PERSPECTIVE

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Differences in the imaging of Crohn's disease patients between North America and Europe: are we ready to bridge the divide?

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Abstract

The emphasis of treatment in Crohn's disease has evolved from a reactive model to "treat-to-target" approaches. Cross-sectional imaging has rapidly evolved in parallel, with a growing evidence base supporting its abilities for diagnosis, monitoring and prognostication. Whilst there are differences in emphasis between Europe and North America, particularly around the type of imaging modalities and patterns of multidisciplinary care, there is increasing convergence. This perspective piece provides an overview of the evolving role of cross-sectional imaging in Crohn's disease, discusses practice differences between North America and Europe and provides suggestions on areas for future collaboration and research priorities.

Keywords Crohn disease · MRI enterography · CT enterography · Cross-sectional imaging · Ultrasound

Introduction

Management of Crohn's disease has traditionally been reactive and based around controlling patient symptoms, with stepwise escalation of therapy over time. In recent years, however, the emphasis of treatment has switched to early aggressive control of inflammation, with the goal of achieving mucosal healing and reducing long-term bowel damage. For example, in the REACT trial, early combined immunosuppression reduced major adverse events such as surgery and hospitalization compared to conventional therapy [1]. This change in paradigm has occurred in parallel with rapid developments in cross-sectional imaging, resulting in unprecedented opportunities for radiologists to contribute to the care of patients with Crohn's disease. Radiological imaging has evolved from simply aiding diagnosis and detecting complications to playing a central role in quantifying inflammatory activity, monitoring treatment response and potentially facilitating prognostication. Several important publications in 2018 reflect this expanding role, including the METRIC trial [2], Society of Abdominal Radiology (SAR) Crohn's disease-focused panel consensus guidelines on the utilization of CT and MRI in Crohn's disease [3], and the joint European Crohn's and Colitis Organization (ECCO), European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus guidelines on diagnostic assessment in inflammatory bowel disease [4, 5]. Whilst the direction of travel is very similar between the radiological communities in North America and Europe, there remain practice differences. These must be recognized so that efforts to unify approaches either side of the Atlantic can be made where appropriate to fully realize the potential of cross-sectional imaging. This perspective piece provides an overview of the evolving role of cross-sectional imaging in Crohn's disease, discusses practice differences between North America and Europe and provides suggestions on areas for future collaboration and research priorities.

Modalities used in Crohn's disease imaging

Europe

In Europe, there is increased emphasis on MR enteography (MRE) and ultrasound (US) over CT enterography (CTE)

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for imaging Crohn's disease. This mainly stems from fears about cumulative radiation exposure in this often young patient cohort who frequently undergo repeat imaging over the course of their disease, but may also be influenced by reimbursement patterns in individual healthcare systems. This influences both the research and clinical communities. For example, the English National Institute of Health Research commissioned the METRIC trial, whose remit was specifically to compare diagnostic accuracy of MRE and US (rather than CTE) [2]. Consensus guidelines also reflect this approach; the ECCO-ESGAR consensus guidelines on diagnostic assessment in inflammatory bowel disease states "Radiation exposure is a limitation of CT and should only be used if MRI or ultrasound is not available". Small bowel imaging is mandated at diagnosis and cross-sectional imaging (using MRE or US) is already considered a robust alternative to ileocolonoscopy (IC) in treatment monitoring [5]. In the UK, annual assessment of patients on biological therapy is mandated by the National Institute for Health and Care Excellence (NICE), and increasingly MRE or US form part of this assessment. Although the METRIC trial showed that in a national health service setting MRE is more accurate than US for diagnosing and staging small bowel Crohn's disease [2], US itself performed well and has many advocates. For example, US has a high sensitivity for small bowel disease and is often used to investigate patients with nonspecific abdominal symptoms, usually in conjunction with biochemical markers such as calprotectin. It also is widely used in treatment follow-up. Physicians performing US examinations is gaining acceptance, driven by acute care and emergency medicine [6]. In continental Europe, gastroenterologists (as opposed to radiologists) commonly perform small bowel US; US technology is easily accessible with hand-held bedside devices increasingly available [7]. The ECCO, for example, is very active in prompting US training and education amongst gastroenterologists. In some countries, such as Germany, abdominal US is part of the training program for gastroenterologists, and US performed by nonradiologists may achieve acceptable diagnostic accuracy [8]. Furthermore, the ability of the gastroenterologist to interpret the findings real time within the clinical context may be advantageous [9], and such interactions could strengthen the physician–patient relationship [8]. CTE is of course undoubtedly used in Europe particularly in older patients and in some centers in patients with nonspecific abdominal symptoms in whom enteropathy is being excluded. However, if available, MRE and US are recommended as first line in the Crohn's disease population.

North America

There has been a rapid growth in the use of CT and MR enterography throughout the United States in the last two decades, and these tests are now widely available. Compared to Europe, practice pressures within most United States have precluded routine use of specialized bowel ultrasound, which requires dedicated individuals with clear expertise. Additionally, while MR enterography is generally preferred for pediatric and younger patients, and patients undergoing imaging to determine response to therapy [10], there is increased utilization of CT enterography for the imaging of small bowel diseases for several reasons, despite the requirement for low-dose radiation at CT. First, CT is ubiquitous and widely available and accessible in most emergency rooms and outpatient radiology practices, it is quick and the performance of CT and MR enterography are felt to be identical for the detection and staging of active inflammatory Crohn's disease [11]. As cross-sectional enterography is used for an expanding list of indications, the MR scanners in many radiology practices cannot accommodate small bowel imaging in a timely fashion, so patients with diarrhea (potentially due to pancreatic disease, or with IBS symptoms) or with other suspected indications (e.g., NSAID enteropathy) are imaged with CT enterography. Low-dose CT techniques such as iterative reconstruction and kV selection are now widely available, and United States radiologists have become more accustomed to interpreting noisier, lower dose images such as their European colleagues, so CT imaging can be performed in most practices at doses that are similar to annual background doses [12, 13]. Moreover, multiple studies have demonstrated the benefit of CT in detecting unanticipated complications in both the emergency room and outpatient setting [14–16].The United States has a larger number of new Crohn's disease diagnosed at age 60 years or older, in addition to those being treated for existing Crohn's disease [17]. While these older patients tend to have less aggressive disease, they have worse outcomes [17–19], and CT enterography is often a more attractive alternative in elderly patients owing to the speed of acquisition, its ability to identify other pathologies, and the decreased perceived risk of low-dose radiation. For all these reasons, many gastroenterologists now involve their Crohn's disease patients in the selection of cross-sectional bowel imaging tests, and refer many patients with non-Crohn's alternatives for initial CT imaging.

National and international oversight

Europe

Multidisciplinary management of Crohn's disease is well established in Europe and regular face to face multidisciplinary team meetings including gastroenterologists, radiologists, surgeons, and nurses are often mandated for hospitals running inflammatory bowel disease services, a concept long

implemented in the UK for example [20]. Indeed, management of complex Crohn's disease is on a par with cancer management, and team approach is deemed essential. The multidisciplinary nature of managing Crohn's disease is reflected by the established international joint consensus guidelines published by ECCO and ESGAR, originally in 2013 [21] and recently updated [4, 5]. National guidelines are also truly multidisciplinary, for example those developed the British Society of Gastroenterology in the UK. Such consensus documents repeatedly emphasize the complementarity of cross-sectional imaging and IC alongside biochemical markers such as CRP and calprotectin in all aspects of Crohn's disease management. This is exemplified by many statements in 2018 ECCO/ESGAR guidelines, for example "Endoscopic or cross-sectional reassessment in CD should be considered in cases of relapse, persistent disease activity, new unexplained symptoms, and before switch of therapy" [5], and "Magnetic resonance [MR] enterography-based indexes have high accuracy for assessing luminal CD activity and can be used in clinical trials for measuring activity and response to pharmacological interventions" [4]. Multidisciplinary conferences such as the United European Gastroenterology week have long-hosted educational sessions with gastroenterological and radiological speakers, reflecting this multidisciplinary approach.

North America

In the United States, outside of major academic centers, radiologists, gastroenterologists, and colorectal surgeons have traditionally tended to attend their individual subspecialty medical meetings. With the formation of the Society of Abdominal Radiology (SAR), Crohn's disease-focused panel, which includes non-radiology gastroenterologist IBD experts as well as pediatric, European and Asian radiologists, there has been increasing collaboration with the American Gastroenterology Association (AGA) imaging and advanced technology (IAT) and inflammatory bowel disease (IBD) sections, as well as the Society of Pediatric Radiology (SPR). After the creation of technical specifications for MR and CT enterography [22, 23], the SAR Crohn's disease-focused panel worked with AGA-IAT, AGA-IBD, and SPR members to develop the aforementioned consensus recommendations for the utilization and interpretation of cross-sectional enterography in small bowel Crohn's disease [3]. Concurrent with this process has been the increasing realization in the need for and complementarity of cross-sectional enterography in identifying substantial small bowel inflammation in both adult and pediatric Crohn's patients that is not identified by ileocolonoscopy alone [24, 25], and that cross-sectional and optical imaging are complementary rather than competing techniques: cross-sectional enterography cannot visualize the mucosa (or mucosal healing) or perform cancer

surveillance or biopsies, and many features of Crohn's disease (e.g., colorectal strictures, stricturing of the ileocecal valve, skipping of the terminal ileum) hamper endoscopic diagnosis. Additionally, there is increasing understanding of how serum markers such as CRP and fecal markers such as calprotectin can be used to guide management decisions in conjunction with cross-sectional imaging [26, 27]. These parallel developments have led to an increasing number of interdisciplinary inflammatory bowel disease conferences within institutions patterned after multidisciplinary tumor boards, as well as increasing interdisciplinary session at major gastroenterology meetings in IBD such as the combined meeting of the Crohn's and Colitis Congress supported by the Crohn's and Colitis Foundation and the AGA IBD section [28]. There is also increasing focus on the use of imaging endpoints in therapeutic studies and their joint development by gastroenterologists and radiologists [29].

Treatment strategy and evolving role of imaging

As can be seen from the above discussion, although differences exist between Europe and North America, there is increasing convergence in recommendations from multidisciplinary bodies. The SAR/SPR/AGA consensus recommendations indicate that MR and CT enterography be performed not only at diagnosis of small bowel Crohn's disease, but considered in surveillance when assessing response to therapy. Similar recommendations (for MRE and US) are also made by the joint ECCO/ESGAR consensus statements [4, 5]. Mucosal healing at endoscopy is associated with longer periods of subsequent clinical remission [30]. Building upon the knowledge that mucosal healing is achieved in only a minority of patients, Colombel and colleagues recently demonstrated in the CALM study that escalation of treatment based on objective markers of disease progression led to better clinical and endoscopic outcomes [31]. This has important implications for cross-sectional imaging given its ability to quantify disease burden and activity. Complete response to therapy as shown by resolution of all imaging findings of inflammation at US, CT and MR enterography is termed "transmural healing", as these cross-sectional techniques image the bowel wall. Of note, abnormalities on cross-sectional imaging, such as wall thickening, strictures and creeping fat, frequently persist, despite achieving endoscopic remission [32]. MR enterography has an approximately 90% accuracy for mucosal healing [33], and other studies have demonstrated improved outcomes or prediction of clinical remission with transmural healing [34, 35]. In contrast to transmural healing, response to therapy can also be seen with cross-sectional enterography [36, 37]. Deepak et al. have shown that response (defined by decrease in length or

severity of inflammation for all inflamed bowel segments) results in lower rates of hospitalization and surgery, and that maintaining patients in a state of response on imaging dramatically reduces the risk of small bowel surgery [38, 39].

Next steps (near future)

In recent years, the treat-to-target paradigm has gained significant traction in the care of Crohn's disease patients [40]. This strategy involves setting of a specific goal, such as mucosal or transmural healing, that signals low or absent disease activity. This goal is then evaluated frequently to monitor progress and the treatment plan adjusted if the target is not achieved. Cross-sectional imaging may have a crucial role in this monitoring strategy as it is non-invasive with a lower complication rate then invasive colonoscopy, providing greater patient comfort and safety [41]. To achieve this, we must embed cross-sectional imaging into large clinical trials, so we can truly establish its added value, not only in monitoring disease response (for example as an endpoint in clinical trials of novel therapies), but also predicting longer term outcomes. Whilst the CALM study provides evidence that objective monitoring leads to better outcomes [31], it is unclear if imaging targets are superior to cheaper and simple biochemical markers. It is very possible that the goal of treatment will shift from mucosal to transmural healing, but such an evolution will require more compelling evidence, in particular on the natural history of Crohn's disease. We imagine that the future will continue to bring consensus, refinement and reproducibility to cross-sectional imaging criteria for treatment response (regardless of the chosen modality), as well as developing algorithms to combine imaging with other biomarkers. Cross-sectional imaging holds many advantages over other monitoring techniques in several situations, such as isolated small bowel Crohn's disease or perianal Crohn's disease and is already forming an important part of assessment of new therapies such as janus kinase inhibitors (NCT03046056 and NCT03077412). Emphasis is currently increasingly placed on MRE, but we must not forget the undoubted strengths of US and CTE, both of which will play an important role in this evolution. Their exact place in the future management algorithms will need to be defined. Teaching the skills of enteric US and fully utilizing the dose reduction techniques available for CT should continue. Whilst it is essential to address technical questions, for example the added value of diffusion-weighted imaging and motility quantification as part of MRE, importantly this should not distract radiologists from collaborating externally. We must emerge from our radiological silos and develop (and if possible, combine) the existing international consensus groups involving radiological (such as SAR, ESGAR) and clinical societies (such as AGA, ECCO,

and UEG). We must fully involve patients in our work-patients are not only involved in their own care, but play an increasingly important role in setting the agenda of the major funding agencies and our imaging technologies must be developed with them. In parallel, we must reach out to other disciplines such as computationalists, physicists and mathematicians. Interdisciplinary groups are essential. For example, current MRI activity scores are too time consuming and cumbersome for use in day to day clinical practice. However, radiomics or artificial intelligence techniques will likely make annotation of disease severity and length for inflamed bowel segments rapid, reproducible and available in the clinic. Indeed, some progress has already been made in automated measurement of bowel wall thickness and enhancement [42]. In the clinical care of our patients, we must embrace multidisciplinary team working; we anticipate that interdisciplinary inflammatory bowel disease boards will become the norm at individual institutions in North America, as well as Europe.

Future areas that will require interdisciplinary expertise, are the imaging of Crohn's disease-associated strictures and fibrosis. This is perhaps one of the largest areas of unmet need in Crohn's disease, and research is urgently needed given the absence of validated definitions or response parameters. Based on prior experience, this area is now being jointly and systematically developed by gastroenterologists, radiologists and clinical trialists to standardize definitions, diagnosis and treatment targets for stricturing Crohn's disease [43]. In parallel, several novel imaging techniques are being developed to differentiate inflammation from fibrosis, a critical step towards future anti-fibrotic therapies [44].

Summary

In the recent years, the emphasis of treatment in Crohn's disease has evolved from a reactive model to "treat-to-target" approaches. Cross-sectional imaging has rapidly evolved in parallel, with a growing evidence base supporting its abilities for diagnosis, monitoring and prognostication. Whilst there are differences in emphasis between Europe and North America, particularly around the type of imaging modalities and patterns of multidisciplinary care, there is increasing convergence. This is exemplified by multidisciplinary consensus statements which have emerged on either side of the Atlantic in 2018. Although it seems likely US will remain primarily practiced in Europe, there is clear commonality in approaches to MRE, as well as CTE. This is a time of unparalleled opportunity for radiologists to meaningfully impact on the care of Crohn's disease long into the future. By engaging widely, both with each other, and with other disciplines, we will be able to realize the potential of cross-sectional imaging in the management of Crohn's disease.

Compliance with ethical standards

References

1. Khanna R, Bressler B, Levesque BG, Zou G, Stitt LW, Greenberg GR, Panaccione R, Bitton A, Pare P, Vermeire S, D'Haens G, MacIntosh D, Sandborn WJ, Donner A, Vandervoort MK, Morris JC, Feagan BG (2015) Early combined immunosuppression for the management of Crohn's disease (REACT): a cluster randomised controlled trial. Lancet (London, England) 386(10006):1825-1834. https://doi.org/10.1016/s0140-6736(15)00068-9

2. Taylor SA, Mallett S, Bhatnagar G, Baldwin-Cleland R, Bloom S, Gupta A, Hamlin PJ, Hart AL, Higginson A, Jacobs I, McCartney S, Miles A, Murray CD, Plumb AA, Pollok RC, Punwani S, Quinn L, Rodriguez-Justo M, Shabir Z, Slater A, Tolan D, Travis S, Windsor A, Wylie P, Zealley I, Halligan S (2018) Diagnostic accuracy of magnetic resonance enterography and small bowel ultrasound for the extent and activity of newly diagnosed and relapsed Crohn's disease (METRIC): a multicentre trial. The lancet Gastroenterology & hepatology 3 (8):548-558. https://doi.org/10.1016/s2468-1253(18)30161-4

3. Bruining DH, Zimmermann EM, Loftus EV, Jr., Sandborn WJ, Sauer CG, Strong SA, Society of Abdominal Radiology Crohn's Disease-Focused P (2018) Consensus Recommendations for Evaluation, Interpretation, and Utilization of Computed Tomography and Magnetic Resonance Enterography in Patients With Small Bowel Crohn's Disease. Gastroenterology 154 (4):1172-1194. https://doi.org/10.1053/j.gastro.2017.11.274

4. Sturm A, Maaser C, Calabrese E, Annese V, Fiorino G, Kucharzik T, Vavricka SR, Verstockt B, van Rheenen P, Tolan D, Taylor SA, Rimola J, Rieder F, Limdi JK, Laghi A, Krustins E, Kotze PG, Kopylov U, Katsanos K, Halligan S, Gordon H, Gonzalez Lama Y, Ellul P, Eliakim R, Castiglione F, Burisch J, Borralho Nunes P, Bettenworth D, Baumgart DC, Stoker J (2018) ECCO-ESGAR Guideline for Diagnostic Assessment in Inflammatory Bowel Disease. Journal of Crohn's & colitis. https://doi.org/10.1093/ecco-jcc/jjy114

5. Maaser C, Sturm A, Vavricka SR, Kucharzik T, Fiorino G, Annese V, Calabrese E, Baumgart DC, Bettenworth D, Borralho Nunes P, Burisch J, Castiglione F, Eliakim R, Ellul P, Gonzalez-Lama Y, Gordon H, Halligan S, Katsanos K, Kopylov U, Kotze PG, Krustins E, Laghi A, Limdi JK, Rieder F, Rimola J, Taylor SA, Tolan D, van Rheenen P, Verstockt B, Stoker J (2018) ECCO-ESGAR Guideline for Diagnostic Assessment in Inflammatory Bowel Disease. Journal of Crohn's & colitis. https://doi.org/10.1093/ecco-jcc/jjy113

6. Dietrich CF, Goudie A, Chiorean L, Cui XW, Gilja OH, Dong Y, Abramowicz JS, Vinayak S, Westerway SC, Nolsoe CP, Chou YH, Blaivas M (2017) Point of Care Ultrasound: A WFUMB Position Paper. Ultrasound in medicine & biology 43 (1):49-58. https://doi.org/10.1016/j.ultrasmedbio.2016.06.021

7. Kjesbu IE, Laursen CB, Graven T, Holden HM, Romo B, Newton Andersen G, Mjolstad OC, Lassen A, Dalen H (2017) Feasibility and Diagnostic Accuracy of Point-of-Care Abdominal Sonography by Pocket-Sized Imaging Devices, Performed by Medical Residents. Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine 36 (6):1195-1202. https://doi.org/10.7863/ultra.16.05077

8. Atkinson NS, Bryant RV, Dong Y, Maaser C, Kucharzik T, Maconi G, Asthana AK, Blaivas M, Goudie A, Gilja OH, Nolsoe C, Nurnberg D, Dietrich CF (2016) WFUMB Position Paper. Learning Gastrointestinal Ultrasound: Theory and Practice. Ultrasound in medicine & biology 42 (12):2732-2742. https://doi.org/10.1016/j.ultrasmedbio.2016.08.026

9. Novak K, Tanyingoh D, Petersen F, Kucharzik T, Panaccione R, Ghosh S, Kaplan GG, Wilson A, Kannengiesser K, Maaser C (2015) Clinic-based Point of Care Transabdominal Ultrasound for Monitoring Crohn's Disease: Impact on Clinical Decision Making. Journal of Crohn's & colitis 9 (9):795-801. https://doi.org/10.1093/ecco-jcc/jjv105

10. Guimaraes LS, Fidler JL, Fletcher JG, Bruining DH, Huprich JE, Siddiki H, Sandborn WJ, Loftus EV, Jr., Pardi DS, McCollough CH (2010) Assessment of appropriateness of indications for CT enterography in younger patients. Inflamm Bowel Dis 16 (2):226-232. https://doi.org/10.1002/ibd.21025

11. Liu W, Liu J, Xiao W, Luo G (2017) A Diagnostic Accuracy Meta-analysis of CT and MRI for the Evaluation of Small Bowel Crohn Disease. Academic radiology 24 (10):1216-1225. https://doi.org/10.1016/j.acra.2017.04.013

12. Del Gaizo AJ, Fletcher JG, Yu L, Paden RG, Spencer GC, Leng S, Silva AM, Fidler JL, Silva AC, Hara AK (2013) Reducing radiation dose in CT enterography. Radiographics 33 (4):1109-1124. https://doi.org/10.1148/rg.334125074

13. Rosenfeld G, Brown J, Vos PM, Leipsic J, Enns R, Bressler B (2018) Prospective Comparison of Standard- Versus Low-Radiation-Dose CT Enterography for the Quantitative Assessment of Crohn Disease. AJR Am J Roentgenol 210 (2):W54-W62. https://doi.org/10.2214/AJR.17.18296

14. Bruining DH, Siddiki HA, Fletcher JG, Sandborn WJ, Fidler JL, Huprich JE, Mandrekar JN, Harmsen WS, Evans PE, Faubion WA, Hanson KA, Ingle SB, Pardi DS, Schroeder KW, Tremaine WJ, Loftus EV, Jr. (2012) Benefit of computed tomography enterography in Crohn's disease: effects on patient management and physician level of confidence. Inflamm Bowel Dis 18 (2):219-225. https://doi.org/10.1002/ibd.21683

15. Bruining DH, Siddiki HA, Fletcher JG, Tremaine WJ, Sandborn WJ, Loftus EV, Jr. (2008) Prevalence of penetrating disease and extraintestinal manifestations of Crohn's disease detected with CT enterography. Inflamm Bowel Dis 14 (12):1701-1706. https://doi.org/10.1002/ibd.20529

16. Kerner C, Carey K, Mills AM, Yang W, Synnestvedt MB, Hilton S, Weiner MG, Lewis JD (2012) Use of abdominopelvic computed tomography in emergency departments and rates of urgent diagnoses in Crohn's disease. Clin Gastroenterol Hepatol 10 (1):52-57. https://doi.org/10.1016/j.cgh.2011.09.005

17. Taleban S, Colombel JF, Mohler MJ, Fain MJ (2015) Inflammatory bowel disease and the elderly: a review. Journal of Crohn's & colitis 9 (6):507-515. https://doi.org/10.1093/ecco-jcc/jjv059

18. Everhov AH, Halfvarson J, Myrelid P, Sachs MC, Nordenvall C, Soderling J, Ekbom A, Neovius M, Ludvigsson JF, Askling J, Olen O (2018) Incidence and Treatment of Patients Diagnosed With Inflammatory Bowel Diseases at 60 Years or Older in Sweden. Gastroenterology 154 (3):518-528 e515. https://doi.org/10.1053/j.gastro.2017.10.034

19. Taleban S (2015) Challenges in the Diagnosis and Management of Inflammatory Bowel Disease in the Elderly. Curr Treat Options Gastroenterol 13 (3):275-286. https://doi.org/10.1007/s11938-015-0059-6

20. Mowat C, Cole A, Windsor A, Ahmad T, Arnott I, Driscoll R, Mitton S, Orchard T, Rutter M, Younge L, Lees C, Ho GT, Satsangi J, Bloom S (2011) Guidelines for the management of inflammatory bowel disease in adults. Gut 60 (5):571-607. https://doi.org/10.1136/gut.2010.224154

21. Panes J, Bouhnik Y, Reinisch W, Stoker J, Taylor SA, Baumgart DC, Danese S, Halligan S, Marincek B, Matos C, Peyrin-Biroulet L, Rimola J, Rogler G, van Assche S, Ardizzone S, Ba-Ssalamah A, Bali MA, Bellini D, Biancone L, Castiglione F, Ehehalt R, Grassi R, Kucharzik T, Maccioni F, Maconi G, Magro F, Martin-Comin J, Morana G, Pendse D, Sebastian S, Signore A, Tolan D, Tielbeek JA, Weishaupt D, Wiarda B, Laghi A (2013) Imaging techniques for assessment of inflammatory bowel disease: joint ECCO and ESGAR evidence-based consensus guidelines. Journal of Crohn's & colitis 7 (7):556-585. https://doi.org/10.1016/j.crohns.2013.02.020

22. Baker ME, Hara AK, Platt JF, Maglinte DD, Fletcher JG (2015) CT enterography for Crohn's disease: optimal technique and imaging issues. Abdom Imaging 40 (5):938-952. https://doi.org/10.1007/s00261-015-0357-4

23. Grand DJ, Guglielmo FF, Al-Hawary MM (2015) MR enterography in Crohn's disease: current consensus on optimal imaging technique and future advances from the SAR Crohn's disease-focused panel. Abdom Imaging 40 (5):953-964. https://doi.org/10.1007/s00261-015-0361-8

24. Mansuri I, Fletcher JG, Bruining DH, Kolbe AB, Fidler JL, Samuel S, Tung J (2017) Endoscopic Skipping of the Terminal Ileum in Pediatric Crohn Disease. AJR Am J Roentgenol 208 (6):W216-W224. https://doi.org/10.2214/AJR.16.16575

25. Samuel S, Bruining DH, Loftus EV, Jr., Becker B, Fletcher JG, Mandrekar JN, Zinsmeister AR, Sandborn WJ (2012) Endoscopic skipping of the distal terminal ileum in Crohn's disease can lead to negative results from ileocolonoscopy. Clin Gastroenterol Hepatol 10 (11):1253-1259. https://doi.org/10.1016/j.cgh.2012.03.026

26. Faubion WA, Jr., Fletcher JG, O'Byrne S, Feagan BG, de Villiers WJ, Salzberg B, Plevy S, Proctor DD, Valentine JF, Higgins PD, Harris JM, Diehl L, Wright L, Tew GW, Luca D, Basu K, Keir ME (2013) EMerging BiomARKers in Inflammatory Bowel Disease (EMBARK) study identifies fecal calprotectin, serum MMP9, and serum IL-22 as a novel combination of biomarkers for Crohn's disease activity: role of cross-sectional imaging. The American journal of gastroenterology 108 (12):1891-1900. https://doi.org/10.1038/ajg.2013.354

27. Sandborn WJ (2014) Crohn's disease evaluation and treatment: clinical decision tool. Gastroenterology 147 (3):702-705

28. (2018). www.crohnscolitiscongress.org. Accessed 10-29-2018

29. Coimbra AJ, Rimola J, O'Byrne S, Lu TT, Bengtsson T, de Crespigny A, Luca D, Rutgeerts P, Bruining DH, Fidler JL, Sandborn WJ, Santillan CS, Higgins PD, Al-Hawary MM, Vermeire S, Vanbeckevoort D, Vanslembrouck R, Peyrin-Biroulet L, Laurent V, Herrmann KA, Panes J (2016) Magnetic resonance enterography is feasible and reliable in multicenter clinical trials in patients with Crohn's disease, and may help select subjects with active inflammation. Alimentary pharmacology & therapeutics 43 (1):61-72. https://doi.org/10.1111/apt.13453

30. Shah SC, Colombel JF, Sands BE, Narula N (2016) Systematic review with meta-analysis: mucosal healing is associated with improved long-term outcomes in Crohn's disease. Alimentary pharmacology & therapeutics 43 (3):317-333. https://doi.org/10.1111/apt.13475

31. Colombel JF, Panaccione R, Bossuyt P, Lukas M, Baert F, Vanasek T, Danalioglu A, Novacek G, Armuzzi A, Hebuterne X, Travis S, Danese S, Reinisch W, Sandborn WJ, Rutgeerts P, Hommes D, Schreiber S, Neimark E, Huang B, Zhou Q, Mendez P, Petersson J, Wallace K, Robinson AM, Thakkar RB, D'Haens G (2018) Effect of tight control management on Crohn's disease (CALM): a multicentre, randomised, controlled phase 3 trial. Lancet (London, England) 390 (10114):2779-2789. https://doi.org/10.1016/S0140-6736(17)32641-7

32. Rimola J, Alfaro I, Fernandez-Clotet A, Castro-Poceiro J, Vas D, Rodriguez S, Masamunt MC, Ordas I, Ricart E, Panes J (2018) Persistent damage on magnetic resonance enterography in patients with Crohn's disease in endoscopic remission. Alimentary pharmacology & therapeutics 48 (11-12):1232-1241. https://doi.org/10.1111/apt.15013

33. Ordas I, Rimola J, Rodriguez S, Paredes JM, Martinez-Perez MJ, Blanc E, Arevalo JA, Aduna M, Andreu M, Radosevic A, Ramirez-Morros AM, Pino S, Gallego M, Jauregui-Amezaga A, Ricart E, Panes J (2014) Accuracy of magnetic resonance enterography in assessing response to therapy and mucosal healing in patients with Crohn's disease. Gastroenterology 146 (2):374-382 e371. https://doi.org/10.1053/j.gastro.2013.10.055

34. Fernandes SR, Rodrigues RV, Bernardo S, Cortez-Pinto J, Rosa I, da Silva JP, Goncalves AR, Valente A, Baldaia C, Santos PM, Correia L, Venancio J, Campos P, Pereira AD, Velosa J (2017) Transmural Healing Is Associated with Improved Long-term Outcomes of Patients with Crohn's Disease. Inflamm Bowel Dis 23 (8):1403-1409. https://doi.org/10.1097/MIB.0000000000001143

35. Sauer CG, Middleton JP, McCracken C, Loewen J, Braithwaite K, Alazraki A, Martin DR, Kugathasan S (2016) Magnetic Resonance Enterography Healing and Magnetic Resonance Enterography Remission Predicts Improved Outcome in Pediatric Crohn Disease. J Pediatr Gastroenterol Nutr 62 (3):378-383. https://doi.org/10.1097/MPG.0000000000000976

36. Bruining DH, Loftus EV, Jr., Ehman EC, Siddiki HA, Nguyen DL, Fidler JL, Huprich JE, Mandrekar JN, Harmsen WS, Sandborn WJ, Fletcher JG (2011) Computed tomography enterography detects intestinal wall changes and effects of treatment in patients with Crohn's disease. Clin Gastroenterol Hepatol 9 (8):679-683 e671. https://doi.org/10.1016/j.cgh.2011.04.025

37. Wu YW, Tang YH, Hao NX, Tang CY, Miao F (2012) Crohn's disease: CT enterography manifestations before and after treatment. Eur J Radiol 81 (1):52-59. https://doi.org/10.1016/j.ejrad.2010.11.010

38. Deepak P, Fletcher JG, Fidler JL, Barlow JM, Sheedy SP, Kolbe AB, Harmsen WS, Loftus EV, Hansel SL, Becker BD, Bruining DH (2016) Radiological Response Is Associated With Better Long-Term Outcomes and Is a Potential Treatment Target in Patients With Small Bowel Crohn's Disease. The American journal of gastroenterology 111 (7):997-1006. https://doi.org/10.1038/ajg.2016.177

39. Deepak P, Fletcher JG, Fidler JL, Barlow JM, Sheedy SP, Kolbe AB, Harmsen WS, Therneau T, Hansel SL, Becker BD, Loftus EV, Jr., Bruining DH (2018) Predictors of Durability of Radiological Response in Patients With Small Bowel Crohn's Disease. Inflamm Bowel Dis. https://doi.org/10.1093/ibd/izy074

40. Peyrin-Biroulet L, Sandborn W, Sands BE, Reinisch W, Bemelman W, Bryant RV, D'Haens G, Dotan I, Dubinsky M, Feagan B, Fiorino G, Gearry R, Krishnareddy S, Lakatos PL, Loftus EV, Jr., Marteau P, Munkholm P, Murdoch TB, Ordas I, Panaccione R, Riddell RH, Ruel J, Rubin DT, Samaan M, Siegel CA, Silverberg MS, Stoker J, Schreiber S, Travis S, Van Assche G, Danese S, Panes J, Bouguen G, O'Donnell S, Pariente B, Winer S, Hanauer S, Colombel JF (2015) Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE): Determining Therapeutic Goals for Treat-to-Target. The American journal of gastroenterology 110 (9):1324-1338. https://doi.org/10.1038/ajg.2015.233

41. Miles A, Bhatnagar G, Halligan S, Gupta A, Tolan D, Zealley I, Taylor SA (2018) Magnetic resonance enterography, small bowel ultrasound and colonoscopy to diagnose and stage Crohn's disease: patient acceptability and perceived burden. European radiology. https://doi.org/10.1007/s00330-018-5661-2

42. Puylaert CAJ, Schuffler PJ, Naziroglu RE, Tielbeek JAW, Li Z, Makanyanga JC, Tutein Nolthenius CJ, Nio CY, Pendse DA, Menys A, Ponsioen CY, Atkinson D, Forbes A, Buhmann JM, Fuchs TJ, Hatzakis H, van Vliet LJ, Stoker J, Taylor SA, Vos FM (2018) Semiautomatic Assessment of the Terminal Ileum and Colon in Patients with Crohn Disease Using MRI (the VIGOR++ Project). Academic radiology 25 (8):1038-1045. https://doi.org/10.1016/j.acra.2017.12.024

43. Rieder F, Bettenworth D, Ma C, Parker CE, Williamson LA, Nelson SA, van Assche G, Di Sabatino A, Bouhnik Y, Stidham RW, Dignass A, Rogler G, Taylor SA, Stoker J, Rimola J, Baker ME, Fletcher JG, Panes J, Sandborn WJ, Feagan BG, Jairath V (2018) An expert consensus to standardise definitions, diagnosis and treatment targets for anti-fibrotic stricture therapies in Crohn's disease. Alimentary pharmacology & therapeutics 48 (3):347-357. https://doi.org/10.1111/apt.14853

44. Stidham RW, Higgins PD (2016) Imaging of intestinal fibrosis: current challenges and future methods. United European gastroenterology journal 4 (4):515-522. https://doi.org/10.1177/2050640616636620