastography Ultrasound makes the diagnosis objective because it can be standardized, but it needs to be studied more.

Diagnosis of thyroid cancer in clinical is mainly based on assessment of stiffness through palpation, however, it is difficult to detect small and deep thyroid nodules. Elastography ultrasound (US elastography) is an ultrasound method based on the variation of propagating waves in the organization to evaluate stiffness, this method has been studied and step by step to applied in distinguished diagnosis benign or malignant thyroid nodules [3]. However, how to apply for this method is necessary to study and consider in a scientific, objective, honest and truth. That's why, we researched with 2 main objectives: Study on benign and malignant nucleation characteristics on US elastography; Evaluation of the US elastography in the differential diagnosis of benign and malignant thyroid nodules.

2. Subject and method

2.1. Subject

From September 2019 to August 2020, 535 patients with 557 thyroid nodules were included in this study. All the patients were prospectively selected on the basic of ultrasound (US), US elastography and histopathology examination. Of these 557 thyroid nodules, 92 had benign and 465 malignant nodules. The diagnoses for all 557 nodules were confirmed by histopathologic examination with the specimens obtained by thyroid surgical resection.

2.2. Equipment

The ultrasonographic equipment used in this study was an Logiq S8 Healthcare machine (GE, Korean) with a linear transducer with frequency of 10MHz. The Shear Wave Elastography software in the system with qualified method.

2.3. Ultrasound elastography examination

Thyroid US and US elastography were performed using a real-time instrument (Logiq S8 machine with a linear transducer with central frequency of 10MHz; GE Heathcare Systems, Korean). A careful evaluation of the following US parameters was performed on all thyroid nodules: US elastographic measurement was performed during the US examination, using the same real-time instrument and the same probe. The probe was placed on the neck with light pressure, and a box was highlighted by the operator that included the nodule to be evaluated. The principle of US 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. The US elastogram was displayed over the B-mode image in a color scale that ranges from red, for components with greatest elastic strain (i.e.softest components), to blue for those with no strain (i.e. hardest components) (Figure 1).

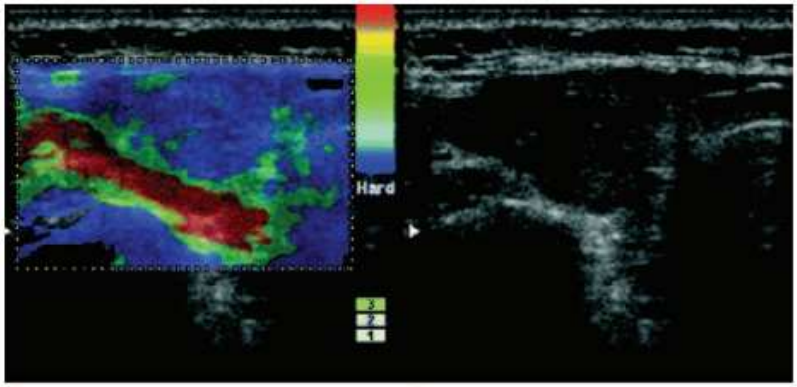

Figure 1. Thyroid nodule images obtained on US elastography

The US elastographic image was matched with an elasticity color scale and classified using the elasticity score (Table 1).

Table 1. Elastography score

Score	
1	Elasticity in the whole nodule
2	Elasticity in a large part of the nodule
3	Elasticity only at the peripheral part of the nodule
4	No elasticity in the nodule
5	No elasticity in the nodule and in the posterior shadowing

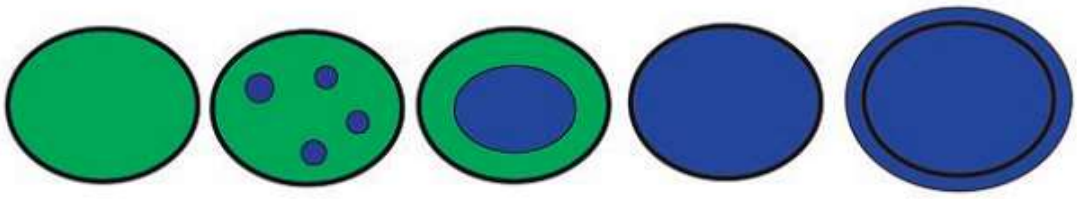

Figure 2. Five pattern scoring system of thyroid nodules arrcoding to Rago T. (2007):

Score 1 - the nodule is entirely elastic (green);

Score 2 - the nodule is mostly elastic (green, with some blue areas);

Score 3 - the nodule is elastic only at the periphery (blue core, green periphery);

Score 4 - the nodule is entirely rigid (blue);

Score 5 - the nodule and the surrounding tissue is rigid (blue).

To minimize the interobserver and intraobserver variability, the freehand compression applied on the neck region was standardized by real-time measurement displayed on a numerical scale (score 1 to 5; Figure 2), to maintain an intermediate level optimal for US elastographic evaluation (3 to 4). It is important that the level of pressure is maintained constant throughout the examination.

2.4. Histopathologic evaluation

All patients had confirmed by histopathology. The histopathologic specimens were reviewed by a single pathologist who was blinded to the US

elastography findings. The results was categorized according to the World Health Organization Classification.

2.5. Statistical analysis

A Student t test were used to compare the differences in perfusion parameters between the groups. A χ^2 test was used to compare the enhancement patterns between the groups. Quantitative data are expressed as mean ± SD. $p<0.05$ was considered statistically significant. Statistical analysis was performed using SPSS version 20.0 for Windows software.

3. Result

Table 2. The characterization of patients

No. of patients	535	
No. of thyroid nodules	557	
Sex	Male	78 (14.6%)
	Female	457 (85.4%)
	Male / Female	~ 1 / 5.85
Age (years)	X ± SD (Min - Max)	44.9 ± 11.5 (11 - 77)

The study included 535 patients with 557 thyroid nodules, mainly female with the rate of 85.4%. The average age of the study was 44.9 ± 11.5 years.

Table 3. The characterization of pathology

Thyroid nodules (n = 557)		**n**	**%**
Benign (n = 92)	Colloid	64	11.5
	Thyroditis	4	0.7
	Adenoma	24	4.3
Malignant (n = 465)	Papillary microcarcinoma	151	27.1
	Classic papillary carcinoma	302	54.2
	Papillary carcinoma mixed follicular variant	7	1.3
	Papillary carcinoma mixed columnar cell variant	1	0.2
	Papillary carcinoma mixed encapsulated variant	1	0.2
	Follicular variant	3	0.5

The colloid accounts for the majority with 64 nodules per 92 benign nodules, the mainly group was papilloma thyroid cancer with 302 nodules per 654 malignant nodules.

Table 4. The size of thyroid nodules

Size of thyroid nodules (mm)		**All (n = 557)**	**Benign (n = 92)**	**Malignant (n = 465)**
$\bar{X}$ ± SD (Min - Max)		12.13 ± 9.25 (3.0 - 65.9)	21.26 ± 12.76 (3.4 - 65.9)	10.32 ± 7.13 (3.0 - 44.9)
	< 5mm	68	5	63
	5 - < 10mm	261	17	244
	10 - < 20mm	139	23	116
	≥ 20mm	89	47	42

The size of the benign was larger than that of the malignant and concentrated mainly in the size over 20mm. The rate of mainly malignant was concentrated in the size from 5 to under 10mm.

Tab 5. The classification of thyroid nudules by US Elastography (classed by Rago T. (2007))

Classification	All (n = 557)	Benign[1] (n = 92)	Malignant[2] (n = 465)	*p[1,2]*
Score 1	7 (1.3)	3 (3.3)	4 (0.9)	
Score 2	78 (14.0)	37 (40.2)	41 (8.8)	*<0.05*
Score 3	197 (35.4)	44 (47.8)	153 (32.9)	*>0.05*
Score 4	170 (30.5)	5 (5.4)	165(35.5)	*<0.05*
Score 5	105 (18.8)	3 (3.3)	102 (21.9)	*<0.05*

The low group's score (score 2), the rate of benign thyroid nodules was significantly higher than that of the malignant group (with p<0.05). In contrast, the high group's score (score 4, 5), the rate of malignant thyroid nodules was significantly higher than that of the benign group (with p<0.05). In the medium group (score 3), the incidence of malignant and benign thyroid nodules was the same.

Table 6. The correlation of size to US elastography for diagnosing thyroid cancer

	Benign (n = 92)	Malignant (n = 465)	*p*	*Se*	*Sp*
All					
US Elastography (+)	8	267	<0.001	57.4	91.3
US Elastography (-)	84	198			
< 10mm					
US Elastography (+)	5	173	<0.001	56.4	77.2
US Elastography (-)	17	134			
> 10mm					
US Elastography (+)	3	94	<0.001	59.5	95.7
US Elastography (-)	67	64			

Se - sensitivity, Sp - specificity.

US Elastography diagnosis of malignant thyroid nodules with high score (4, 5) and negative with low (score 1 - 2) and medium score (score 3). The results in Table 6 shows that the difference between the groups benign and malignant of thyroid nodules by US Elastography had a suspected benign and malignant estimate with p<0.0001 (Q = 72.9449). Diagnosis of a malignant thyroid nodules by US elastography had a sensitivity of 57.4% and a specificity of 91.3%. The benign thyroid nodules usually have medium to low score. The accuracy of the diagnosis was 63%. Thyroid nodules size < 10mm, US Elastography had a sensitivity of 56.4%, specificity 77.2% and the size ≥ 10mm, the sensitivity of 59.5%, the specificity of 95.7%.

4. Discussion

The number of patients studied is 535, included 453 patients with thyroid cancer and 82 patients with benign. The number of thyroid nodules was 557, included 465 were thyroid cancer (mean size 10.32 ± 7.13mm) and 92 benign (mean size 21.26 ± 12.76mm). The group of thyroid cancer is mainly found in the group with the size from 5mm up to 10mm

(approximately 52.5%, highest in the malignant group), while the main benign group has size ≥ 20mm (approximately 51.0%, highest in benign group). Due to the research in patients with thyroid surgery, the thyroid cancer is high, and the benign thyroid using surgery is less that undergoes surgery when there is a large size nodules causing clinical symptoms such as swallowing problems, aestheticsless, difficulty breathing or hoarseness ...

Characteristics of pathology: The patient with thyroid cancer has mainly papillary carcinoma (302 of 465 malignant nodules) and mixed papillary variations, benign patients mainly with colloid (64 of 92 benign nodules) and adenoma.

By the results of Table 4 shows the group of benign thyroid nodules with low stiffness (score 2) and which is higher than malignant ones, the score 1 is not comparable due to the small number of study, may be it not correct. In contrast, in the thyroid nodules group with high stiffness (score 4 - 5), the rate of malignant nodules was higher than benign, which shows that the benign nodules have lower stiffness to malignant. At the medium stiffness level (score 3), the incidence of benign and malignant nodules is the same, but the tendency to thyroid malignant is higher. There is the same to Rago T (2007), studied in 31 malignant thyroid nodules, the results showed there are 30 of 31 malignant nodules has a high stiffness (score 4 - 5) [4]. Thus, it is possible to base on the difference in stiffness between benign and malignant of thyroid nodules on the US Elastography to diagnose thyrroid malignant. Rago T. used the cut-off value to diagnose thyroid malignant with high stiffness (score 4 - 5), with the sensitivity of 100% and the specificity of 100%. Applying this diagnostic criterion with the cut-off value of score 4 - 5, in our study, the diagnosis of malignant neoplasm by tissue elastomeric ultrasound has a sensitivity of 57.4% and a specificity of 91.3% (Table 6).

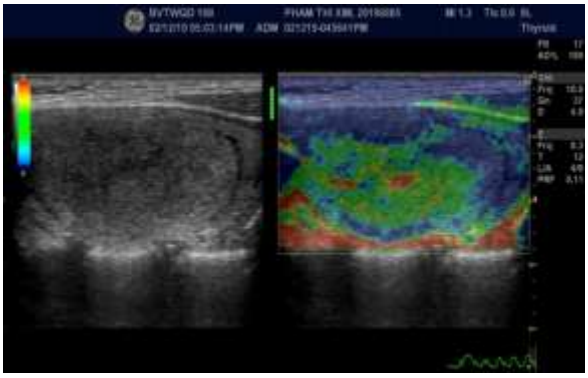

Figure 3a. US Elastography in the 51 years-old female with benign thyroid nodule (colloid) had score 2 on.

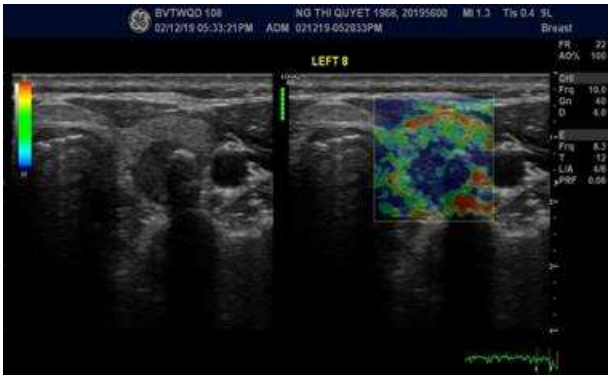

Figure 3b. US Elastography in the 52 years-old female with malignant thyroid nodule (papillary carcinoma) had score 4.

The difference in sensitivity can be seen that in fact, the study of author Rago T is not much (included 61 benign and 31 malignant nodules) and the failure founded in the cancer group as the result of other researchs [3]. According to the study of Arslan H (2017) showed that based on the high stiffness of the thyroid nucleus on US Elastography, the diagnosis of malignant nodules had a sensitivity of 77.3% and a specificity of 87. 6% (research based on data including 135 nodules of which 113 nodules are benign and 22 nodules are malignant) [5]. This result is quite similar to the results of our study, although the number of patient with malignant is not much.

The correlation of size and the sensitivity and specificity in the diagnosis of malignant thyroid

based on stiffness by US elastography, our research shows that the size of the thyroid nodules under 10mm with sensitivity and specificity has lower than the size larger from 10mm (Table 6). Comparing the diagnostic value to Moon HJ (2012) [2], as this result:

The size of thyroid nodules	Moon H.J. (2012)		Our research	
	Se (%)	Sp (%)	Se (%)	Sp (%)
< 10mm	12.2	93.1	56.4	77.2
≥ 10mm	23.2	97.5	59.5	97.5

The results show that the US elastography is influenced by the size of the nodules, this result is completely consistent with the study of Xing P et al (2011) [6].

So that, diagnosis of a malignant thyroid nodules by US elastography has a rather high specificity, for benign thyroid have low stiffness (score 1 - 2), however for thyroid malignant nodules, the nodules with low stiffness is quite high rate, that takes the sensitivity is low. In our study, the benign thyroid nodules was 92 of 557, the data in the study of Moon HJ (2012) was mainly of benign nodules (included 486 of 703 nodules), thus giving different sensitivity.

Thus, the diagnotic evaluation of the thyroid cancer nodules is based on US elastography with high specificity, but the sensitivity is low due to the structural differences between benign and malignant nodules, the benign due to the feature of high fluid content (colloid, bleeding, vascular…), it usually has coming a soft structure, especially those with small nodules with size under 5mm which has the low sensitivity [2], [6]. The value of diagnosis of malignant nodules by US ealstography has different sensitivity and specificity [7], many studies have high sensitivity and specificity over 85% [8], [9], but there are many studies with low sensitivity [2], [10]. So that, many authors have studied the combination of US ealstography with conventional US to increase the accuracy of diagnosis [2], [11].

5. Conclusion

The stiffness of the malignant thyroid nodules was higher than that of benign thyroid nodules by elastography ultrasound; The diagnostic value of the malignant thyroid nodules had a sensitivity of 57.3% and a specificity of 91.3%.

References

1. La Vecchia C et al (2015) *Thyroid cancer mortality and incidence: A global overview.* Int J Cancer 136(9): 2187-2195.
2. Moon HJ et al (2012) *Diagnostic performance of gray-scale US and elastography in solid thyroid nodules*. Radiology 262(3): 1002-1013.
3. Dudea SM and Jid CB (2015) *Ultrasound elastography in thyroid disease.* Medical ultrasonography 17(1): 74-96.
4. Rago T et al (2007) *Elastography: new developments in ultrasound for predicting malignancy in thyroid nodules.* The Journal of Clinical Endocrinology & Metabolism 92(8): 2917-2922.
5. Arslan H et al (2017) *Contribution of ultrasound strain elastography to the differentiation of benign and malignant thyroid lesions: Randomized controlled study.* Van Medical Journal 25(1): 51-56.
6. Xing P et al (2011) *Differentiation of benign from malignant thyroid lesions: Calculation of the strain ratio on thyroid sonoelastography.* Journal of ultrasound in medicine 30(5): 663-669.
7. Kwak JY and Kim EK (2014) *Ultrasound elastography for thyroid nodules: Recent advances.* Ultrasonography 33(2): 75.
8. Cantisani V et al (2015) *Diagnostic accuracy and interobserver agreement of quasistatic ultrasound elastography in the diagnosis of thyroid nodules.* Ultraschall in der Medizin-European Journal of Ultrasound 36(02): 162-167.

9. Dighe M et al (2013) *Efficacy of thyroid ultrasound elastography in differential diagnosis of small thyroid nodules.* European journal of radiology 82(6): 274-280.
10. Park AY et al (2015) *Shear wave elastography of thyroid nodules for the prediction of malignancy in a large scale study*. European journal of radiology 84(3): 407-412.
11. Afifi AH et al (2017) *Diagnostic accuracy of the combined use of conventional sonography and sonoelastography in differentiating benign and malignant solitary thyroid nodules.* Alexandria Journal of Medicine 53(1): 21-30.