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ROLE OF CONTRAST-ENHANCED ULTRASONOGRAPHY IN THE MANAGEMENT OF CHRONIC INFLAMMATORY BOWEL DISEASE

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The incidence of inflammatory bowel disease (IBD) has increased over the past few decades.[1] Also, the management of patients with IBD is associated with a relevant use of healthcare resources, and requires a multidisciplinary approach, with patients being cared for in monographic units.[2 3] The umbrella term IBD includes ulcerative colitis (UC) and Crohn's disease (CD). The former condition involves the colonic mucosa alone, from the rectum in a cephalad direction with a variable extent, whereas the latter is a segmental transmural condition that may involve any portion of the gastrointestinal (GI) tract. Ileocolonoscopy is the gold standard for the diagnosis and follow-up of IBD, but can only assess intraluminal findings, hence it must be supplemented with techniques capable of transmural evaluation and of exploring scarcely accessible bowel segments, namely gastrointestinal ultrasound (GIUS), computed tomography (CT), and MR enterography (MRE).[4]

Systematic reviews and meta-analyses have shown that GIUS, CT, and MRE have similar diagnostic accuracies for the initial assessment of CD, the follow-up of disease activity and progression, and the evaluation of complications (strictures, fistulas, abscesses).[5,6.]

The most recent guidelines by the European Crohn's and Colitis Organisation (ECCO) and the European Society of Gastrointestinal and Abdominal Radiology (ESGAR) recommend using GIUS or MRE for CD.[7] They do not recommend CT because of its associated ionizing radiation. GIUS has the advantage of being better tolerated, repeatable, cheaper, and readily available, and allows real-time exploration of the bowel and its physiological status in order to assess morphological and functional aspects such as peristalsis and transit, as well as its relations to other organs.[8] It is

considered a first-line technique for the diagnosis and follow-up of CD.[9]

The use of contrast-enhanced ultrasound (CEUS) for IBD complements B-mode and color Doppler to improve diagnostic power. A CEUS procedure has two phases, arterial and venous, for two minutes, where we may assess the local vascularization of the target area; its use is recommended by the EFSUMB guidelines.[9] Among its limitations, the heterogeneity of quantification curves between different devices stands out.

CEUS in CD is very useful to assess inflammatory activity, to provide a differential diagnosis between fibrotic and inflammatory stenosis, and to evaluate extraintestinal complications out of endoscopic reach.

The most widely used sonographic parameter in the diagnosis of CD is intestinal wall thickening, with intact or distorted sonographic pattern (both intermingled occasionally). Loss of wall stratification correlates with clinical and biochemical activity, prevalent histological inflammation, and higher risk for surgery.[10-11] Color Doppler allows a semi-quantitative assessment of vascularization in thickened segments; while highly specific, the technique is poorly accurate to identify slow blood flow in smaller vessels, and vascularization in deeper layers of the intestinal wall.[12]

CEUS has high diagnostic accuracy for detecting inflammatory activity in active CD when compared to CDAI, and is superior to B-mode and color Doppler.[13] CEUS analysis includes qualitative, semi-quantitative, and quantitative parameters; the former two include several contrast enhancement and perfusion patterns. Quantitative parameters are measured at selected target areas, and include multiple measurements that differ according to each piece of equipment. Peak of maximum intensity (PMI), area under the curve (AUC), and wash-in area are most commonly used as they are the most reproducible and reliable parameters.[14]

CEUS provides relevant information postoperatively on CD response to medical therapy and recurrence.[15] In a study using CEUS and color Doppler in 180 patients with CD, those where Doppler found grade 2 or 3 loop hyperemia according to Limberg's classification, as modified, showed good correlation with endoscopic activity, with a positive predictive value of 96 %; therefore, CEUS could be held back

in this setting, but would however take precedence in cases with grade 0 or 1 hyperemia.[16]

GIUS is highly effective in the detection of strictures in CD; it provides a clear view of the dilated pre-stenotic segment and impaired peristalsis, and may also differentiate hypervascular (inflammatory) from hypovascular (fibrotic) stenoses, albeit both types usually coexist, with one of them predominating. A quantitative analysis of increased contrast uptake percentage greater than > 46 % in inflammatory strictures has shown correlation with inflammatory findings during endoscopy (St: 96 %, Sp: 73 %), whereas the likelihood of fibrosis is very high with lower percentages.[17] Other authors have reported differences in PMI, AUC, wash-in area, and slope of wash-in.[18] Shear-wave elastography (SWE) has also demonstrated good correlation with fibrosis extent.[19] When GIUS, CEUS, and SWE are combined sensitivity and specificity improve in the differential diagnosis of strictures.[20] The main component of fibrotic stenosis has been shown to be muscle layer hypertrophy, which bears a moderate relation to SWE, and an inverse relation to PMI with CEUS.[21]

Regarding extraintestinal complications, it is in the characterization of inflammatory masses where CEUS is more relevant, as it may clearly differentiate a phlegmon from an abscess, with the clinical and therapeutic implications this entails. CEUS clearly tells a phlegmon with increased intralesional uptake from an abscess with absence of increased intralesional uptake and presence of peripheral enhancement.[22]

Few studies have dealt with the role of CEUS in the management of UC. With B-mode ultrasound a thickening of the intestinal wall > 4 mm may be seen at the expense of the mucosa and submucosa, the latter more hyperechogenic, without compromise of the muscularis propria or surrounding fat tissue. With Doppler, increased vascularization is associated with both clinical and endoscopic activity. CEUS is superior to B-mode and Doppler for identifying disease activity, the association between CEUS and clinical, endoscopic, and histological activity being fairly good.[23,24]

However, ultrasound has limitations in UC. On occasion, all intestinal segments cannot be clearly visualized because of superposition of other structures, and the ability to visualize the rectum is very limited, with a sensitivity of 15 %; therefore,

severe distal disease may be underdiagnosed by CEUS.[13]

In this issue of the *Revista Española de Enfermedades Digestivas,* Martin et al. review the scientific evidence available on the usefulness of ultrasound contrast enhancement for IBD, clearly defining its utility and usage recommendations for diagnosis, follow-up monitoring, complications assessment, and postsurgical recurrence identification — all in all, an excellent update.[25]

To conclude, CEUS allows the assessment of transmural disease and extraintestinal complications; furthermore, quantitative analysis allows to assess inflammatory activity and treatment response during follow-up, which results in reduced numbers of endoscopic procedures.

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