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PICTORIAL ESSAY

Real-time elastography in Crohn's disease: feasibility in daily clinical practice

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Abstract Ultrasound (US) is the first-line investigation in patients with abdominal symptoms and it has a role in the diagnosis and monitoring of inflammatory bowel diseases. Strain elastography (SE) is a US method for estimating tissue elasticity. This method is still not routinely used in clinical practice, although it is suggested by the EFSUMB Guidelines for the characterization of intestinal stenosis in Crohn's disease. The purpose of this Pictorial Essay is to confirm the feasibility of elastography in Crohn's disease in clinical practice by comparing elastography images with corresponding endoscopic or radiological images. At present, diagnostic accuracy of SE is reported in the literature only in connection with detection of bowel wall fibrosis in advanced cases of Crohn's disease. However, in our opinion, SE can add useful diagnostic information to grayscale and color Doppler US by providing a more accurate characterization of the bowel wall in the various manifestations of Crohn's disease.

Keywords Gastrointestinal ultrasound · Strain elastography · Bowel strain elastography · Crohn's disease

Sommario L' ecografia è indagine di primo livello nei pazienti con sintomatologia addominale ed ha un ruolo nella diagnosi e monitoraggio delle malattie infiammatorie croniche intestinali. L' elastografia strain (metodica ecografica per la stima dell'elasticità tissutale) viene suggerita dalle Linee Guida EFSUMB per la caratterizzazione dei tratti intestinali stenotici nel morbo di Crohn, ma la metodica è ancora poco utilizzata nella pratica clinica. Lo scopo di questo Pictorial Esssay è di confermare la "feasibility" dell' elastografia nel morbo di Crohn nella pratica clinica e confrontare le immagini elastografiche con le corrispondenti endoscopiche o radiologiche. Attualmente l'accuratezza diagnostica della metodica è confermata in Letteratura soltanto per quanto concerne la documentazione della fibrosi viscerale nelle forme di Crohn evolute E' nostra opinione che la elastografia "strain" possa fornire informazioni aggiuntive all' ecografia in scala dei grigi e color doppler nella caratterizzazione della parete intestinale nelle differenti manifestazioni di questa patologia.

Introduction

Ultrasonography (US) is the first-line investigation in patients with abdominal symptoms. US diagnostic accuracy is considered equivalent to that of CT enterography and MRI enterography in the evaluation of the terminal ileum in patients with Crohn's disease [1].

Strain elastography (SE) is a US method which can add information to grayscale US by assessing tissue elasticity and recently SE has been suggested for the characterization of bowel wall elasticity. SE is based on the concept of elastic modulus: a material subjected to a uniform stress deforms along its axis proportionally to the intensity of the applied compression and depending on its elasticity.

Real-time elastography examination consists in applying a light rhythmic probe pressure perpendicular to the target tissue. A dedicated software (in our scanner: ElaXto, Esaote, Genova, Italy) evaluates the changes in the echo signal after compression of the target tissues and calculates

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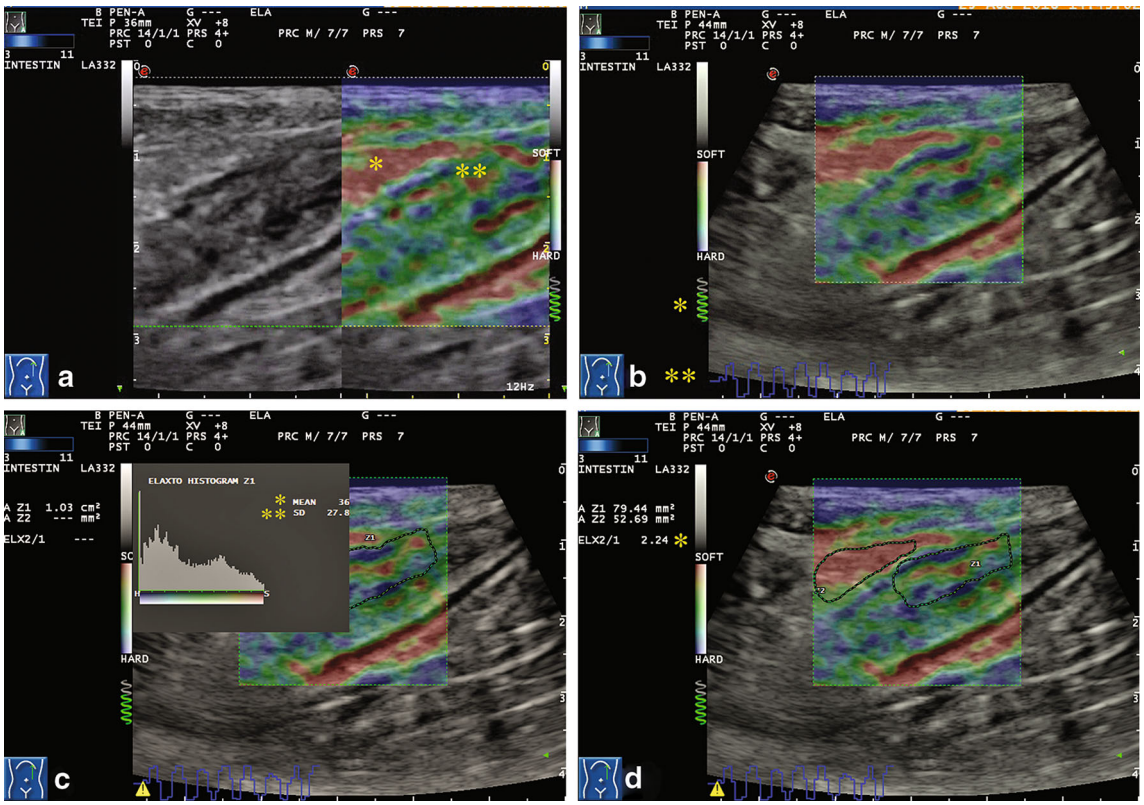

Fig. 1 Longitudinal scan of the descending colon. **a** SE visual score—dual display: the target bowel is located at the center of the image, the ROI is large and includes the abdominal wall and the adjacent mesentery (*). The elastography image shows *colored layers* of the intestinal wall** with *shades of blue* representing the mucous layer, a *red–green pattern* representing the submucosal layer and *shades of blue* representing the muscle layer. **b** SE visual score—single display: the elastography image is superimposed on the B-mode image; the *green* spring* and the motion indicator ** show that probe compression movements are correct. **c** Same bowel tract as (**b**), SE-histogram: a ROI is manually drawn on the anterior bowel wall and the measured area (Z1) is calculated. ElaXto software displays the histogram showing the various degrees of elasticity of the tissues included in the selected Z1 zone [distribution from hard (H) to soft (S) is on a 0–100 numerical scale]. The system also computes the mean value "MEAN"* and the standard deviation SD** of all data included in the selected Z1 zone. **d** Same bowel tract as (**b**), strain ratio: the value ELX2/1* is the ratio between the average strains produced on zone Z2 manually drawn on the mesentery and the average strains produced on zone Z1 manually drawn on the bowel wall

how much the tissues deform or partially move (if they are hard) according to the position of the probe. The result of this computation is shown in real-time on a color image superimposed on the B-mode image and visualized in single or dual display. The different degrees of strain are displayed in a color scale of 100 shades ranging from blue for maximum stiffness to red for maximum elasticity [2]. Strain information is shown in relation to the surrounding tissues. Targets will appear soft/hard, if they are softer/harder than the average strain value of the tissues within the region of interest (ROI).

SE of the gastrointestinal tract presents additional difficulties because the structures to be examined are thin and difficult to compress correctly. The underlying supporting structures are sometimes curved, such as the psoas major muscle, or located deep in the abdomen, such as the posterior abdominal wall.

A good B-mode image is required to acquire a reliable elastographic image. Probe frequency, dynamic range, gain and transparency of the elastography map are, therefore, monitored to obtain the best results. The target bowel should be positioned centrally in the ROI and the elastogram must be reproduced several times to be considered reliable. If the anterior and posterior bowel walls present different elastic properties, the values obtained on the anterior bowel wall should be considered correct as the slight pressure applied with the probe loses efficacy in deeper located structures.

There are different workflow tools available, all displayed on the monitor, which provide a real-time elastography acquisition feedback. Dual display allows a correct identification of the targeted bowel (Fig. 1a) and the ElaXto spring series as well as the motion indicator (Fig. 1b) provides information on the quality of the

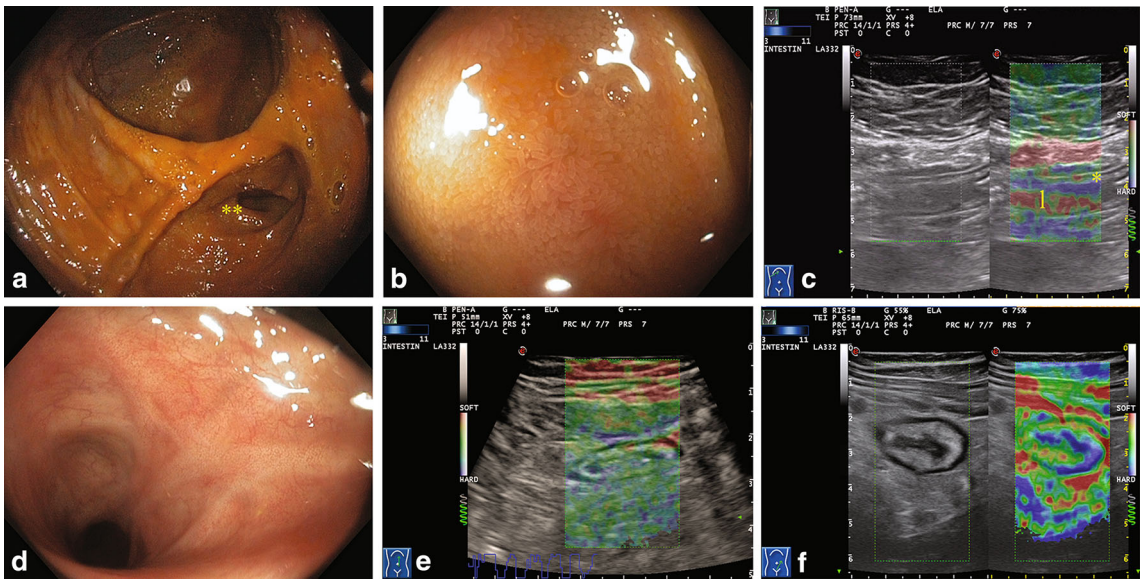

Fig. 2 SE images classified Type A (Fufezan et al.) suggesting absence or remission of disease. **a** Patient who had undergone ileocolic resection: endoscopy shows the ileocolic anastomosis**. **b** Endoscopy of the anastomotic ileum: the mucosa appears normal. **c** The same bowel tract as (**b**), SE classifies the anastomotic ileum* as Type A. **d** Patient with Crohn's disease affecting the descending colon after 2 years of biological therapy: endoscopy shows only scarring and mild deformation of the bowel lumen. **e** The same bowel tract as (**d**), SE classifies this colon tract as Type A. **f** The same bowel tract as (**e**), follow-up of the previous year, SE classified the colon tract as Type B

acquisition correlated to the probe compression movements [2].

The software provides advanced information including calculation of the distribution of strain values within a manually drawn ROI, presenting the results obtained in this region in a histogram (Fig. 1c). Moreover, the ratio between the average strain values in a ROI manually drawn on a reference tissue and the average strain values in the ROI drawn on the bowel wall can provide numerical and reproducible data (Fig. 1d) [2].

In our Institution, the affected bowels are evaluated using a LA332 linear probe (MyLab^{TM} Twice, Esaote, Genova ,Italy), but a CA541 convex probe is preferred when the bowel is located deep in the abdomen. The US operator (AG) has 15 years' experience in bowel US. The aim of this Pictorial Essay is to evaluate the feasibility of SE in Crohn's disease in daily clinical practice by comparing elastography maps with the corresponding endoscopic or radiological images.

Strain elastography in Crohn's disease

In the presence of disease, the bowel wall is usually thickened, and the SE map will show color stratification of the bowel wall in shades of blue and turquoise if the bowel wall is stiffer than normal, but mainly green with shades of yellow or red if the bowel wall is more elastic than normal.

To obtain a better reproducibility and comparability of the results, the outcome of SE can be categorized according to the classification methods already proposed in the literature [3–7].

Havre et al. [3] classified the lesions according to the distribution of colors in the bowel wall: category 1 = the bowel wall appears homogeneous in a predominant color; category 2 = inhomogeneous appearance in 2–3 colors in various patterns, but not fragmented; category 3 = inhomogeneous appearance in a "honeycomb" pattern due to fragmentation of the colors.

Baumgart et al. [4] used a second box drawn on the upper part of the cross-sectioned bowel wall to obtain a strain histogram and its mean. They used the mean of relative strain values to compare the normal bowel wall with the bowel wall affected by Crohn's disease before, during and after surgery.

Sconfienza et al. [5] divided the circular image of the bowel wall (axial scans) into eight concentric sections and converted the color map obtained on each segment of the bowel wall to a numerical scale according to the predominant color (1 = mainly red; 2 = mainly green; 3 = mainly blue). Thus, the total score ranged from 8 (8 × 1, minimal fibrosis) to 24 (8 × 3, maximal fibrosis).

Fufezan et al. [6] proposed a visual score that divided Crohn's disease in pediatric patients into three categories according to the different elastographic images. Type A: a normal bowel wall or disease remission (SE shows normal

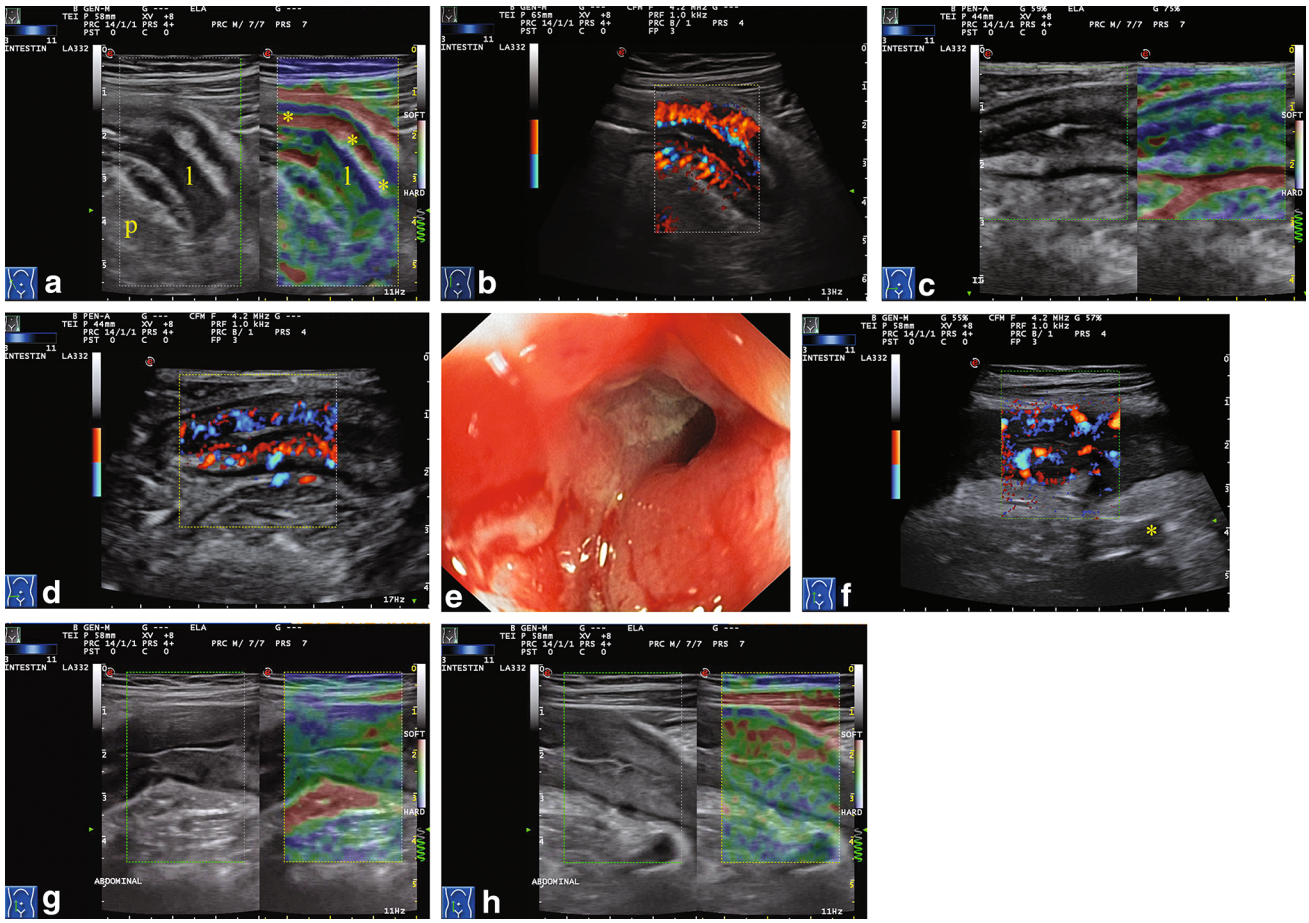

Fig. 3 Three patients with Crohn's disease and bowel wall thickening >5 mm; SE images classified Type B (Fufezan et al.) suggesting bowel inflammation. **a** SE shows the terminal ileum with preserved color echo-stratification layers: *blue* (mucosal layer), *red–green* (*submucosal layer), *blue* (muscle layer), with a prevalence of *red*. **b** The same bowel tract as (**a**), CDUS shows bowel vascular signals, Limberg score 4. **c** SE shows the terminal ileum with preserved color echo-stratification layers: *blue* (mucosal layer), *green with brown and yellow shades* (submucosal layer), *blue* (muscle layer) with a prevalence of *green*. **d** The same bowel tract as (**c**), CDUS shows bowel vascular signals, Limberg score 3. **e** Endoscopy shows the terminal ileum and substenosis of the lumen due to mucosal edema, concomitant hyperemia and linear serpiginous ulcer. **f** The same bowel tract as (**e**), CDUS shows bowel vascular signals, Limberg score 3. **g** The same bowel tract as (**e**), SE shows preserved color echo-stratification layers, *blue* (mucosal layer), *green with yellow and red shades* (submucosal layer), *blue* (muscle layer) with a prevalence of *green*. **h** The ileal tract adjacent to (**g**), SE shows preserved color echo-stratification layers, *blue* (mucosal layer), *red–green* (submucosal layer), *blue* (muscular layer) with a prevalence of *red–green colors*

bowel wall thickness and color stratification in a blue–green–blue pattern); type B: the inflammatory phase of the disease (SE shows a thickened bowel wall and color stratification with a thick green–blue submucosal layer); type C: the fibrotic phase of the disease (SE wall pattern is mainly or completely blue).

According to Fraquelli et al. [7] calculation of strain ratio between the affected bowel wall and the adjacent mesentery as reference tissue is feasible and able to provide more objective and reproducible data than the visual score.

In everyday clinical practice, SE is performed in connection with B-mode US and color Doppler US (CDUS). In our opinion, the visual score is sufficient in most cases for differentiating moderate and severe bowel wall fibrosis, and the classification recently published by Fufezan et al. is useful thanks to its simplicity.

"**Type A**" of the classification proposed by Fufezan et al. refers to normal bowel or remission of bowel wall disease. SE of a Type A bowel wall is difficult; grayscale US shows normal thickness (≤3 mm) and the SE image shows an echo-stratification pattern which is predominantly green with linear or punctiform shades of blue in the mucosal and muscularis layers (Fig. 2).

"**Type B**" of the classification proposed by Fufezan et al. refers to a bowel wall affected mainly by inflammation. We present images of Crohn's disease affecting the terminal ileum suggestive of moderate-intense inflammatory activity (Fig. 3) and mild inflammatory activity (Fig. 4).

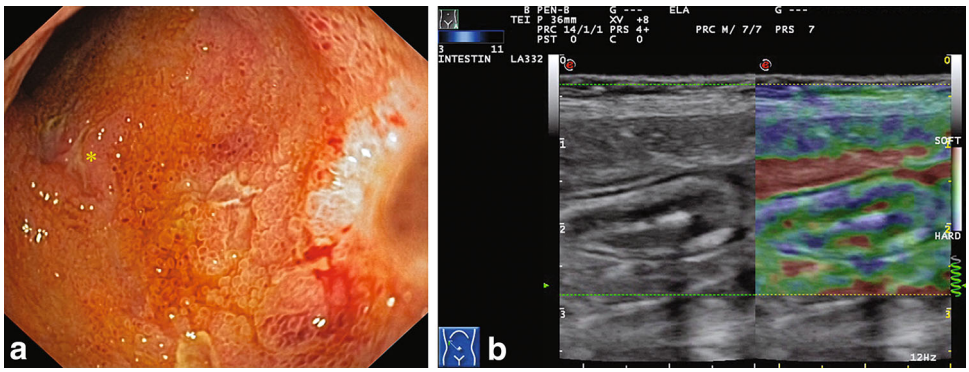

Fig. 4 Crohn's disease with bowel wall thickening <5 mm: SE image is classified Type B (Fufezan et al.). **a** Endoscopy shows the terminal ileum with mucosal edema, bleeding mucosal suffusions, one small serpiginous ulcer* and dystrophic appearance of the villi. **b** The same bowel tract as (**a**), SE shows preserved color echo-stratification layers, prevalence of *green with shades of blue* (submucosal layer)

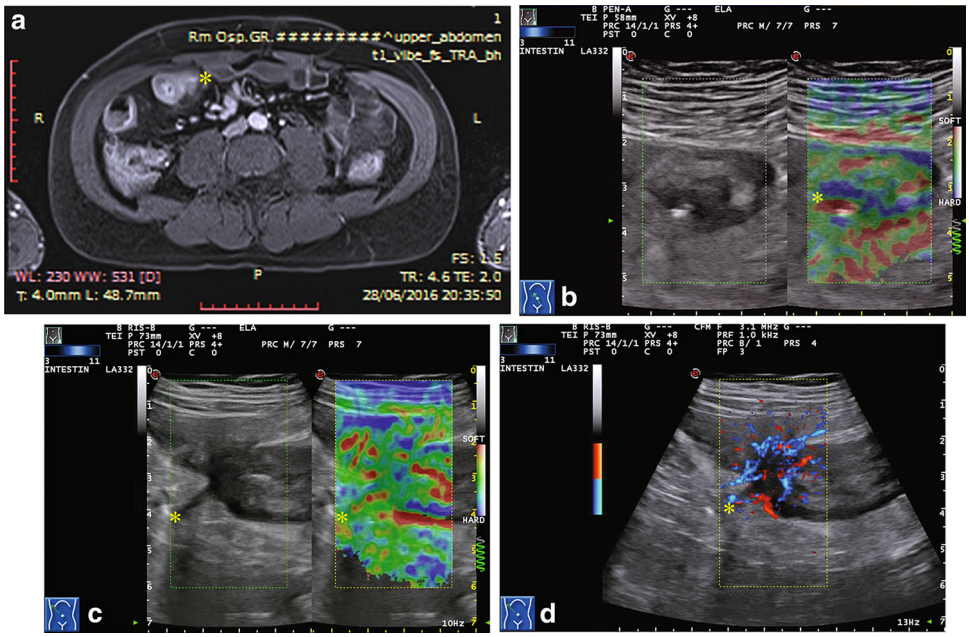

Fig. 5 Two patients with Crohn's disease in the fistolizing phase. First patient (**a**) Contrast-enhanced MR enterography transverse scan of the distal ileum shows a small area of inflammation* adjacent to the ileal wall. **b** The same bowel tract as (**a**), SE image of the ileal wall is classified Type B, the small area of inflammation* appears as a *mix of colors*. **c** Second patient: Crohn's disease affecting the distal ileum and cecum; SE image of the ileal wall classified as Type B: the fistula tract* appears as a mix of colors, mainly *red*. **d** The same bowel tract as (**c**), CDUS shows a thickened ileal wall and vascular wall signals, Limberg score 3, the path of the fistula tract* at the ileocecal valve is identified by vascular signals at CDUS

The combination of grayscale US showing bowel wall thickness >5 mm, CDUS detecting vascular signals within the bowel (Limberg score 3–4) and endoscopy revealing mucosal hyperemia with deep ulcerations suggest moderate-intense inflammation. SE usually shows bowel wall thickening with color stratified appearance and prevalence of the intermediate layer (submucosa) with color shades ranging from red to yellow to green. SE depicts mucosal and muscularis layers mainly in linear shades of blue (Fig. 3).

Grayscale US showing bowel wall thickness <5 mm and endoscopy revealing mucosal hyperemia with aftae or superficial ulcerations suggest mild inflammation. SE shows preserved color echo-stratification of the bowel wall, which is mainly green with a peripheral rim of blue shades (Fig. 4).

Fistulas occur as a result of transmural inflammation involving other structures such as the mesentery, other loops, the abdominal wall, etc. SE image of a fistula is similar to that of inflammation and is shown in a mixture of colors, mainly red, green and blue (Fig. 5).

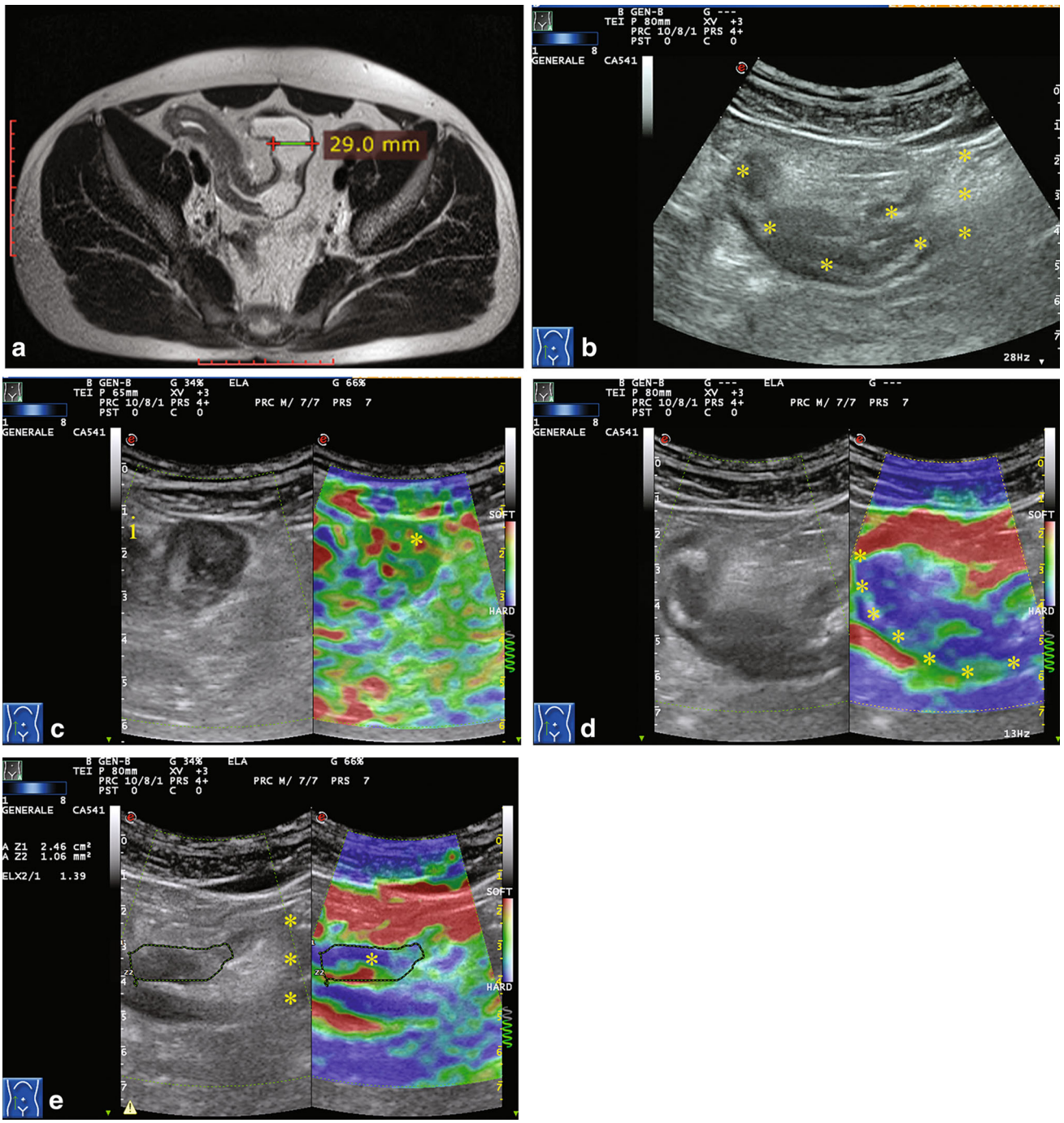

Fig. 6 SE images classified Type C (Fufezan et al.) show color pattern (mainly *blue*) suggestive of bowel wall fibrosis. **a** MR enterography (HASTE sequence, transverse scan of the pelvis) shows terminal ileum stricture with wall thickening and dilatation of upstream lumen. **b** B-mode US showing the same tract of the ileum with bowel wall thickening * and dilatation of upstream lumen***. **c** SE image of the terminal ileum* adjacent to the iliac vessel (i), classified as Type B (mainly *green*). **d** SE image showing the same tract of the ileum as (**b**), classified as Type C (mainly *blue*). **e** SE image showing the tract of the ileum adjacent to (**d**), classified as Type B (*green–red* thick submucosa and *blue* muscularis)

"**Type C**" of the classification proposed by Fufezan et al. refers to bowel wall fibrosis, a common complication occurring in Crohn's disease.

We present US, radiological and endoscopic images of Crohn's disease affecting the terminal ileum and transverse colon suggestive of fibrotic changes in the intestinal wall.

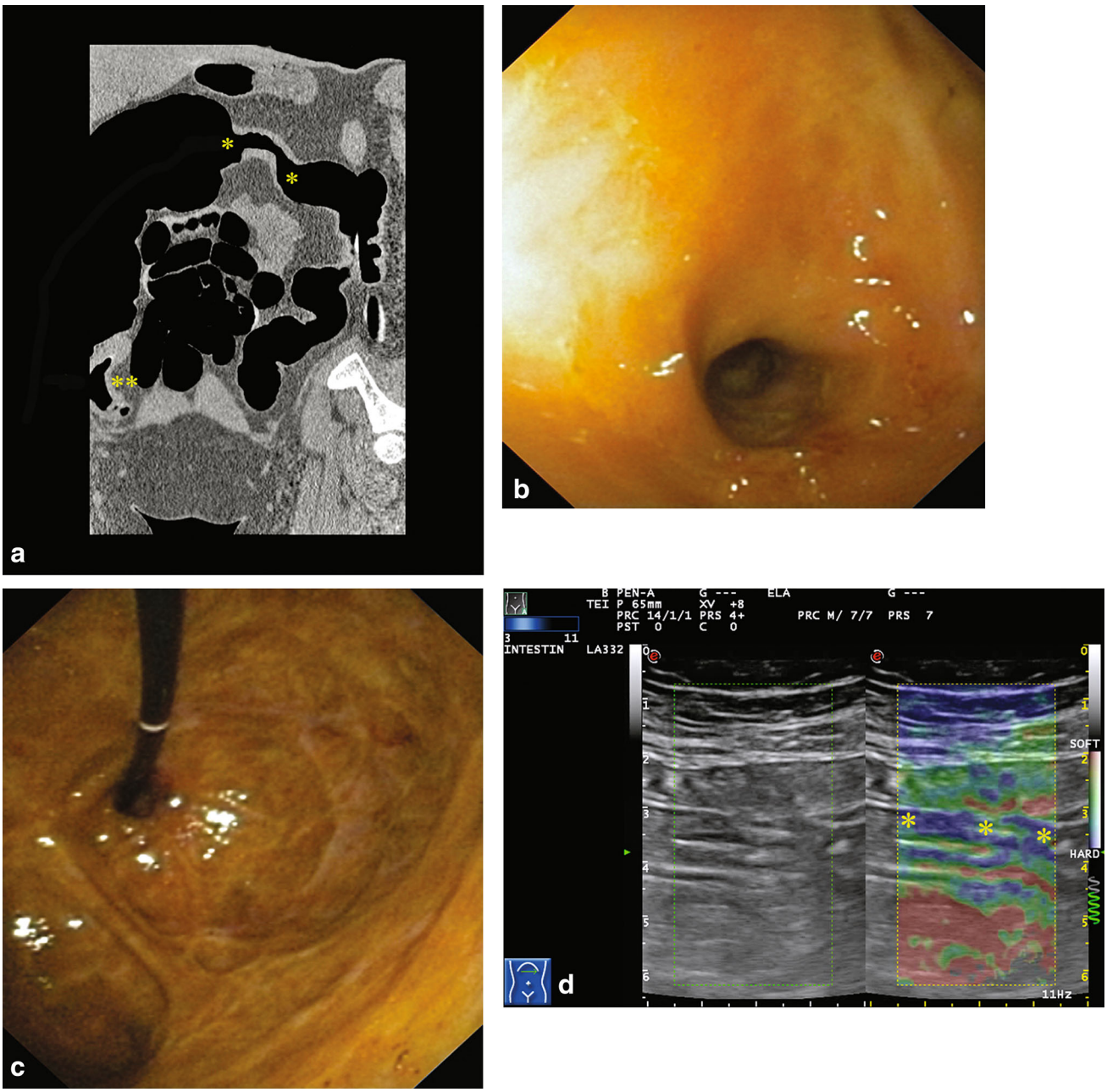

Fig. 7 Patient with ileocolic Crohn's disease, receiving biological therapy. **a** Virtual CT colonoscopy, coronal plane, shows stenosis of the transverse colon* with dilatation of the proximal bowel and thickening of the terminal ileum wall**. **b** Endoscopy showing the distal orifice of the colic stenosis. **c** Endoscopy, retroversion of the endoscope showing the proximal orifice of the colic stenosis, the mucosa presents scar formation. **d** SE showing the transverse colon stricture (*) classified Type C (wall pattern mainly *blue*)

At grayscale US, the bowel wall of the terminal ileum appears markedly thickened (Fig. 6) whereas the transverse colon wall appears only slightly thickened (Fig. 7) with dilatation of the upstream lumen. Fibrosis can affect the submucosa and muscularis to varying degrees, and SE image shows this increased stiffness in extended areas of turquoise and blue colors. If fibrosis affects the entire thickness of the bowel wall, it usually appears completely blue on the SE image.

Conclusions

US has become a useful imaging method for diagnosis and management of inflammatory bowel diseases thanks to its high diagnostic accuracy, repeatability, low cost, and the lack of side effects. Newer applications such as small intestine contrast US (SICUS) using an oral contrast agent and contrast-enhanced US (CEUS) using intravenous contrast agent have proven effective in Crohn's for

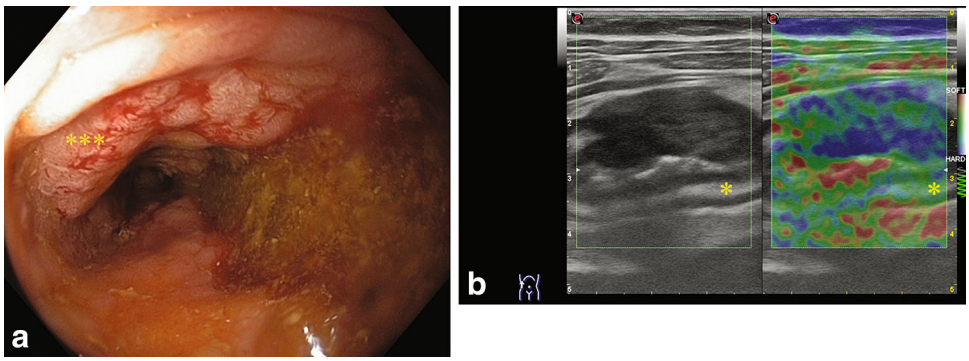

Fig. 8 Patient with a 20-year history of inflammatory bowel disease. **a** Endoscopy of the ascending colon: the mucosa presents focal thickening with hyperemia, edema and adenomatous appearance***; histological examination revealed fragments with severe dysplasia and adenocarcinoma. **b** The same bowel tract as (**a**), SE shows increased stiffness of the focally thickened portion compared to the adjacent bowel wall*

evaluating the extension of the disease (SICUS) and the inflammatory activity within the bowel walls (SICUS and CEUS) as well as the complications (SICUS and CEUS) [8].

Recently also SE has been used in some diseases of the gastrointestinal tract and in the most recent EFSUMB guidelines [9, 10] SE has been reported as a useful method for characterizing pathologically thickened bowel walls.

However, there are several reasons why SE is not routinely performed in clinical practice. SE is operator-dependent and requires additional training, as the examination technique and evaluation of the obtained images are different from those applied in grayscale US and CDUS. SE is not always adequate in the study of the gastrointestinal tract and finally the results obtained with scanners produced by competitor companies (using different algorithms to calculate the strain) are not readily compared despite the use of similar colorimetric maps.

Only a few studies of these issues are reported in the literature and the examined patient populations are small. Nevertheless, the Authors obtained statistically significant results using elastography and the chosen method of measurement to differentiate fibrotic bowel walls from normal and inflammatory bowel walls [4–7].

The aim of this Pictorial Essay is to evaluate the feasibility of SE in Crohn's disease in daily clinical practice and to compare SE images with corresponding endoscopic or radiological images.

In our experience, SE provides additional information on the degree of stiffness and/or elasticity of the affected bowel walls and it is, therefore, useful in combination with grayscale US, CDUS and CEUS for staging and monitoring of Crohn's disease.

The usefulness of SE in the evaluation of intestinal fibrosis and stenosis in Crohn's disease is already confirmed in the literature. Also in cases of stenosis defined as "inflammatory stenosis" due to intense vascular signals within the bowel walls at CDUS or enhancement at CEUS, SE can document coexistence of fibrotic phenomena and have a significant impact on the management of the disease [11].

It is hard to predict the future possibilities of SE in the management of Crohn's disease in addition to characterization of the bowel wall in patients with bowel strictures.

SE does not provide a differential diagnosis between Crohn's and other different gastrointestinal diseases [12], however, it may occasionally raise suspicion of supervening intestinal neoplasia if a focally thickened bowel wall is stiffer than the adjacent bowel wall (Fig. 8).

SE may be a promising tool in the assessment of inflammatory activity in cases remaining uncertain after grayscale US and CDUS (e.g. marked thickening of the bowel wall without vascular signals). In these patients, an elastography pattern Type B, which is suggestive of inflammatory activity, may constitute an indication for further endoscopic or contrast enhanced investigation, whereas elastography pattern Type C may confirm that bowel wall thickening is caused by a prevalence of fibrosis.

Finally, in patients receiving medical therapy and in clinical remission of symptoms, SE pattern Type A may be suggestive of full recovery, whereas documentation of increased bowel wall stiffness (Type C pattern) may suggest that the patient is developing bowel wall fibrosis.

Compliance with ethical standards

Conflict of interest Authors have no conflict of interest to declare related to this study.

Ethical approval All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki declaration of 1975, as revised in 2000.

Informed consent The patients provided written informed consent to the publication of information that could potentially lead to their identification.

Human and animal studies The study described in this article does not involve the use of animal subjects.

References

1. Panes J, Bouhnik Y, Reinisch W, Stoker J, Taylor SA et al (2013) Imaging techniques for assessment of inflammatory bowel disease: joint ECCO and ESGAR evidence-based consensus guidelines. J Crohns Colitis 7(7):556–585
2. Satragno L, Forzoni L, De Beni S, Biordi F, Dellacasa R, Faraggi M (2012) Esaote: ElaXto Sonoelastography. In: Calliada F, Canepari M, Ferraioli G, Filice C (eds) Sono-elastography main clinical application. EDIMES Srl Edizioni Medico Scientifiche, Pavia, pp 142–145
3. Havre RF, Leh S, Gilja OH et al (2014) Strain assessment in surgically resected inflammatory and neoplastic bowel lesions. Ultraschall Med 35(2):149–158
4. Baumgart DC, Muller HP, Grittner U, Metzke Fischer A et al (2015) US-based real-time elastography for the detection of fibrotic gut tissue in patients with structuring Crohn disease. Radiology 275(3):889–899
5. Sconfienza LM, Cavallaro F, Colombi V, Pastorelli L, Tontini G et al (2016) In-vivo axial-strain sonoelastography helps distinguish acutely-inflamed from fibrotic terminal ileum strictures in patients with Crohn's disease: preliminary results. Ultrasound Med Biol 242(4):855–863
6. Fufezan O, Asavoaie C, Tamas A, Farcau D, Serban D (2015) Bowel elastography a pilot study for developing an elastography scoring system to evaluate disease activity in pediatric Crohn's disease. Med Ultrason 17(4):422–430
7. Fraquelli M, Branchi F, Cribiù FM, Orlando S, Casazza G et al (2015) The role of ultrasound elasticity imaging in predicting ileal fibrosis in Crohn's disease patients. Inflamm Bowel Dis 21:2605–2612
8. Schiavone C, Romano M (2015) EDITORIAL Diagnosis and management of Crohn's disease. J Ultrasound 18:1–2
9. Cosgrove D, Piscaglia F, Bamber J, Bojunga J, Correas JM et al (2013) EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 2: clinical applications. Ultraschall Med 34(3):238–250
10. Nylund K, Maconi G, Hollerweger A, Ripolles T, Pallotta N et al (2016) EFSUMB recommendations and guidelines for gastrointestinal ultrasound. Part 1: examination techniques and normal findings. Ultraschall Med. doi:10.1055/s-0042-115853
11. Giannetti A, Biscontri M, Matergi M, Stumpo M, Minacci C (2016) Feasibility of CEUS and strain elastography in one case of ileum Crohn stricture and literature review. J Ultrasound 19:231–237
12. Giannetti A, Biscontri M, Matergi M (2014) Feasibility of real-time strain elastography in colonic diseases. J Ultrasound 17:321–330