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Endoscopic Ultrasound Elastography in Inflammatory Bowel Disease

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1. Introduction

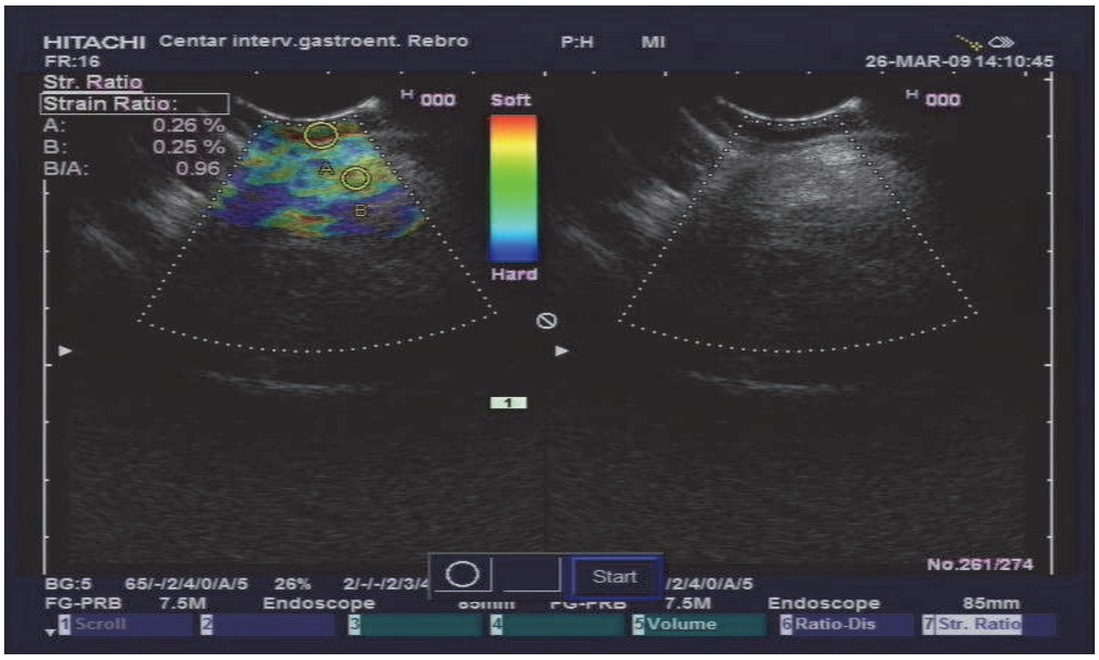
The diagnosis of inflammatory bowel disease (IBD) is based on clinical, endoscopic, radiologic and histologic criteria[1]. There are two main IBD phenotypes – Crohn's disease (CD) and ulcerative colitis (UC). In some circumstances, especially when disease extension is restricted to the colon or in cases of acute severe pancolitis, recognition of specific IBD phenotype is very difficult. Recognition of the exact IBD phenotype is essential for guiding therapeutic decisions and detection of complications that warrant treatment.

Endoscopic examination is the mainstay in the diagnosis of IBD. Endoscopic appearance (distribution and shape of lesions) helps to differentiate CD from UC in most cases. Pathohistologic analysis confirms the elements of chronic inflammation but it is frequently not diagnostic. Patients with UC may have atypical histological features such as microscopic inflammation of the ileum, patchiness of inflammation and rectal sparing at the time of diagnosis prompting physicians to make the diagnosis of CD in UC cases. Other endoscopic findings such as cobble stoning, segmental colitis, ileal stenosis and ulceration, perianal disease and pathologically confirmed multiple granulomas in the small bowel or colon strongly suggest a diagnosis of CD.

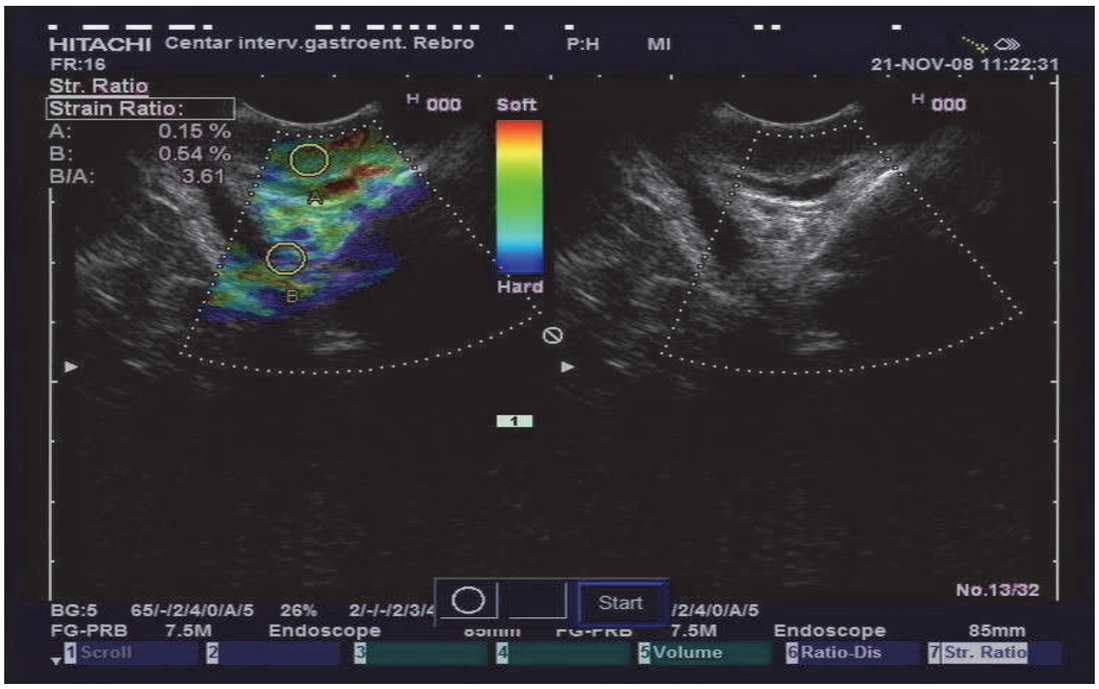
The progress in genetics, serological markers and imaging studies will lead to more reliable determination of exact IBD phenotype in the future[2]. In the meantime, it is reasonable to explore other diagnostic options for better differentiation between different IBD phenotypes. We think that endoscopic ultrasound (EUS) elastography is a promising method to achieve this goal, picture 1 and 2. It is a new endoscopic procedure which can differentiate the stiffness of normal and pathological tissue by ultrasound. This finding is based on B-mode scanning during compressions[3]. There are some data on elastography applied on the GI tract, biliary tract, kidney, muscle, breast and the heart[3-5].

Primary sclerosing cholangitis (PSC) is a chronic liver disease of unknown etiology, characterized by cholestasis, inflammation, fibrosis and stricture formation of the biliary ducts. The pathophysiology of PSC is a complex multistep process included unclear immunological mechanisms, genetic susceptibility and various defects of the biliary epithelial cells.

The disease is rare in the general population but is strongly associated with inflammatory bowel disease. The prevalence of IBD, predominantly ulcerative colitis, among PSC patients is approximately 70-90% while only 5% of patients with UC develop PSC. The percentage of



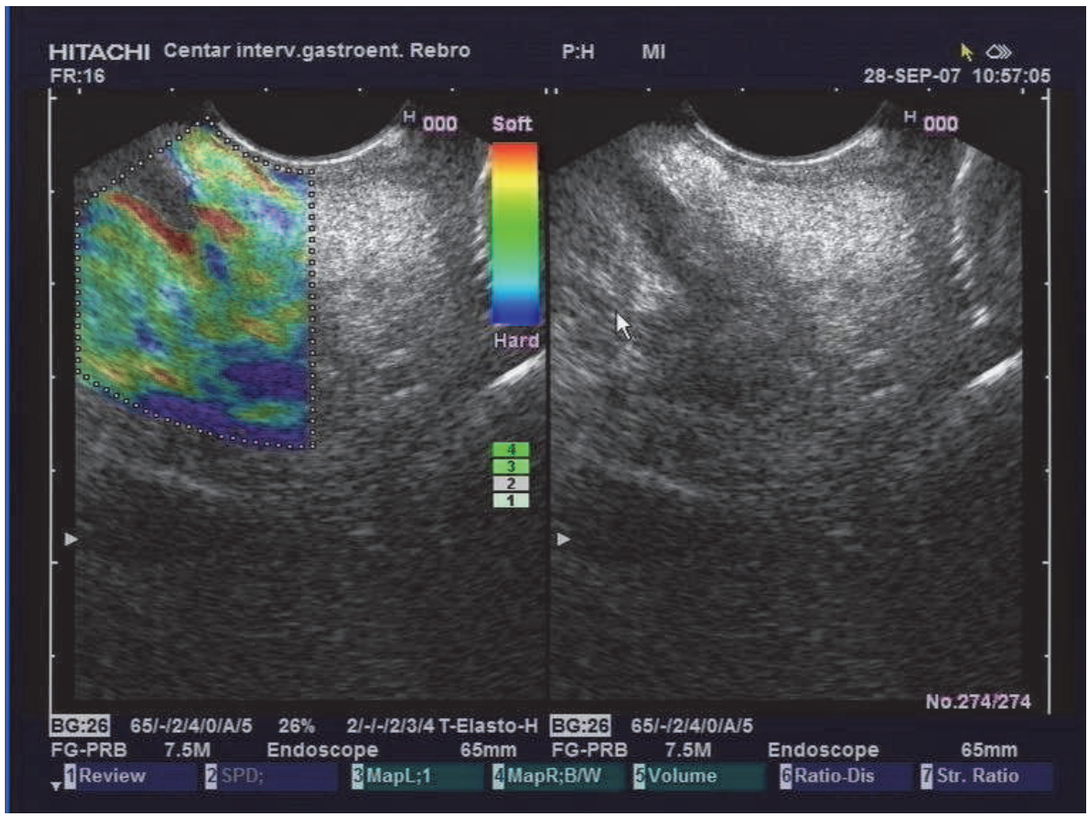
Picture 1. TRUS elastography in a UC patient



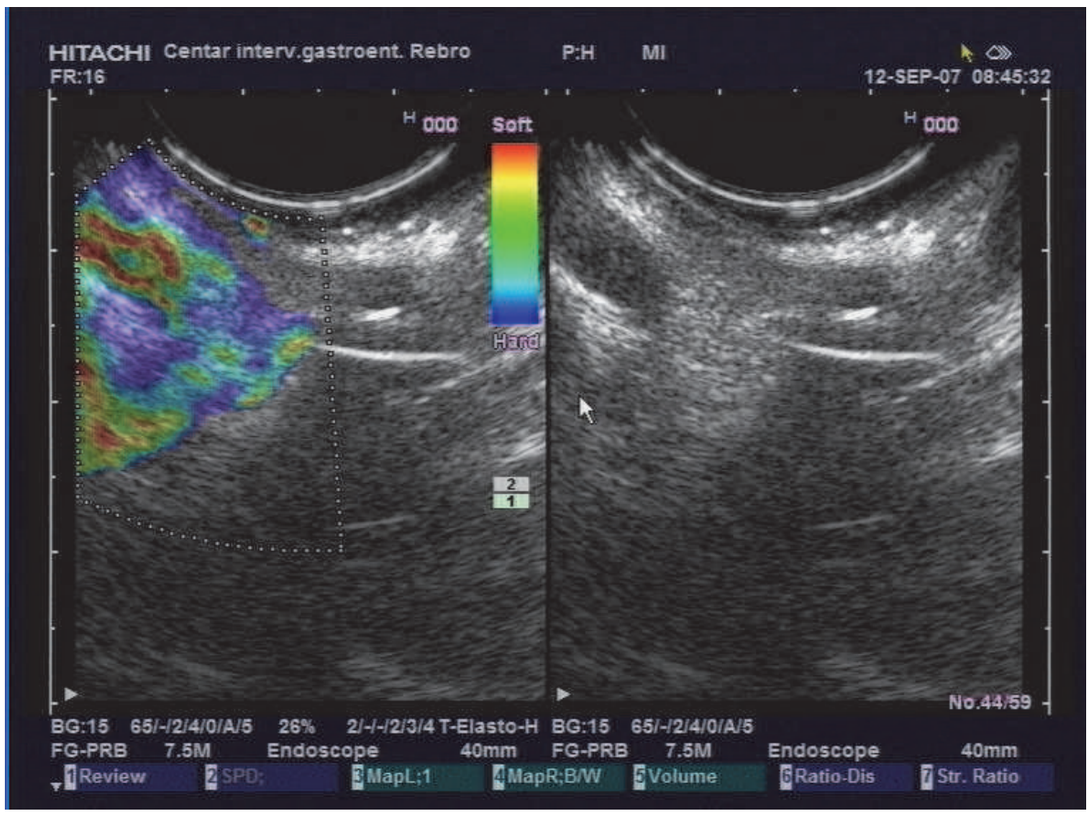
Picure 2. TRUS elastography in a CD patient

Crohn's disease patients affected by PSC is much smaller. Recently, it was recognized that PSC-IBD is a distinct IBD phenotype. Ulcerative colitis associated with PSC is usually mild, quiet, is associated with rectal sparing, more intensive right sided disease, and backwash ileitis and has a significant risk of developing pouchitis after colectomy.

In advanced cases symptoms include icterus, itch and lethargy but almost 45% of patients have no symptoms and increasing numbers of asymptomatic patients are being identified.
Primary sclerosing cholangitis is generally aggressive disorder and can progress in cirrhosis. In that setting, liver transplantation is the only therapeutic option with cure potential because median survival without liver transplantation after diagnosis is approximately 12 years.
PSC is associated with a 10%-15% lifetime risk of developing cholangiocellular carcinoma which often presents in advanced stage with a poor prognosis. Primary sclerosing cholangitis also has a risk of developing colorectal dysplasia and neoplasia in IBD. Treatment with high dose ursodeoxycholic acid has chemoprotective effects against potential neoplasia.
Magnetic resonance cholangiography (MRC) and endoscopic retrograde cholangiography (ERC) are diagnostic procedures which confirm multifocal strictures and dilatation of biliary ducts, characteristic for PSC. Both procedures, ERC and MRC are comparable for diagnosing PSC but there are conflicting data regarding the role of ERCP in patients with PSC. It seems that elective ERCP has a modest risk of ERCP-related complications in patients with PSC. However, ERCP in severe ill IBD patients increases the probability of post procedure complications. Because of its noninvasive nature, MRCP may have advantages over invasive cholangiography when diagnosis is the main goal of the procedure.
According to evident well-documented risk of malignant disease during the life course, early identification of PSC patients is very important for establishing adequate surveillance strategy.
Elastography is a method which can differentiate the stiffness of normal and pathological tissue by ultrasound which is based on B-mode scanning during compressions, picture 3 and 4.



Picture 3. Normal bile duct.



Picture 4. PSC patient.

Regarding to the fact that imaging of ultrasound tissue elasticity is a way to distinct normal from abnormal tissue we analyzed the role of EUS elastography in assessing ductus choledochus properties in patients with and without PSC. EUS elastography has a potential to define tissue characteristics but specificity has to be improved[4].

Based on the idea that imaging of ultrasound tissue elasticity is a way to differentiate tissue characteristics, we hypothesized that EUS elastography has the role in assessing the thickness of bowel wall in patients with IBD and in differentiation between types of colonic inflammation in Crohn's colitis and ulcerative colitis[6,7] based on the fact that CD is a transmural disease and UC is limited to the mucosa and submucosa of the bowel wall.

2. Discussion

There are numerous papers in the current literature on the issue of EUS elastography. The method was initially inaugurated to distinguish benign from malignant pancreatic lesions[6,9,10]. Although it cannot replace biopsy and histological confirmation of cancer, „virtual biopsy" done by EUS elastography could provide good information of the consistency of the tissue of interest[11].

We hypothesized that „virtual biopsy" technique might be implemented in differentiating colonic tissue between CD and UC[4,12]. IBD phenotyping is clinically very important because of three specific reasons. Firstly, Crohn's colitis and UC have different risk of complications (fistulas, strictures, extraintestinal manifestations) that require specific therapeutic approach.

Secondly, regarding the drugs, there is a clear difference in the efficacy of mesalazine in active Crohn's colitis and ulcerative colitis[15,16]. Delay of introduction of immunosuppressive agents in misdiagnosed patients with Crohn's colitis can be deleterious. Thirdly, accurate determination of disease phenotype is important in cases were surgical intervention becomes necessary, since continent proctocolectomy is inappropriate method in Crohn's colitis where pelvic reservoir in case of unrecognized CD gets complicated by fistulas, stenosis and pelvic sepsis[17]. To conclude, present serologic and genetic markers cannot always confirm the phenotypic diagnosis and predict the clinical course in IBD patients [18, 19, 20]. EUS elastography could be, therefore, a new diagnostic option with the potential to recognize differences in the UC tissue and Crohn's colitis tissue.

In order to clearly define the differences between the colonic wall in CD and UC, our investigation was focused on the characteristics of the rectal wall and perirectal tissue, observed by the EUS elastography with SR calculation. Perirectal tissue in UC patients is supposed to be soft, without inflammation. In CD patients, „hard tissue" reflects the transmural nature of inflammation. These qualitative and quantitative elastography data could lead to accurate differentiation of IBD phenotypes.

Our pilot study revealed a significant difference in rectal wall thickness between IBD group as a whole and controls which is in agreement with other reports from the literature[21,22]. Interestingly, we also found a significant difference in rectal wall thickness between CD patients without rectal involvement and controls. The significance of this finding in our pilot study is unclear but it could suggest a possible predictive role of TRUS elastography in CD. Bearing in mind the fact that CD can involve any part of the GI tract, it would be interesting to identify such patients early in the course of the disease and follow them prospectively to see whether rectal involvement or perianal disease will develop. In UC patients, a significant difference in rectal wall thickness but not strain ratio was found between active UC patients and controls. This finding reflects the fact that inflammatory process in UC is confined to the mucosa and submucosa leading to the thickening of the rectal wall in acute inflammation but without changes in perirectal tissue as measured by strain ratio. A significant difference was detected in rectal wall thickness and strain ratio between CD and UC patient group reflecting the difference in pathogenetic mechanisms driving these diseases with CD being characterized by transmural inflammation as opposed to UC. Finally, we detected a significant difference in both rectal wall thickness and strain ratio between CD patients with rectal involvement and UC patients with active disease.

There was unfortunately significant difference in age between control group and IBD group. The results of TRUS elastography show that control group and UC group had comparable strain ratios, while CD group had statistically higher strain ratio. Based on the available literature, there are no significant changes in the rectal wall thickness with aging[23,24].

We believe that the results of our study confirm the potential usefulness of TRUS elastography in determining the exact phenotype of IBD. Currently, about 10% of patients with inflammation restricted to the colon can not be accurately classified using standard diagnostic techniques[25,26]. More importantly, 4-6 % of patients with presumably UC undergoing proctocolectomy with ileoanal anastomosi and pelvic pouch formation turned out to have CD resulting in significant morbidity and high rate of pouch failure[27,28]. Although we found a significant difference in rectal wall thickness and significant difference in strain ratio between CD patients with rectal involvement and active UC patients, our

study has a limitation due to a small number of patients included. There is a need for a prospective study with inclusion of a greater number of patients and for the construction of receiver operating characteristics (ROC) curve to definitely assess the value of TRUS elastography in IBD.

3. Conclusion

TRUS elastography with strain ratio calculation provides valuable information regarding the stiffness of the rectal and perirectal tissue and can help to differentiate CD from UC. Our study indicates that TRUS elastography could be one of the perspective and promising diagnostic tools in IBD. A prospective study on a large cohort of patient is necessary to consolidate and confirm the results and establish the role of TRUS in distinguishing Crohn's colitis and UC. In addition, one of the important benefits of EUS elastography in the long run could be the possibility of identifying individuals at risk of developing a transmural disease, thereby facilitating appropriate action for prevention of disease complications.

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