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Elastography and Strain Ratio in Diagnosing Different Body Masses, Could They Solve the Puzzle?

Hussein Okasha, Shaimaa Elkholy, Wael Aref, Ahmed Abdel-Moaty, Ahmed Mostafa, Asem Ashraf, Ramy El-Husseiny, Yehia Elsherif, Amr Abo El-Magd, Moustafa Saeed, Ahmed Salman*, Reem Ezzat Mahdy

Faculty of Medicine-Internal Medicine, Cairo University, Egypt

***Corresponding author:** Salman A, Faculty of Medicine-Internal Medicine, Cairo University, Egypt, Tel: 00966507862399; E-mail: awea844@gmail.com

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Abstract

Background: Different real time elasticity scores were developed to distinguish between benign and malignant lesions, yet the most important drawback is that they are very subjective. Strain ratio as a semi-quantitative method developed by dividing the area of interest by the normal tissue to improve objectivity and reach a better diagnosis.

Aim: To validate the accuracy of elastography and strain ratio in diagnosing stiffness of different body masses.

Patients and methods: This prospective study included 568 patients with different body masses and lymph nodes. We reached diagnosis in 427 patients by FNA, tru-cut and/or excision biopsy. Real time Elastography and strain ratio were assessed in all patient by US or EUS-elastography.

Results: The best cut off value of strain ratio in differentiating benign from malignant lesions was 6.5 with 86% sensitivity, 84% specificity, 85% accuracy, 91% PPV and 76% NPV. Elastography score had sensitivity, specificity, accuracy, PPV and NPV of 94, 78, 88, 88, 87% respectively. Adding both results to each other resulted in sensitivity of 94%, specificity of 78%, accuracy, PPV and NPV of 88%.

Conclusion: Using both strain ratio and elastography increases the accuracy of differentiating benign from malignant body lesions.

Keywords: Elastography; Strain ratio; Body masses

Introduction

Elastography and strain ratio (SR) have been used extensively in the past few years as tools assisting in differentiating malignant from benign lesions by determining organ stiffness. FNA is a good positive test, however, negative results does not exclude malignancy. Accordingly, elastography and strain ratio were added to help in diagnosing the nature of the examined lesion. Elastography and SR were studied in different body masses as pancreatic [1] and rectal masses and lymph nodes [2], some studied their role on measuring liver stiffness [3]. Esophageal, mediastinal masses, breast [4] and thyroid gland [5] were also included in similar studies. In our study, we aimed at estimating the ability of both techniques to predict tissue stiffness correctly when compared to the final diagnosis of the lesion. We validated the tests by calculating their sensitivity, specificity, accuracy, positive predictive value and negative predictive value.

Materials and Methods

Patients

This study included 568 patients with body masses in different sites identified by different imaging techniques. The inclusion criteria were patients with an identified mass from prior radiological imaging and patients between 18 and 80 years old. The exclusion criteria included patients that declined to participate in the study and patients with contraindication to the procedure as patients unfit for Propofol injection or patients with bleeding tendency contraindicating tissue biopsy. Informed consent was obtained from all patients prior to the procedure.

Methods

This study was conducted as a prospective study starting from Jan. 2013 to Oct. 2017, through which ultrasound (US) or endoscopic ultrasound (EUS) and FNA were carried to patients eligible for the work, and the ethical committee approved the study.

Full history and clinical examination were performed with complete routine lab work up according to the site of the examined lesion.

Conscious sedation with Propofol was given to the patients undergoing EUS examination, and local anesthesia was used in those undergoing ultrasound examinations prior to FNA.

EUS examination was performed using a linear Echo-endoscope Pentax EG3830UT (HOYA Corporation, PENTAX Lifecare Division, Showanomori Technology Center, Tokyo, Japan) connected to an ultrasound unit Hitachi EUB-7000 HV (Hitachi Medical Systems, Tokyo, Japan). All examinations were performed by one operator. For EUS-FNA biopsies, we used the Cook needle 22G (Echotip®; Wilson-Cook, Winston Salem, NC).

Qualitative score

We used the "Elastic score" reported by Giovannini et al. [6] Score 1 indicated a homogeneous hypoechoic area (soft, green); Score 2 was for heterogeneous elastogram which still within the soft-tissue range. Elastographic images that were largely blue with minimal heterogeneity were given a score of 3. Score 4 represented a hypoechoic region in the center, with a green appearance within a small area and surrounded by blue, or harder tissue.

US elastography scoring (patterns) system was done according to Furukawa et al. [7]

- Pattern 1: 80% or more of the cross-sectional area of the mass is red or green, i.e., soft as shown in Figure 1.
- Pattern 2: 50% or more and less than 80% is red or green.
- Pattern 3: 50% or more and less than 80% are blue.
- Pattern 4: 80% or more of the cross-sectional area of the mass is blue i.e., hard as shown in Figures 2 and 3.

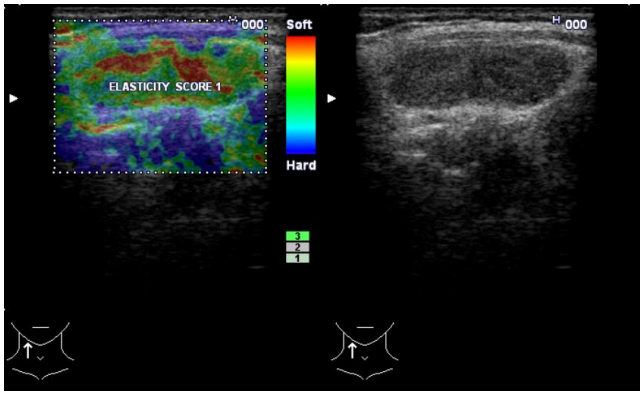

Figure 1: Benign cervical LN with elasticity score 1.

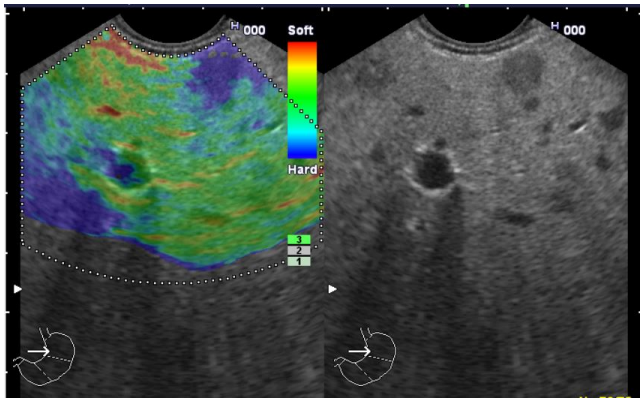

Figure 2: EUS picture of liver metastasis with elasticity score 4.

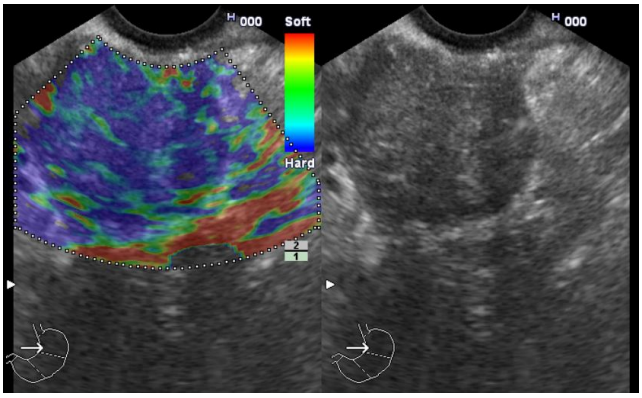

Figure 3: Malignant pancreatic head mass with elasticity score 4.

Quantitative score

The semi-quantitative score of elastography was represented by the strain ratio method. Two areas were selected, area (A) representing the region of interest and area (B) representing the normal area. Area (B) is then divided by area (A). For masses with homogeneous pattern of elasticity, area A was chosen from any region, but, in those with heterogeneous ones, area A was chosen to cover all heterogeneous area as much as possible (Figures 4 and 5). Both areas were manually selected by these criteria. Means of SR were calculated and used as final results for each patient. Subsequently, the best cut-off value was calculated and was used for the calculation of diagnostic value. Its value in our study is 6.5 with very high significant value on applying t-test. The best cut-off value of strain ratio was also combined with results of elastography for calculation of diagnostic value.

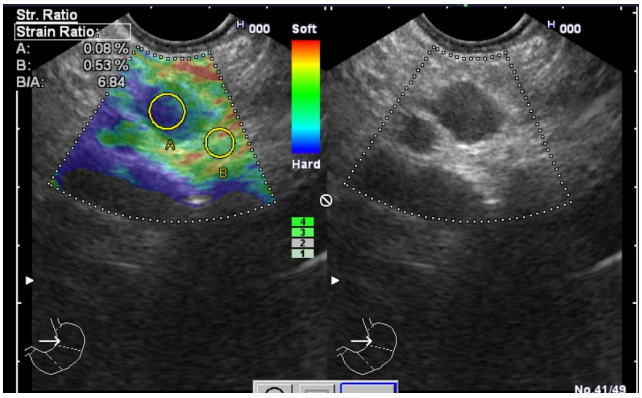

Figure 4: Malignant peripancreatic LN with high strain ratio.

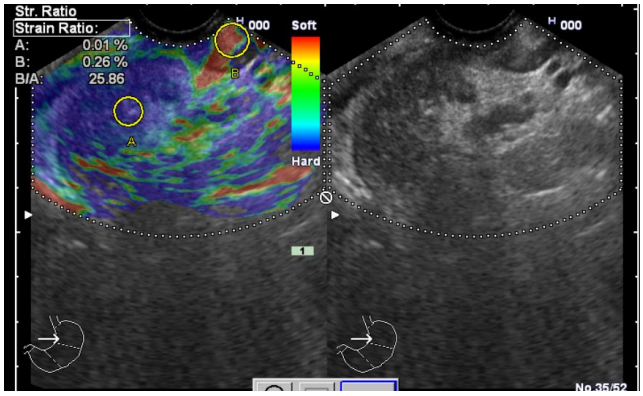

Figure 5: Malignant pancreatic head mass with very high strain ratio.

Final diagnosis

Final diagnosis was reached in 427 out of 568 patients. It was reached by FNA (356 patients), tru-cut sonar guided biopsy (8 patients), excision biopsy (5 patients), or follow up ranging from 6 months up to 3 years with no progression of the mass denoting its benign nature (51 patients), presence of metastasis (7 patients). Patients with positive FNA was considered malignant due to the very high positive predictive value (PPV) reaching up to 95-100%. However, due to its rather low negative predictive value, patients with negative FNA were followed up for at least 6 months with no progression of the mass denoting its benign nature.

Data analysis

Descriptive data are demonstrated in the form of mean and percentage. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated by comparing diagnoses made by elastography, strain ration (SR) and final diagnoses. Data analysis was performed by Microsoft office 2010.

Results and Discussion

The study started with 568 patients, 219 females and 349 males. Final diagnosis was reached in 427 patients while 141 patients were excluded due to unavailable results of cytology or patients lost for follow up. Malignant lesions were proved in 277 (64.87%) patients while 150 (35.13%) patients were proved to have benign lesion. Half of the lesions (51%) were pancreatic lesions, (32%) were lymph nodes and the rest (17%) were different body masses as illustrated in Table 1.

Site	Number	Distribution
Pancreatic masses	217 (51%)	138 head 29 body 6 tail 28 diffuse 4 papillary 9 uncinate process 3 distal cholangio-carcinoma
Lymph nodes	136 (32%)	43 peri-pancreatic 23 cervical 14 celiac 32 portahepatis, 6 mediastinal 2 sub-mandibular 9 peri-gastric 1 pre-tracheal 1 submental 1 porto-caval 2 para-rectal 1 para-aortic 1 femoral
Body masses	74 (17%)	20 gastric 7 breast 20 hepatic 5 papillary 4 mediastinal 2 recto-sigmoid 4 oesophageal 3 duodenal 2 splenic 1 thyroid 1 parotid 1 retroperitoneal 2 suprarenal 1 sub-diaphragmatic 1 pre-sacral

Table 1: Site and distribution of diagnosed lesions

Total 217 patients	Score 1	Score 2	Score 3	Score 4	Total
Chronic pancreatitis	7	22	9	4	42 (19.3%)
Autoimmune pancreatitis	-	5	5	1	7 (3.2%)
Papillary adenoma	-	-	-	1	1 (0.46%)
Neuroendocrine tumour	-	1	-	1	2 (0.92%)
Cystic lesion	-	3	1	-	4 (1.8%)
Pancreatic cancer	-	1	40	116	157 (72.35%)

Table 2: Pancreatic lesions and elastography scores

Total Number	Score 1	Score 2	Score 3	Score 4	Total
-136					
Malignant	-	7	27	29	63 (46.32%)
Benign	18	43	10	2	73 (53.67%)

Table 3: Lymph nodes and elastography scores

Total Number	Score 1	Score 2	Score 3	Score 4	Total
-74					
Benign	5	14	4	2	25 (33.8%)
Malignant	-	6	24	19	49 (66.2%)

Table 4: Different body masses and elastography scores

The elastography score in different diagnoses of pancreatic lesions (Table 2). While the elastography score of benign and malignant lymph nodes and different body masses respectively (Tables 3 and 4).

	Elastography (%)	SR (6.5) (%)	Elastography and SR (%)
Sensitivity	94	86	94
Specificity	78	84	78
Accuracy	88	85	88
PPV	88	91	88
NPV	87	76	87

Table 5: Diagnostic value of elastography score and strain ratio of all lesions

Site	Cutoff values	Sensitivity	Specificity	Accuracy	PPV	NPV
		(%)	(%)	(%)	(%)	(%)
Pancreatic masses	12.8	71	83	73	96	35
Lymph nodes	3.9	91	76	85	85	85
Body masses	7.8	65	84	72	89	57

Table 6: Sensitivity, specificity, PPV, NPV and Accuracy of each item at the best cut off level

The sensitivity, specificity, accuracy, positive predictive values (PPV), negative predictive values (NPV) of elastography, strain ratio and both combined elastography and strain ratio collectively in all body masses (Table 5). These values differ when illustrating sensitivity, specificity, accuracy, positive predictive values (PPV), negative predictive values (NPV) of elastography, strain ratio and both combined elastography and strain ratio separately in different tissues as Pancreas, lymph nodes and other body masses (Table 6).

Diagnosing the nature of a body mass with minimal error is required to reach the correct management. Different imaging techniques were developed along the past years to minimize the risk of false negative results.

Elastography is a technique that depends on the degree of tissue stiffness based on the concept that healthy tissues deform more easily than diseased ones [8]. Its major disadvantage is that it is a qualitative method and operator dependent. SR allows semi-quantitative measurement of the average elasticity of a lesion for overcoming the limitation of the elasticity score. SR is measured by taking area (A) from the lesion and area (B) from a normal tissue (control point) and dividing (B) by (A) values.

Adding elastography and SR to ultrasound examination, being qualitative and semi-quantitative methods to decrease rely on observer opinion increased the chance of better differentiation of the type of the lesion.

We examined 568 patients with different body masses for which ultrasound or endoscopic ultrasound, elastography, SR and FNA were performed. We reached a diagnosis in 427 of them. Malignancy was more recorded than benign diagnosis being 277:150. We considered lesions with score 1 and 2 as benign lesions while scores 3 and 4 as malignant ones. Examined lesions included the pancreas, different groups of lymph nodes, gastric submucosal lesions, liver, thyroid gland, breast, rectal, retroperitoneal, spleen, suprarenal gland, esophageal duodenal, papillary, presacral masses and mediastinal lesions. In pancreatic lesions, elastography recorded score 4 in 5 chronic pancreatitis cases mostly due to increased calcifications with the chronic inflammation and one case of autoimmune pancreatitis while 1 pancreatic malignancy recorded score 2. For lymph nodes, 7 malignantly diagnosed nodes recorded score 2 while 2 benign lymph nodes scored 4 on elastography, one of them was inflammatory condition and the other was diagnosed as TB. On validating the elastography as a diagnostic test it had a sensitivity of 94%, specificity of 78%, accuracy and PPV of 88% and NPV of 87%.

Being relatively depending on the operator pressure applied upon the examined lesion, we used the strain ratio (SR) as a semi-quantitative measurement to assess degree of tissue stiffness. We calculated the cut off value for SR of different examined lesions. This resulted in a cut off value of 12.8 for pancreatic masses, 3.9 for lymph nodes and 7.8 for different body masses. Then the best cut off value for strain ratio for all the examined lesions was calculated, being with the highest significant value for differentiating between malignant and benign lesions. The calculated value was 6.5 which showed sensitivity of 86%, specificity of 84%, and accuracy of 85%, PPV of 91% and NPV of 76%. This is near to a cut off value of 6.04 [9,10] used in previous studies for evaluating pancreatic lesions. In a study done by Dana Stoian and his colleagues [11], 4.88 was the cut off value for breast masses. Another study done on thyroid lesions had a cut off value of 1.94 (SD 2) for benign lesions and 7.07 (SD 5) for malignant lesions [12]. The cut off value for lymph nodes was different from a study carried out by Ales and his colleagues [13] as he documented a cut off value of 8 for lymph nodes, but it was near to a study done by Zhang and his colleagues [14] which showed a cut off value of 2.39.

We suggest that reaching such a cut off value for our study depends on having different body masses all over the body with different criteria according to the region of the mass as facing the trachea at the site of thyroid which increases the resistance or the far position of the pancreas in relation to the endoscopic ultrasound probe rendering the calculations more difficult. This hypothesis could also be applied to the liver, spleen and rectum where there is the behavior of surrounding body structures which will affect the degree of deformability of tissues

under the probe. Also, facing heterogeneous lesions as pancreatic malignancies will cause area (A) to be large to cover all the region of interest which would affect the readings and increases the strain ratio.

A previous study performed on image quality on phantom, indicated that strain elastography is better in solid lesions than soft ones [15]. This was similar to our studies where the true positive cases according to the calculated cut off value were 243 out of 277 diagnosed malignant cases.

On adding both tests and comparing them to the final diagnosis we had high sensitivity reaching 94% but the specificity decreased to 78% with accuracy and PPV of 88% and NPV of 87%. This indicates that adding elastography to strain ratio would be more sensitive than either of using each of them alone.

Our study has many points of strength, being done on a large number of patients, being a prospective study with long periods of follow up and being performed on different sites to validate the accuracy of the tests at different positions.

The major weak point is the different types of examined masses including pancreatic, lymphadenopathy and different masses all over the body. To avoid this weak point, we calculated the elastography score and SR of each group with similar cases sepataely as pancreatic masses and lymphadenopathy.

Conclusion

Adding elastography score with SR increases the accuracy of differentiating benign from malignant body masses and lymphadenopathy, which on turn would assess the need of tissue diagnosis by FNA, tru-cut or excision biopsy which should remain the gold standard for diagnosis of different body lesions.

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