

Usefulness of Endoscopic Ultrasound Elastography Combined with the Strain Ratio in the Estimation of Treatment Effect in Autoimmune Pancreatitis

Takuya Ishikawa¹, MD, PhD, Hiroki Kawashima¹, MD, PhD, Eizaburo Ohno¹, MD, PhD, Hiroyuki Tanaka¹, MD, Keiko Maeda², MD, PhD, Tsunaki Sawada², MD, PhD, Takeshi Yamamura², MD, PhD, Kazuhiro Furukawa¹, MD, PhD, Masanao Nakamura¹, MD, PhD, Ryoji Miyahara¹, MD, PhD, Masatoshi Ishigami¹, MD, PhD, Mitsuhiro Fujishiro¹, MD, PhD

1. Department of Gastroenterology, Nagoya University Graduate School of Medicine, Nagoya, Japan
2. Department of Endoscopy, Nagoya University Hospital, Nagoya, Japan

Corresponding author: Takuya Ishikawa

E-mail: ishitaku@med.nagoya-u.ac.jp

ADDRESS: 65 Tsuruma-cho, Showa-ku, Nagoya, 466-8550, Japan

TEL.: +81-52-744-2602 FAX: +81-52-744-2785

Running head: EUS Elastography for Autoimmune Pancreatitis

Disclosure: The authors declare no conflict of interest.

To the Editor:

Autoimmune pancreatitis (AIP) is a peculiar type of chronic pancreatitis typically showing a diffusely enlarged pancreas with a dramatic response to steroids.¹ However, some patients present with atypical imaging that requires differentiation from pancreatic cancer. In such cases, a 2-week steroid trial may be helpful in confirming the diagnosis². However, it is not always easy to evaluate the treatment effect in a short period. The purpose of this study was to evaluate the usefulness of endoscopic ultrasound elastography (EUS-EG) combined with strain ratio (SR) in the estimation of short-term treatment effects in patients with AIP.

Materials and Methods

This was a retrospective study performed at Nagoya University Hospital. The study was performed with the approval of the ethics committee of Nagoya University Graduate School of Medicine. We retrospectively reviewed 10 patients out of 147 patients who were diagnosed with AIP in our hospital between May 2001 and May 2019, who underwent EUS-EG before and after 2 weeks of steroid treatment and whose SR could be evaluated. A total of 8 men and 2 women with a median age of 68.5 (interquartile range [IQR], 62-74.5) were included in the study (Table 1). The treatment effect was evaluated after 2 weeks of steroid therapy with contrast-enhanced Computed tomography scanning and EUS-EG, and the SR and the size of the pancreatic parenchyma were compared before and after treatment. All the procedures were performed by either a combination of the EG3670URK/3870UTK (Pentax Co., Ltd, Tokyo, Japan) and the HI VISION Ascendus (Hitachi, Ltd, Tokyo, Japan) or a combination of the GF-UCT-260 (Olympus

Co., Ltd, Tokyo, Japan) and the Arietta 850 (Hitachi), which can provide higher-quality elastographic images than other modalities. The region of interest for the elastographic evaluation was manually selected to include the pancreatic parenchyma and the surrounding tissue with a ratio of 1:1.³ The SR was calculated based on a previous report⁴ by selecting two different areas, area A for pancreatic parenchyma and B for peripancreatic tissue. Because elastographic images tend to show rapidly changing colors, an image that was stable for at least 5 seconds was required for final analysis. The images were recorded as a movie, and three optimal still images automatically selected by the ultrasound system were used for calculation of SR. To limit the selection bias of areas A and B, their elasticity values each were estimated three times in each image in all patients, and the median value was used for the evaluation. Statistical analyses were performed using SPSS Statistics 25.0 (SPSS, Inc., Chicago, Ill). The paired t-test was used to compare SR and size of the pancreatic parenchyma before and after treatment.

Results

Most of the patients showed improvement in pancreatic swelling after 2 weeks of steroid treatment, and the mean size of the pancreatic parenchyma decreased significantly (mean 20.08 [SD, 2.46]mm to 15.9 [SD, 2.49]mm [$P = 0.001$]). However, 2 pancreases remained the same size at 2 weeks. In contrast, all 10 patients showed a decrease in SR, with statistical significance (mean 8.04 [SD, 2.29] to 3.44 [SD, 1.97] [$P < 0.0001$]) (Fig. 1), although the initial SR values varied across a wide range. All 10 patients underwent steroid maintenance therapy, and there was no case of relapse in the mean observation period of 15.6 months (IQR, 3.4-26.1)

Discussion

In this study investigating the usefulness of EUS-EG combined with SR in the estimation of the short-term treatment effect of AIP, all 10 patients showed a decrease in SR at 2 weeks, with statistical significance.

Interestingly, 2 out of 10 patients showed a decrease in SR before radiological improvement in pancreatic swelling, suggesting that the elastic change may happen earlier than the morphological change in AIP.

Strain ratio is a measure that compares the strain between the target area and other reference areas to provide

more objective, quantitative data in strain elastography.⁵ Because of its simplicity, SR has been used in

multiple studies to evaluate solid pancreatic lesions.⁵⁻⁸ Although these reports show the high diagnostic

ability of SR, the cut-off point varies between the reports, and several problems have been raised regarding

SR. For example, there is no standardization for the reference area⁹, and the distance from the reference

area to the ultrasound probe significantly impacts the SR measurements.¹⁰ Due to these problems, the values

of SR may vary according to each individual. To solve these problems, we compared the SR in the same

patient before and after the treatment so that the reference areas and the target areas would be set in similar

positions to ensure reliability. Based on our results, the best use of SR could be the comparison before vs.

after treatment in the same individual. In conclusion, EUS elastography combined with the strain ratio can

be a new early marker to estimate the short-term treatment effect on autoimmune pancreatitis.

References

1. Shimosegawa T, Chari ST, Frulloni L, et al. International consensus diagnostic criteria for

- autoimmune pancreatitis: guidelines of the International Association of Pancreatology. *Pancreas*. 2011;40:352-358.
2. Moon SH, Kim MH, Park DH, et al. Is a 2-week steroid trial after initial negative investigation for malignancy useful in differentiating autoimmune pancreatitis from pancreatic cancer? A prospective outcome study. *Gut*. 2008;57:1704-1712.
 3. Ignee A, Jenssen C, Arcidiacono PG, et al. Endoscopic ultrasound elastography of small solid pancreatic lesions: a multicenter study. *Endoscopy*. 2018;50:1071-1079.
 4. Iglesias-Garcia J, Lindkvist B, Larino-Noia J, et al. Differential diagnosis of solid pancreatic masses: contrast-enhanced harmonic (CEH-EUS), quantitative-elastography (QE-EUS), or both? *United European Gastroenterol J*. 2017;5:236-246.
 5. Itokawa F, Itoi T, Sofuni A, et al. EUS elastography combined with the strain ratio of tissue elasticity for diagnosis of solid pancreatic masses. *J Gastroenterol*. 2011;46:843-853.
 6. Dawwas MF, Taha H, Leeds JS, et al. Diagnostic accuracy of quantitative EUS elastography for discriminating malignant from benign solid pancreatic masses: a prospective, single-center study. *Gastrointest Endosc*. 2012;76:953-961.
 7. Iglesias-Garcia J, Larino-Noia J, Abdulkader I, et al. EUS elastography for the characterization of solid pancreatic masses. *Gastrointest Endosc*. 2009;70:1101-1108.
 8. Kongkam P, Lakananurak N, Navichareern P, et al. Combination of EUS-FNA and elastography (strain ratio) to exclude malignant solid pancreatic lesions: A prospective single-blinded study. *J Gastroenterol Hepatol*. 2015;30:1683-1689.
 9. Hirooka Y, Kuwahara T, Irisawa A, et al. JSUM ultrasound elastography practice guidelines: pancreas. *J Med Ultrason (2001)*. 2015;42:151-174.
 10. Havre RF, Waage JR, Gilja OH, et al. Real-Time Elastography: Strain Ratio Measurements Are Influenced by the Position of the Reference Area. *Ultraschall Med*. 2011.

Table 1. Patient Characteristics

	n = 10
Age, median (IQR)	68.5 (62-74.5)
Sex, n	
Male	8
Female	2
Parenchymal imaging, n	
Diffuse	8
Focal enlargement	2
Serum IgG4, median (IQR), mg/dl	578 (181-1055)
Diabetes mellitus, n (HbA1c > 6.5% at diagnosis)	7
OOI, n	3
Dose of steroid, mg/day	
30	9
35	1
Final diagnosis, n	
Definitive type 1	9
NOS	1

IQR: Interquartile range, OOI: Other organ involvement; NOS: Not otherwise specified

Figure legend

Figure 1. Endoscopic ultrasound elastography images of a patient with autoimmune pancreatitis before (A) and after steroid treatment for 2 weeks (B). A: Three elastic images of the pancreas prior to treatment automatically selected by the ultrasound system, showing a homogenous, predominantly blue pattern with a median SR value of 9.15. B: Elastic images after steroid treatment for 2 weeks showing a heterogeneous, predominantly green pattern with a median SR value of 3.39.

Figure 1

