Thieme

EFSUMB Recommendations and Clinical Guidelines for Intestinal Ultrasound (GIUS) in Inflammatory Bowel Diseases

EFSUMB-Empfehlungen und klinische Leitlinien für den gastrointestinalen Ultraschall (GIUS) chronisch entzündlichen Darmerkrankungen (CED)

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Key words

Gastrointestinal tract, inflammatory bowel diseases, guidelines, ultrasound, Crohn's disease, ulcerative colitis, IBD, ultrasonography

received 03.07.2017
accepted 05.12.2017

Bibliography

DOI https://doi.org/10.1055/s-0043-125329
Published online: March 22, 2018
Ultraschall in Med 2018; 39: 304–317
© Georg Thieme Verlag KG, Stuttgart · New York
ISSN 0172-4614

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ABSTRACT

The accuracy and usefulness of gastrointestinal ultrasound (GIUS) for detecting activity and complications of inflammatory bowel diseases (IBD), has been reported in studies, promoting this technique as an important tool for the management of IBD patients. Whilst well recognised by international guidelines, standardization and general agreement in the definition of the luminal and extra-intestinal features, still need to be well defined.

A task force group of 17 experts in GIUS faced this issue, by developing recommendations and clinical guidelines for the use of GIUS in IBD, under the auspices of EFSUMB. This article presents the consensus on the current data on sonographic features of IBD and summarises the accuracy of different sonographic modalities for the management of IBD patients.

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ZUSAMMENFASSUNG

Über die Genauigkeit und den Nutzen des gastrointestinalen Ultraschalls (GIUS) zum Nachweis von Aktivität und Komplikationen bei entzündlichen Darmerkrankungen (IBD „inflammatory bowel disease“) wurde in Studien berichtet, die diese Technik als wichtige Methode beim Management von IBD-Patienten propagieren. Die Standardisierung und der allgemeine Konsens bei der Definition der luminalen und extra-intestinalen Merkmale ist zwar von internationalen Leitlinien anerkannt, muss aber noch genau definiert werden. Eine Arbeitsgruppe von 17 GIUS-Experten hat sich diesem Problem angenommen und entwickelte unter der Schirmherrschaft des EFSUMB Empfehlungen und klinische Leitlinien für den Einsatz von GIUS bei IBD. Dieser Artikel präsentiert den Konsens über die sonografischen Merkmale bei IBD aufgrund der aktuellen Datenlage und fasst die Genauigkeit verschiedener sonografischer Verfahren für das Management von IBD-Patienten zusammen.

Introduction

Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory bowel diseases (IBD) with increasing incidence and prevalence worldwide [1]. The onset of IBD may occur in different decades of life with CD being more frequent in the second and third decade. Many patients are still faced with a diagnostic delay [2, 3].

Diagnostic imaging in the management of IBD

IBD patients need clinical, biochemical, endoscopic, and cross-sectional assessment to confirm the diagnosis and flares of the disease, to detect complications and to guide treatment. To date, endoscopy remains the main diagnostic procedure since it allows biopsy and histological evaluation [4]. However, it has limitations with respect to the assessment of the complications and proximal ileal extension of CD [5]. Furthermore, European guidelines on diagnostics in IBD have recommended complementary imaging methods, such as gastrointestinal ultrasound (GIUS), computed tomography enterography (CTE) and magnetic resonance enterography (MRE) for the diagnosis and determination of the location, extent and complications of CD [6].

Gastrointestinal ultrasound and other imaging tools in IBD

Systematic reviews and meta-analyses have shown that GIUS, CTE and MRE have comparable diagnostic accuracy for the initial assessment of CD, the monitoring of disease activity and progression, and for assessing its main complications (stenoses, fistulae and abscesses) [7 – 10] The latest consensus guidelines by the European Crohn's and Colitis Organization (ECCO) and European Society of Gastrointestinal Radiology (ESGAR) for imaging in IBD have recommended GIUS, CTE, or MRE to detect small bowel CD at its first presentation, to assess disease activity of the terminal ileum, to diagnose stenoses of the small bowel and to assess penetrating complications [11]. Among these techniques, GIUS has the advantage of being well-tolerated, radiation-free, repeatable, generally available and less expensive [12].

Advantages and limitations of GIUS

The increasing worldwide interest in GIUS for IBD has been recently pointed out [12 – 14], but issues need to be faced before widespread use, such as standardization and general agreement regarding the definition of the intestinal and extra-intestinal features, and the criteria for the detection of IBD, which are still not well defined. Indeed the sensitivity and specificity of the technique may vary according to the criteria and cut-offs used [7, 8, 15 – 19].

For this reason our international team of GIUS experts, under the umbrella of the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB), cooperated in order to establish GIUS recommendations for assessing IBD.

Methodological structure and classification of the consensus levels

The creation of the Task Force Group (TGF) of GIUS experts, the development of guidelines according to a modified Delphi method and all steps that have led to the statements regarding the definition criteria and landmarks of the US features of IBD, with their Level of Evidence (LoE) and Grade of Recommendation (GoR) [20] have been reported in detail in the online version of this issue. All statements in this issue include an agreement/disagreement level that has been scored on a five-point Likert scale as follows: A+: agree; A-: rather agree; I: indecisive; D-: rather disagree; D+: disagree.

RECOMMENDATION

1. GIUS is recommended to be used to detect IBD at its first presentation, and to assess CD location, activity and possible complications [LoE 1a, GoR A]. Consensus levels of agreement: A+ 17/17;

Features of Crohn's disease

Crohn's disease, especially when located in the small bowel, can be difficult to detect and challenging to follow-up, since it presents with both intestinal and extra-intestinal features. Transabdominal GIUS can assess luminal, parietal and extra-parietal features of CD and allows the detection and assessment of its severity.

Luminal and parietal features

Thickening

Bowel wall thickening (BWT) is by far the most important and most used parameter when diagnosing CD, and it is the most consistently used parameter in systematic reviews and meta-analyses

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to detect the disease [7, 8]. Indeed, BWT is also a reproducible parameter between investigators [21]. We recommend measuring wall thickness in the anterior wall of the bowel (or where it is better visible) in the longitudinal direction, avoiding haustrations and mucosal folds. The cursor/calipers should be placed at the end of the interface echo between the serosa and the proper muscle to the start of the interface echo between the lumen and the mucosa [22, 23].

The cut-off for the detection of CD varies among studies. However, the latest meta-analysis, which included 15 prospective studies, showed that a cut-off value of 3 mm had a sensitivity and specificity of 89 % and 96 %, respectively, while other cut-off values (4 mm or more) yielded a sensitivity of 87 % and a specificity of 98 % [16]. Moreover, this study also showed that increased BWT is the best parameter to detect CD located in the small bowel.

The thickening of each single layer of the bowel wall and its clinical significance in CD have been poorly investigated so far. It seems that the proper muscle layer and submucosal layer are thicker in patients with poor response to medical treatment and higher risk of surgery [24, 25] and that the increased thickening of the submucosa is associated with active CD [26]. Overall the degree of BWT is correlated with clinical and biochemical activity of CD, but the correlation is weak [27 – 30]. The increased BWT is also the most common parameter to detect CD recurrence after surgery and its degree seems to be correlated with the severity of endoscopic recurrence (see below).

Furthermore, improvement or even normalization of BWT after immunosuppressive treatment takes a long time and occurs only in a small percentage of patients [27, 31 – 33]. Conversely, the lack of improvement or the increase of BWT after treatment is correlated with high risk of surgery [33, 34].

RECOMMENDATIONS

2. Bowel wall thickening measured by GIUS can be used to accurately evaluate Crohn's disease, in particular when located in the small bowel [LoE 1a, GoR A].
   Consensus levels of agreement: A+ 14/17; A- 2/17; I 1/17
3. Bowel wall thickening > 3 mm as measured with GIUS should be used as a cut-off for the detection of Crohn's disease when a high sensitivity is preferred while bowel wall thickening > 4 mm should be used when a high specificity is preferred [LoE 1a, GoR A].
   Consensus levels of agreement: A+ 15/17; A- 1/17; D- 1/17
4. Clinical disease activity in Crohn's disease is correlated with bowel wall thickness and can be estimated using GIUS [LoE 2b, GoR A].
   Consensus levels of agreement: A+ 14/17; A- 1/17; D- 2/17

Echo pattern

The bowel wall echo pattern may have variable features in CD. The wall layers may be intact and all clearly visible with preserved stratification but may also be focally or extensively disrupted (disrupted or hypoechoic echo pattern). The diseased bowel may also show tracts with preserved stratification alternating with a disrupted echo pattern.

Changes in the predominance of the layers or loss of stratification may be related to different disease aspects [26, 35, 36]. The loss of mural stratification (the disrupted or hypoechoic echo pattern) correlates with clinical and biochemical CD activity [27, 37, 38] with prevalent histological inflammation [39] and with increased risk of surgery [40 – 42]. In vitro studies revealed that the focal disappearance sign or focal destruction of wall stratification is caused by deep longitudinal ulcerations [43 – 45].

RECOMMENDATIONS

5. GIUS can demonstrate preserved or disrupted stratification of a thickened bowel wall in Crohn's disease [LoE 4, GoR C]
   Consensus levels of agreement: A+ 16/17; A- 1/17
6. The focal or extensive disruption of bowel wall layers can be detected by GIUS and suggests severe disease, possibly with ulcerations [LoE 4, GoR C]
   Consensus levels of agreement: A+ 15/16; A- 1/16
7. Increased bowel wall thickening and loss of stratification as detected by GIUS suggest a higher risk of surgery in patients with Crohn´s disease [LoE 4, GoR C]
   Consensus levels of agreement: A+ 15/17; A- 1/17; D- 1/17

Vascularity

Splanchnic vascularity in CD

Crohn's disease affects the in- and outflow of splanchnic vessels that can be assessed using pulse wave Doppler. Clinical disease activity, namely disease activity established by clinical indices such as Crohn's Disease Activity Index (CDAI) or Harvey Bradshow Index (HBI), is associated with increased flow in the mesenteric and portal vein or mesenteric arteries, either shown as increased maximum velocity, time-averaged mean velocity, flow volume or reduced resistive index in fasting patients in some studies [46 – 52], but with more controversial results in other studies [52 – 54]. Studies have also compared Doppler US of mesenteric blood flow with endoscopic activity of CD or a combination of clinical, endoscopic and radiological findings with conflicting results [55 – 58].

The rather disappointing results indicated by measuring flow parameters in splanchnic vessels are probably related to the extensive physiological variability in the flow, also well-known in the healthy population [59, 60]. Furthermore the intra-subject, inter-observer and inter-equipment variability of color Doppler imaging (CDI) measurements are well documented [61 – 63].

RECOMMENDATION

8. Doppler US of the large mesenteric vessels is not routinely recommended for estimation of disease activity in IBD [LoE 4, GoR B]
   Consensus levels of agreement: A+ 17/17

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Color Doppler assessment of bowel wall in CD

A more focused approach on CD is the measurement of the vascularity in the affected bowel wall. Bowel wall vascularity can be determined at the level of the most thickened segments, by color or power Doppler US, using special presets optimized for slow flow detection [23]. Color Doppler flow is usually semi-quantitative and graded subjectively. There are scoring systems assessing the degree of vascularity based on thickening of the bowel wall coupled with the number, size and extent of the power Doppler signals [64, 65].

This subjective assessment of vascularity seems to reflect vessel density and inflammatory activity in the histologically examined bowel wall [66 – 69]. Furthermore, bowel wall vascularity seems to be correlated with endoscopic activity [67, 69 – 71] and clinical activity (e. g., Harvey-Bradshaw index score of ≥ 4 or Crohn's disease activity index ≥ 150) [27, 33, 58, 68, 71 – 75] and to a lesser degree with biochemical activity (e. g., C-reactive protein or fecal calprotectin) of CD [58]. Moreover, persistence of increased vascularity despite clinical remission after treatment may suggest an increased risk of relapse [74].

RECOMMENDATION

9. Semi-quantitative assessment of bowel wall vascularity using color Doppler techniques is useful to evaluate Crohn's disease activity [LoE 2b, GoR B]
   Consensus levels of agreement: A+ 16/17; A- 1/17

Contrast-enhanced US assessment of bowel wall in CD

Despite the capabilities of US color Doppler to suggest CD activity, its accuracy in detecting slow-moving blood flow in small vessels and vascularity in deep-lying bowel wall segments is low. Contrast-enhanced ultrasound (CEUS) overcomes these limitations, improving the detection of hypervascularity and perfusion, also in the deep-seated bowel wall and in the capillaries.

Assessing contrast-enhanced blood flow in the bowel wall is more complex [23]. Studies show considerable heterogeneity with regard to CEUS techniques and contrast parameters to assess bowel wall vascularity in CD [76 – 78]. The main parameters could be simply subdivided into qualitative, semi-quantitative and quantitative. The main qualitative and semi-quantitative parameters include different patterns of contrast enhancement, such as variation of layer enhancement of the bowel wall [79] and patterns of perfusion, such as submucosal enhancement and inward and outward transparietal enhancement [71]. Among the several quantitative parameters investigated, the relative peak enhancement and the area under the curve seem to be most reproducible, reliable and widely used to discriminate disease activity and to assess the histological features of the bowel wall [25, 78, 80].

Several studies and meta-analyses have shown that CEUS has high accuracy in the detection of active CD using endoscopy or clinical index as the reference standard [18, 19]. CEUS also seems to provide relevant prognostic information regarding treatment efficacy in patients with CD. In fact, improvement of several perfusion parameters, such as peak contrast enhancement, rate of wash-in and wash-out and, in particular, the area under the time intensity curve of the intestinal wall, 4 – 6 weeks after starting anti-inflammatory treatment (anti-TNF-alpha), correlated with a favorable response [25, 80].

Furthermore, CEUS showed excellent accuracy for the diagnosis of postoperative CD recurrence. In particular, the peak contrast enhancement > 46 % over baseline showed a 10 % increase in accuracy compared with conventional parameters such as BWT > 3 mm and the assessment of color Doppler flow [81]. Likewise, the pattern of enhancement showed a sensitivity and specificity of 94 % for identifying endoscopic recurrence compared with a modified endoscopic Rutgeerts score [71].

Several studies assessed the accuracy of CEUS for evaluating various aspects of disease activity. The endoscopic activity has been assessed by CEUS using parameters derived by the time enhancement intensity curves, such as maximum peak intensity or relative peak enhancement, showing a sensitivity of 68 – 100 % and a specificity of 73 – 96 % for discriminating endoscopically active from inactive disease [70, 82 – 85]. In contrast, the correlation between CEUS and clinical and biochemical activity of CD is more controversial [71, 79, 85 – 88].

RECOMMENDATIONS

10. CEUS of the bowel may be used to estimate endoscopic activity in Crohn's disease [LoE 1b, GoR A]
    Consensus levels of agreement: A+ 11/16; A- 4/16; D+ 1/16
11. CEUS methods and parameters for assessing Crohn's disease are heterogeneous and should be kept stable over time when monitoring disease activity [LoE 2b, GoR A]
    Consensus levels of agreement: A+ 16/16

Extraintestinal features

Lymph nodes

Mesenteric loco-regional lymph nodes are a common finding in healthy subjects, particularly in children [89], and in CD patients. Enlarged inflammatory mesenteric lymph nodes related to CD are usually described at US as oval or elongated with lesser diameter > 5 mm and seem to be correlated with young age, early disease, or disease with shorter duration, and with the presence of fistulae and abscesses [90 – 92]. However, enlarged mesenteric lymph nodes do not seem to be strongly correlated with clinical disease activity and also appear in other intestinal disorders [27, 90].

RECOMMENDATION

12. Regional mesenteric lymphadenopathy is a common but non-specific sonographic finding in early Crohn's disease and can be detected by GIUS [LoE 3b, GoR C]
    Consensus levels of agreement: A+ 15/17; A- 1/17; D+ 1/17

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Mesenteric fat hypertrophy

Mesenteric fat hypertrophy or creeping fat is a common feature of active CD. Although it seems to be associated with transmural inflammation, fibrosis, muscular hypertrophy and stricture, its role in the onset and development of CD is not fully understood [93]. Creeping fat appears on US as hyperechoic tissue or "mass effect" encircling the diseased bowel. It is found by US in approximately 40 – 50 % of CD patients with a reported sensitivity and specificity > 83 % compared to multi-detector CT scan [94 – 96]. However, this finding is associated with clinical and biochemical disease activity, and it may disappear or improve in patients who have responded to medical treatment [27, 96].

RECOMMENDATION

13. Mesenteric hypertrophy can be detected by GIUS as hyperechoic tissue or "mass effect wrapping" around the diseased bowel and reflects clinical and biochemical disease activity [LoE 3b, GoR C]
Consensus levels of agreement: A+ 15/17; A- 1/17; I 1/17

Abdominal free fluid

A small amount of free fluid, close to the affected bowel segments, is a common, easily detectable and reproducible US finding in CD patients, but its prevalence and significance have not been fully investigated [21]. However, it seems to be a nonspecific finding, as it can been found in most patients irrespective of their underlying disease [97].

RECOMMENDATION

14. Free fluid in the abdomen can be detected using GIUS and is an nonspecific finding with no clear significance in Crohn's disease [LoE 4, GoR C]
Consensus levels of agreement: A+ 17/17

Appendiceal involvement

As CD at its onset may clinically mimic acute appendicitis, the sonographic recognition of these entities is important to avoid unnecessary laparotomies. Primary involvement of the appendix in CD is rare, sonographically indistinguishable from simple acute appendicitis. It is characterized by markedly thickened and hyperemic walls, frequently associated with a thickened terminal ileum and cecum [98 – 100].

RECOMMENDATION

15. Appendiceal involvement in Crohn's disease may be observed by GIUS and is commonly seen in combination with involvement of the terminal ileum and cecum [LoE 4, GoR C]
Consensus levels of agreement: A+ 17/17

Complications in Crohn's disease

The main abdominal complications of CD are stenoses, fistulae and abscesses. These are the main indications for surgical intervention. Surgery is a frequent treatment in the natural history of CD patients [101, 102].

Stenoses

Stenoses represent the more frequent abdominal complications and the main cause of surgical intervention (70 – 90 %) and their prevalence increases over the course of the disease [103, 104]. Several US diagnostic criteria for stenosis have been described [105]. However, the main ones are: thickened and stiff bowel wall, narrowing of the lumen (diameter less than 1 cm), proximal dilatation (> 25 – 30 mm) and hyperperistalsis of the prestenotic gut [106, 107].

The higher diagnostic accuracy of US is obtained when surgery is considered the reference standard. In a systematic review of literature, US has demonstrated a sensitivity for the diagnosis of stenosis from 74 % to 100 %, with a specificity in the range of 89 % to 93 % [8, 10, 12, 106 – 110]. Irrespective of the gold standard used, X-ray or intraoperative findings, the ingestion of an oral contrast agent such as polyethylene glycol (PEG) solution (500 – 800 ml) drunk approximately 30 minutes before the US examination [also called Small Intestine Contrast US (SICUS)] has been shown to improve the sensitivity of US for identifying patients with at least 1 stenosis (74 % vs. 89 – 98 %) and those with 2 or more strictures (55 % vs. 75 – 77 %) with an overall good specificity (> 93 %) [109, 111]. Moreover, there is a good correlation between the extent of small bowel strictures measured by means of US and X-ray, and between the extent of the disease measured at surgery [109, 112].

Stenoses in CD are often the result of a combination of fibrosis and inflammation, although they are usually classified as predominantly inflammatory or fibrotic. Patients with strictures with prominent inflammation can potentially be managed with medical treatment, whereas patients with narrowed bowel segments and with prevalent fibrosis, in particular if associated with obstructive symptoms, frequently require endoscopic dilatation or surgery [113]. Despite the fact that this issue is much more complicated and likely also involves smooth muscle hyperplasia/hypertrophy that may be correlated with chronic inflammation [114], the US pattern of the bowel wall can help to differentiate between inflammatory and fibrotic stenosis. The hypoechoic pattern is more typical of inflammatory stenosis, while the stratified or nonhomogeneous echo pattern indicates fibrosis [24, 39]. Several studies have shown that the degree of vascularization and hyperemia on color Doppler and CEUS is correlated with the histologically proven degree of inflammation [24, 105, 115]. In particular, CEUS is useful for distinguishing inflammatory from fibrostenotic lesions in CD. Most studies showed that the contrast enhancement of the bowel wall of inflammatory strictures (using surgical pathological specimens as the reference standard) is significantly greater compared to that of fibrotic strictures [24, 82, 116 – 119].

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Recent studies reported a significant correlation between the measurement of transabdominal bowel wall stiffness assessed by sonoelastography and the degree of bowel fibrosis at histology [118, 120 – 123].

RECOMMENDATIONS

16. Stenoses can be visualized by GIUS as segments of bowel wall thickening with luminal narrowing and pre-stenotic dilatation [EL 2a, GoR A].
    Consensus levels of agreement: A+ 16/17; I 1/17
17. Oral contrast agents may be applied to increase the accuracy of GIUS to diagnose patients with Crohn's stenoses, particularly those with multiple stenoses [EL 2a, GoR A].
    Consensus levels of agreement: A+ 16/17; A- 1/17
18. a. Loss of stratification, hyperemia on color Doppler US or CEUS of the bowel wall, at the level of the stricture, suggest its inflammatory nature.
    b. Stratification or hypovascularization of the bowel wall, at the level of the stricture, suggests a higher degree of fibrosis [EL 2a, GoR A].
    Consensus levels of agreement: A+ 14/16; A- 1/16; I 1/16
19. GIUS with elastography may be applied to evaluate the stiffness of a Crohn´s stenosis [EL 2b, GoR B]
    Consensus levels of agreement: A+ 11/15; A- 2/15; I 2/15

Intestinal fistulae

Fistulae, sinus tracts and fissures are hallmarks of CD and lead to peri-intestinal abscesses, loop adhesions and stricture formation. Extramural fissures originating from deep ulcerations of the intestinal wall are visualized as subtle hypoechoic irregularities of the bowel surface, in correspondence with hypoechoic segments of the bowel wall. Fissures result in the formation of sinus tracts and fistulae. Sinus tracts are linear extensions of inflammation that may have a blind end or finish in an inflammatory mesenteric mass [94, 124 – 128].

Abdominal fistulae in CD are classified as internal and external. The internal can be entero-enteric, entero-mesenteric or entero-vesical [129]. The US diagnostic criteria of sinus tracts and fistulae are similar and include: hypoechoic areas or tracts between ileal loops with or without internal gaseous artifacts; hypoechoic peri-intestinal tracts with or without gas within; hypoechoic peri-intestinal areas with a diameter < 2 cm [107 – 110, 129 – 133]. The sensitivity of US for the diagnosis of fistulizing lesions ranged from 67 % to 87 %, with a specificity in the range of 90 % to 100 % [8], similar to CT and MR. The latest consensus guidelines by the ECCO and ESGAR for imaging in IBD have recommended GIUS as one of the diagnostic procedures to assess perforating complications [11].

RECOMMENDATIONS

20. Fistulae in Crohn's disease can be identified by GIUS as hypoechoic tracts with or without air bubbles [LoE 2b, GoR A]
    Consensus levels of agreement: A+ 17/17
21. GIUS can be applied with high sensitivity and specificity, comparable to CT or MRI, for the detection of CD fistulas [LoE 1; GoR A]
    Consensus levels of agreement: A+ 14/17; A- 3/17

Abdominal abscesses

In 12 – 30 % of CD patients, an abscess occurs as a result of a fistula or surgical intervention. The US appearance is characterized by: hypo-anechoic lesions containing fluid and gaseous artifacts; posterior enhancement; irregular margins sometimes within hypertrophic mesentery [107 – 110, 129 – 132, 134].

The sensitivity of US for the diagnosis of abdominal abscesses ranges from 81 % to 100 %, with a specificity in the range of 92 % to 94 % [8], similar to CT and MR, although certain anatomic areas, such as the deep pelvis and left hypochondrium, are difficult to assess by GIUS and lesions can be missed. Abscesses and inflammatory masses or phlegmons can have a similar appearance on conventional US. This limit can be overcome using CEUS [135]. CEUS can demonstrate diffusely increased enhancement in phlegmons, while abscesses enhance only in the peripheral zone, with an avascular central portion, due to the fluid collection. To minimize radiation exposure, US should be preferred over CT for the detection of complications [8, 12]. Particularly, it is useful to monitor CD patients under treatment with biologic agents, which are contraindicated in patients with intra-abdominal abscesses, but may be effective in those with phlegmons [136].

RECOMMENDATIONS

22. Abscesses can be detected using GIUS as organized fluid collections that may contain bubbles of gas [LoE 2a, GoR B]
    Consensus levels of agreement: A+ 17/17
23. CEUS is useful for distinguishing between phlegmons and abscesses [LoE 2a, GoR B]
    Consensus levels of agreement: A+ 17/17
24. GIUS may be applied with high sensitivity and specificity to detect Crohn's abscesses [LoE 2, GoR B]
    Consensus levels of agreement: A+ 17/17

Postoperative recurrence in Crohn's disease

Despite advancement in medical therapy, surgery is still required in more than half of CD patients and reoperation in up to 60 % of these patients [137]. The identification of predictive factors of recurrence and ileo-colonoscopic assessment of postoperative

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recurrence (Rutgeerts score) within the first year after surgery are crucial to optimize therapeutic management [138].

Several studies and systematic reviews have assessed the role of bowel US in postoperative follow-up, showing that the detection of increased bowel wall thickening > 3 mm of the anastomosis or neo-terminal ileum is an accurate indicator for recurrence, with a sensitivity > 80 % and specificity > 88 % [8, 12]. In this regard, prospective studies have shown that the use of PEG solution (SICUS) [139 – 143] and color Doppler or CEUS [81, 144] can increase the sensitivity up to 90 – 98 %, albeit with a decrease in specificity. This is valid for US assessment performed 1 year after surgery. With shorter follow-up, e. g. 3 months, the sensitivity of US in assessing and predicting postoperative recurrence appears inaccurate [141, 145].

Moreover, both GIUS and SICUS, adopting different cut-off levels for bowel thickness (> 5 mm for conventional sonography and > 4 mm for SICUS), can suggest severe endoscopic postoperative recurrence and accordingly could replace endoscopy in the postsurgical follow-up [146]. In CD patients treated with conservative surgery (e. g. stricturoplastics or minimal bowel resections), GIUS is useful to monitor the postoperative behavior of bowel wall thickness and provides prognostic information. US detection of unchanged or worsened wall thickness 6 months after surgery or the postoperative persistence of wall thickness > 6 mm is predictive of a high risk of recurrence [147, 148].

RECOMMENDATIONS

25. Postoperative recurrence can be accurately detected using GIUS by assessing the thickness of ileo-colonic anastomosis or neo-terminal ileum (> 3 mm) 1 year after surgery [LoE 1b GoR A]
    Consensus levels of agreement: A+ 16/17; A- 1/17
26. Doppler US and CEUS assessment of thickened neo-terminal ileum and the use of oral contrast agents can improve the sensitivity of postoperative detection of recurrence [LoE 1b GoR A]
    Consensus levels of agreement: A+ 14/17; A- 2/17; D+ 1/17

Sonographic scores in Crohn's disease

The various US mural and extramural features of CD may have relevant prognostic implications and have been used to build sonographic indexes. The US detection of bowel wall thickness > 7 mm has been shown to be an independent risk of surgery (OR = 19.5, 95 % CI: 5.362 – 71.065) [34]. The short-term risk of surgery has also been evaluated with a score that included weighted parameters such as: wall thickness (> 4.5 mm), wall echo pattern ("disrupted stratification") and presence of fistulae/abscesses and stenoses. Although not validated, this score was able to correctly identify up to 84 % of patients requiring short-term surgery [40]. Following this trend, a numerical index, quantitating small bowel damage as detected by SICUS in CD patients, has been developed more recently with the aim of converting qualitative sonographic images into a numerical index for CD (Sonographic Lesion Index for CD – SLIC). Also this index was able to identify patients with higher lesion indices who underwent surgery more frequently than those with lower indices after one-year follow-up [149], and can be used to monitor changes in transmural bowel damage during anti-TNF therapy for CD [150]. An attempt to develop an ultrasonographic index of inflammatory activity for CD was proposed on the basis of wall thickness and wall stratification of the gut, subdivided into eight segments. The results of this index showed a correlation ($r^2 = 0.62$, $P < 0.01$) with endoscopic/radiological score, but, given its complexity and lack of validation, it has remained unused [38].

RECOMMENDATION

27. Indexes and scores using GIUS may be a tool for predicting the risk of surgery and quantifying bowel damage [LoR 4 GoR C]
    Consensus levels of agreement: A+ 14/16; A- 2/16

Ulcerative colitis

Ulcerative colitis, unlike CD, involves only the colonic mucosa starting from the rectum (proctitis) often ascending to the rest of the colon. Nowadays, colonoscopy is the method of choice and the reference standard in UC [151, 152]. Intestinal US is an accurate tool to detect and assess the extension of active UC and to define disease activity. The typical grayscale US finding in active UC is moderate thickening of the intestinal wall (usually below 9 mm), involving the mucosa and submucosa, sometimes with increased echogenicity of the submucosal layer, without involvement of the proper muscle layer or surrounding fat. Typical findings may be the irregular mucosal surface caused by gas bubbles entrapped among pseudopolyps and in deep ulcerations and the loss of haustration [153]. Because the lesions in UC are not transmural, the colonic wall stratification is usually preserved [154], although it may be disrupted in patients with severe activity. In particular, the diagnosis of ulcerative colitis relies in most studies on the detection of bowel wall thickness > 4 mm in adults [153 – 156] and > 3 mm in children [157 – 159]. Intestinal US can be used to assess UC extension, but is more challenging for rectal involvement, where the sensitivity is approximately 15 %. For the remaining colon the sensitivity is higher than 70 %, i. e., up to 97 % for the sigmoid and descending colon [156].

Wall thickness correlates well with clinical activity [153, 158 – 164], with biological tests like C-reactive protein values [155, 159, 163] and also with endoscopy findings [153, 155, 158, 163, 164]. Loss of bowel wall stratification (hypoechoic pattern) was associated with moderate (55 % of cases) and severe forms (100 % of cases) [165], while normal wall stratification was present in 87 % of mild cases in another study [166]. Increased vascularity assessed by Doppler US of the bowel wall (increased Doppler signals with low resistance) was also associated with both clinical and endoscopic activity of UC [158, 159, 166, 168]. Attempts have been made to establish an ultrasonic activity score. One of these,

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based on extension and degree of colonic wall thickness, showed that it is possible to discriminate severe and moderately severe attacks with a sensitivity of 90 % and a specificity of 96 % [160], but it was not validated due to a lack of large cohort studies.

Transabdominal US can also be used for the assessment of UC response to treatment by assessing wall thickness [160, 163, 169, 170], and vascularity changes by CEUS [171, 172]. Regarding response to treatment, published data are contradictory. One study concluded that color and power Doppler are useful [173], while another showed no correlation [172]. Furthermore, CEUS quantification can be used for noninvasive assessment of activity in UC [172, 174] and for treatment response [171, 172]. Strain elastography of the colonic wall may provide information that correlates with endoscopic and clinical disease activity [175].

Appendiceal involvement is seen in 15 % to 86 % of patients with UC and is more common in proctosigmoiditis, than in more extensive UC. It seems to be related to a better response to therapy and higher risk of pouchitis after ileo-colic anastomosis [152, 176].

RECOMMENDATIONS

28. GIUS can be used to estimate long segment thickening of the colonic wall, usually present in active UC [LoE 1b GoR A]
    Consensus levels of agreement: A+ 17/17
29. In active ulcerative colitis the echo-stratification that can be visualized using GIUS may be preserved, except in severe disease. The thickening involves the mucosa and submucosal layer [LoE 1b GoR B]
    Consensus levels of agreement: A+ 17/17
30. Increased Doppler signals in the thickened bowel wall that can be observed using GIUS should be interpreted as a sign of active inflammation [LoE 1b GoR B]
    Consensus levels of agreement: A+ 16/17; A- 1/17
31. CEUS highlights the inflammatory hypervascularity of the bowel wall and it can be used to evaluate therapy response [LoE 2b GoR B]
    Consensus levels of agreement: A+ 15/17; A-1/17; I 1/17
32. GIUS can be used to differentiate between UC and CD based on the location of the disease, degree of wall thickening, preserved stratification, lack of surrounding fat involvement or penetrating complications [LoE 4 GoR C]
    Consensus levels of agreement: A+ 16/17; A- 1/17

Complications of ulcerative colitis

Ultrasound may detect extra-intestinal complications of UC (e. g., primary sclerosing cholangitis) [177], but findings of intestinal complications have not been validated in prospective studies. Toxic megacolon combines abnormal colonic dilatation (> 6 cm), thin colonic walls (< 2 mm) and fluid-filled bowel [178, 179]. Massive pseudopolyposis as well as cancer in IBD may show irregular thickening of the wall [180] or a pseudokidney sign. However, GIUS does not play a major role in diagnosing these complications. Portomesenteric vein thrombosis may be detected by color Doppler imaging and CEUS in up to 26 % of acute or quiescent IBD patients [76, 181, 182].

RECOMMENDATION

33. Intestinal complications of UC, like toxic megacolon, may show some specific features that can be observed by GIUS [LoE 4 GoR B]
    Consensus levels of agreement: A+ 15/16; D- 1/16

Differential diagnosis among inflammatory colitides

GIUS has limited value compared to histology in differentiating various enterocolitides. However, GIUS assessment of the area of gut involvement and of mural and transmural changes of the bowel and vascularity may help to differentiate CD from UC [36, 156, 183 – 186], and other infectious (e. g. tuberculous, bacterial, pseudomembranous and parasitic) [187 – 191], vascular and inflammatory enterocolitides (e. g. ischemic, NSAID, Henoch-Schönlein purpura) [192 – 196] and to suggest the nature of lesions in most patients [166, 197 – 199].

RECOMMENDATION

34. GIUS detection of specific features of the bowel, mainly the site of bowel involvement and peri-intestinal signs, can be used to differentiate Crohn's disease from ulcerative colitis and other intestinal conditions [LoE 4 GoR C]
    Consensus levels of agreement: A+ 14/16; A- 1/16; I 1/16

Conflict of Interest

These authors declare a possible conflicts of interest: GM: Abbvie, Janssen, Alfa-Sigma Novartis, Allergan, THD, Takeda. KN: AbbVie, Ferring, Meda AS. IS: GE, Philips, Siemens, Abbvie, Bristol Myers Squibb. APH: Toshiba. CFD: Bracco, Hitachi, GE, Mindray, Supersonic, Pentax, Covidien, Boston Scientific, AbbVie, MSD, Falk Foundation, Novartis, Roche, Siemens, Olympus, Fuji. OHG: Abbvie, Bracco, Almirall, GE, Takeda AS, Meda AS, Ferring, Allergan, Samsung. CS: Bracco. DN Falk Foundation. AS, AH, TR, NP, KD, TH, LR, EC, CM no COI.

Acknowledgments

The authors thank Prof. Giovanni Casazza, MD, PhD, from Epidemiology and Biostatistic Unit – Department of Biomedical and Clinical Sciences, "L.Sacco" University Hospital – Milan.

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