Small intestine contrast ultrasonography for the detection and assessment of Crohn disease

A meta-analysis

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Abstract

Background: Crohn disease (CD) is a chronic relapsing disease. Imaging modalities are essential for the diagnosis and assessment of CD. Small intestine contrast ultrasonography (SICUS) is a well-tolerated, noninvasive and radiation-free modality and has shown potential in CD assessment. We aimed at evaluating the diagnostic accuracy of SICUS in the detection and assessment of small-bowel lesions and complications in CD.

Methods: We searched PubMed database for relevant studies published before April 24, 2016. We integrated the true positive, false positive, false negative, and true negative into the pooled estimates of sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio. Forest plots were to represent the pooled results of all studies.

Results: Thirteen articles were finally considered eligible. The pooled sensitivity and specificity of SICUS in detecting small-bowel lesions were 0.883 (95% confidence interval (CI) 0.847–0.913) and 0.861 (95% CI 0.828–0.890), respectively. The pooled diagnostic odds ratio was 39.123 (95% CI 20.014–76.476) and the area under the curve of summary receiver operating characteristic was 0.9273 (standard error: 0.0152). In subgroup analyses, SICUS represented fine sensitivity and specificity in proximal and distal small intestine lesion, as well as in CD-related complications such as stricture, dilation, abscess, and fistula.

Conclusion: SICUS is accurate enough to make a complete assessment about the location, extent, number, and almost all kinds of complications in CD small-bowel lesions.

Abbreviations: AUC = area under the curve, CD = Crohn disease, CI = confidence interval, DOR = diagnostic odds ratio, FN = false negative, FP = false positive, IBD = inflammatory bowel disease, NLR = negative likelihood ratio, PLR = positive likelihood ratio, SICUS = small intestine contrast ultrasonography, SROC = summary receiver operating characteristic, TN = true negative, TP = true positive.

Keywords: Crohn disease, meta-analysis, SICUS

1. Introduction

Crohn disease (CD) is a chronic relapsing inflammatory bowel disease (IBD) that may progressively and destructively involve various parts of the gastrointestinal tract,[1,2] causing irreversible transmural bowel damage that is mainly characterized by stricture and penetration.[3] Imaging modalities assessing the site, number, extent, and complications of bowel inflammatory lesions are essential in the establishment of a detailed diagnosis of CD.[4,5]

Although endoscopy provides a direct vision of bowel lesions,[6] only the intraluminal view can be shown. Transabdominal ultrasonography (TUS) overcomes some of the drawbacks of first-line imaging modalities in CD assessment,[7] but the presence of gas in the intestinal loops often results in suboptimal visualization of the surrounding organs, such as pancreas, duodenal tract, and the extrahepatic bile ducts.[8–10]

By applying a small amount of oral contrast fluid to CD patients, small intestine contrast ultrasonography (SICUS) provides a comprehensive depiction about both intramural and extraluminal bowel lesions with a high contrast ratio.[11,12] Moreover, SICUS has shown its potential in locating the sites of lesion,[13] representing the typical cobblestone-like changing of small-bowel wall and depicting enlarged lymph nodes and swelling mesenteric tissue[14] without radiation exposure. As suffers of CD are mainly at reproductive ages, and they generally need frequent and long-term monitoring due to the relapsing nature of CD,[15] frequent radiation exposure should be avoided. An article analyzing the diagnostic ionizing radiation exposure in a large IBD patients cohort showed that patients with CD received 2.46 times higher total cumulative effective radiation
than patients with ulcerative colitis, potentially leading to a higher risk of cancer.\[16\]

SICUS might be a potential modality in CD assessment with its low-cost, noninvasive, radiation-free nature.\[17\] In this meta-analysis, we analyzed all eligible published studies to evaluate the use of SICUS in detecting CD or its complications in clinical practice.

2. Methods

2.1. Literature search

We searched PubMed database for relevant studies published before April 24, 2016, using “Crohn or Crohn’s” and “contrast or contrast-enhanced” and “ultrasound or ultrasonography or sonography or ultrasound” as our search keywords. We also manually examined the references listed in retrieved eligible articles. As this was a meta-analysis, no ethical approval was required.

2.2. Study selection

Two investigators reviewed and selected studies independently according to the inclusion and exclusion criteria set before the selection, and when disagreements came up, we made a consensus by discussion. The inclusion and exclusion criteria were as follows:

Inclusion criteria: articles assessed the accuracy of SICUS for the detection of sites or complications in CD; the contrast agent was taken orally and was nonabsorbable; the gold standard of CD diagnosis was biopsy, surgical findings, or imaging findings; and articles reported true positives (TP), false positives (FP), true negatives (TN), and false negatives (FN) directly, or the data in the article was sufficient enough to extract a 2 × 2 table of TP, FP, TN, FN manually. For example, Calabrese E\(^2\) reported the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the total number of patients, and we calculated TP, FP, FN, and TN based on these data.

Exclusion criteria: the gold standard of CD diagnosis was not valid enough, such as using C-reactive protein only; the contrast agent was not taken orally or was absorbable; and articles without enough data to extract TP, FP, FN, and TN.

2.3. Data extraction

Two investigators independently extracted data from eligible articles. When any discrepancy appeared, we made a consensus by discussion. The following items were extracted from each article: author, year of publication, number of patients, sex, median age, ultrasound system, duration, contrast agents, gold standard, TP, FP, FN, and TN, and so forth.

2.4. Statistical methods

To evaluate the accuracy of SICUS for CD diagnosis and CD complication assessment, we integrated TP, FP, FN, TN into the pooled estimates of sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR), all given with 95% confidence intervals (CIs).

The heterogeneity of all the eligible studies was assessed using the \(\chi^2\) test (heterogeneity \(\chi^2\)-Qexp) and the consistency index (I\(^2\)). When significant heterogeneity existed, the random-effect model was applied,\[18\] otherwise we used the fixed-effect model (Mantel-Haenszel method). The pooled DOR was calculated as \((\text{TP} \times \text{TN})/(\text{FP} \times \text{FN})\).[19]

Publication bias was examined by Deeks’ funnel plot asymmetry test, and \(P > 0.05\) was considered as no potential publication bias.\[20\] All the above statistical analyses were conducted using STATA 12.0 (STATA Corporation, College
Table 1

Summary characteristics of the included studies.

| First author           | Country  | N (M) | Age (Mean) | US system | Contrast agents | Amount of contrast agent | Duration | Performer | Gold standard | Main variable for diagnosis |
|------------------------|----------|-------|------------|-----------|-----------------|--------------------------|----------|-----------|---------------|-----------------------------|
| Cittadini et al 2001   | Italy    | 43 (25)| 40.5 (M)/41.3 (F) | MACRO-P 1, Prometfarm, Milan | PEG-ELS | 500mL | >30 min | Two sonographers | BE | Intestinal wall thickness > 3 mm |
| Parente et al 2004     | Italy    | 102 (62)| 37.3       | Aoka Prosound 5000; Hitachi 6500 | PEG 3350 | 624mL (500–800 mL) | 31.4 min (20–60 min) | Two sonographers | BE/Ileocolonoscopy | Intestinal wall thickness > 4 mm |
| Pallotta et al 2005    | Italy    | 148 (70)| 12–89      | Toshiba Tosbee | PEG (Prometfarm, Milano, Italy) | 370mL (200–500 mL) | 30 min (12–90 min) | One sonographer | Surgical findings/final diagnosis | Intestinal wall thickness > 3 mm |
| Biancone et al 2007    | Italy    | 22 (11)| 33         | Hitachi, EUB 6500, Japan | PEG (Prometfarm, Milano, Italy) | 375mL (250–500 mL) | 40 min (35–90 min) | One sonographer | Ileocolonoscopy | Intestinal wall thickness > 3 mm |
| Castilgione et al 2008 | Italy    | 43 (24)| 38         | Aoka SSD-1700 | PEG 3350 | 750mL | 30 min | One sonographer | Endoscopy | Intestinal wall thickness > 3 mm |
| Calabrese et al 2009   | Italy    | 72 (34)| 44         | Hitachi, EUB 6500, Japan | PEG (Prometfarm, Milano, Italy) | 375mL (250–500 mL) | 40 min (35–90 min) | One sonographer | Ileocolonoscopy | Intestinal wall thickness > 3 mm |
| Chatu et al 2012       | UK       | 143 (64)| 36 (F)     | Toshiba, Japan; GE Healthcare, USA | PEG | 375mL (250–500 mL) | 30 min | One sonographer | Final diagnosis | Intestinal wall thickness > 3 mm |
| Pallotta et al 2012    | Italy    | 49 (28)| 37.7       | Toshiba Tosbee | PEG (Prometfarm, Milano, Italy) | 375mL (250–500 mL) | 45 min (20–120 min) | One sonographer | Final diagnosis | Intestinal wall thickness > 3 mm |
| Onali et al 2012       | Italy    | 15 (6) | 44         | Hitachi, EUB 6500, Japan | PEG (Prometfarm, Milano, Italy) | 375mL (250–500 mL) | NR | One sonographer | Surgical pathology | Intestinal wall thickness > 3 mm |
| Calabrese et al 2013   | Italy    | 59 (29)| 41         | Esaote, My Lab Twice, Italy | PEG | 375mL (250–500 mL) | 40 min (35–90 min) | One sonographer | CT enteroclysis | Intestinal wall thickness > 3 mm |
| Pallotta et al 2013    | Italy    | 51 (31)| 15         | Toshiba, Tokyo, Japan | PEG (Giuliani, Milano, Italy) | 125–250 mL | 45 min (40–90 min) | One sonographer | SBFT/Endoscopy | Intestinal wall thickness > 3 mm |
| Kumar S. et al 2014    | USA      | 25 (12)| 27.9       | Toshiba, Japan; GE Healthcare, USA | PEG | 1000 mL | 30 min | One sonographer | Surgical findings | Intestinal wall thickness > 3 mm |
| Aloi et al 2015        | Italy    | 34 (23)| 12.2       | Toshiba Medical Systems, Tochigi, Japan | PEG | 125–250 mL | 15 min | One sonographer | Ileocolonoscopy | Intestinal wall thickness > 3 mm |

BE = barium enteroclysis, F = female, M = male, N = patients number, NR = not reported, PEG = polyethylene glycol, SBFT = small-bowel follow-through.
Station, TX) and Meta-Disc 1.4 (Cochrane Colloquium, Barcelona, Spain).

2.5. Quality assessment

A quality assessment tool for diagnostic accuracy studies, Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2), was used to assess the quality of the included studies. Each item is rated “yes,” “no,” or “unclear.” The assessment was measured using Review Manager 5.3 (Copenhagen, Sweden).

3. Results

3.1. Included studies

As is shown in Fig. 1, the initial search yielded a total of 279 articles. After screening titles and abstracts, we excluded 260 because they were either review articles (n = 47), letter to the editor (n = 2), case reports (n = 2), irrelevant to SICUS (n = 209). After the full-text review of the remaining 19 potential candidate studies, 6 were ruled out for insufficient data. Finally 13 articles were considered eligible.[2,11–13,22–30]

3.2. Study characteristics

We listed the main characteristics of the 13 eligible studies in Table 1. The articles were published between 2001 and 2015. The number of the patients in each study ranged from 13 to 148. The contrast agent of all the 13 studies was polyethylene glycol (PEG), which was nonabsorbable and was taken orally. Intestinal wall thickness was the main diagnostic variable for all studies. Of the 13 studies, 12 used 3 mm as the cutoff value while Parente et al[26] used 4 mm.

3.3. Detection of small-bowel lesions

The pooled sensitivity and specificity of the eligible studies were 0.883 (95% CI 0.847–0.913) and 0.861 (95% CI 0.828–0.890), respectively (Fig. 2A and B). The PLR and NLR for SICUS were 5.593 (95% CI 3.317–9.430, I² = 77.5%) and 0.186 (95% CI 0.106–0.326, I² = 77.3%), respectively (Fig. 2C and D). The pooled DOR was 39.123 (95% CI 20.014–76.476) (Fig. 2E).

Summary receiver operating characteristic (SROC) curves for the diagnostic value of SICUS in the detection of small-bowel lesions are illustrated in Fig. 3. The overall area under the curve (AUC) of SROC was 0.9273 (standard error: 0.0152).

3.4. Subgroup analysis

Of the 13 studies enrolled in our meta-analysis, 2 studies[27,30] assessed recurrence of CD, 2 studies[24,25] detected active small-bowel CD. The pooled sensitivity and specificity of SICUS in detecting recurrence of CD were 0.899 (95% CI 0.817–0.953) and 0.808 (95% CI 0.606–0.934), respectively. The pooled sensitivity and specificity for the assessment of active small-bowel CD were 0.885 (95% CI 0.698–0.976) and 0.864 (95% CI 0.651–0.971).

Data from 2 studies[11,24] were detailed enough for us to divide the sites of CD bowel lesions into proximal and distal small intestine subgroup. The pooled sensitivities of SICUS in detecting proximal and distal small intestine lesions were 0.903 (95% CI 0.742–0.980) and 0.968 (95% CI 0.833–0.999). Pooled specificities were 0.929 (95% CI 0.827–0.980) and 0.857 (95% CI 0.572–0.982).

Another subgroup analysis was performed for the accuracy of SICUS for the differentiation of CD-related complications. We analyzed the differentiation accuracy of SICUS in CD
complications, including stricture (n = 5), dilation above stricture (n = 2), abscess (n = 1), and fistula (n = 4). The pooled sensitivity and specificity were 0.883 and 0.861 in the definition of stricture, 0.895 and 0.683 for detecting dilation, 0.875 and 0.962 for abscess assessment, and 0.778 and 0.942 for fistula detection (Table 2).

3.5. Quality assessment

The quality of the 13 eligible studies, as assessed according to the QUADAS criteria, is reported in Fig. 4A and B.

3.6. Publication bias

The evaluation of publication bias of the eligible studies was performed using STATA 12.0 (Fig. 5). Results showed that no significant publication bias existed.

4. Discussion

To the best of our knowledge, this is the first study to evaluate the diagnostic accuracy of SICUS for the detection and assessment of CD. Unlike other inflammatory bowel disease, CD may involve any part of the digestive tract, from oral cavity to rectum, and small intestine is the most predilection site of CD. Lesions of CD are discontinuous and jumpy. Therefore, it is important to detect sites and numbers of lesion precisely, especially for surgical purpose. The sensitivity, specificity, and DOR of SICUS in detecting small-bowel lesions were 0.883, 0.861, and 39.123, respectively, and the area under the curve (AUC) of SROC was 0.9273, which indicated that it is reliable in assessing small-bowel lesions. Moreover, SICUS represented substantial sensitivity and specificity in proximal and distal small-intestine lesion according to our subgroup analyses.

One of the most significant characteristics of CD is its high recurrence rate. Rutgeerts’ studies[31,32] showed that CD patients suffered from a recurrence rate of 50% to 90% 1 year after surgery and what makes CD an intractable disease to manage is that recurrence may happen earlier before clinical symptoms show up. Therefore, early detection of the recurrence is essential. Negative SICUS findings could help prove that the patients are unlikely to have recurrence regarding the substantial risk of CD bowel lesions (Table 2).

### Table 2

| Subgroups                          | No. of studies | SEN (95% CI) | SPE (95% CI) | PLR (95% CI) | NLR (95% CI) | DOR (95% CI) | AUC (SE) |
|------------------------------------|----------------|--------------|--------------|--------------|--------------|--------------|----------|
| Detecting small-bowel lesions      | 13             | 0.883 (0.847–0.913) | 0.861 (0.828–0.890) | 5.593 (3.117–9.430) | 0.186 (0.106–0.326) | 39.123 (20.014–76.476) | 0.9273 (0.0152) |
| Detecting recurrence of CD         | 2              | 0.899 (0.817–0.953) | 0.808 (0.606–0.934) | 4.218 (0.042–427.619) | 0.214 (0.095–0.482) | 16.969 (0.587–490.96) | 0.8480 (0.1108) |
| Detecting active small-bowel CD    | 2              | 0.885 (0.698–0.976) | 0.864 (0.651–0.971) | 6.542 (2.267–18.909) | 0.135 (0.046–0.338) | 52.327 (8.583–319.01) | 0.9791 (0.0642) |
| Sites of CD bowel lesions           |                |              |              |              |              |              |          |
| Proximal small intestine lesions    | 2              | 0.903 (0.742–0.980) | 0.929 (0.827–0.980) | 12.147 (2.020–73.047) | 0.119 (0.044–0.321) | 94.958 (15.792–570.70) |          |
| Distal small intestine lesions      | 2              | 0.968 (0.833–0.999) | 0.857 (0.573–0.982) | 5.045 (1.054–15.394) | 0.050 (0.012–0.293) | 89.826 (10.320–781.87) |          |
| Stenosis                            | 2              | 0.816 (0.657–0.923) | 0.818 (0.746–0.876) | 5.528 (3.634–48.216) | 0.297 (0.009–9.939) | 16.458 (0.218–1241.0) | 0.9788 (0.0716) |
| Differentiation of CD-related        |                |              |              |              |              |              |          |
| complications                       | 5              | 0.895 (0.752–0.971) | 0.681 (0.500–0.797) | 2.588 (1.768–3.789) | 0.189 (0.078–0.456) | 14.265 (4.590–44.287) | 0.8480 (0.1108) |
| Stenosis                            | 3              | 0.875 (0.617–0.964) | 0.926 (0.892–0.952) | 11.100 (2.197–56.071) | 0.215 (0.085–0.544) | 97.141 (14.945–353.67) | 0.9417 (0.0470) |
| Fistula                             | 4              | 0.778 (0.573–0.914) | 0.942 (0.859–0.984) | 12.188 (4.600–32.294) | 0.275 (0.138–0.548) | 50.848 (12.780–202.31) | 0.9791 (0.0642) |

AUC (SE)=area under the curve (standard error). CD =Crohn disease; DOR=diagnostic odds ratio; NLR=negative likelihood ratio; PLR=positive likelihood ratio; SEN=sensitivity; SPE=specificity.
Management strategies of CD patients with different kinds of complications differ a lot. Accurate locating, characterizing, numbering, and grading of the complications are quite crucial for preoperative schemes making. Such assessment is also a necessity before endoscopic examination to avoid unnecessary extra trauma or even the retention of capsule endoscopy. According to our analysis, SICUS turns out to be a reliable modality in CD complication assessment. Of all the complications, SICUS shows a prominent ability in abscess assessment with relatively higher sensitivity and specificity, and if detected, abscess should be handled either by surgery or pharmaceuticals.

SICUS has some merits over the first-line imaging modalities. As we all know, endoscopy is the most direct equipment to visualize small-bowel lesion, and is considered to be the golden standard for intestinal disease diagnosis. However, the invasiveness might increase the risk of penetration of bowel wall and the extremely discomfort experience might lead to lack of cooperation of patients with relapsing diseases such as CD, who need regular follow-up. Also, endoscopy examination could not be accomplished if strictures exist. Most importantly, transmural condition such as bowel wall thickness and stiffness, and perienteric condition such as lymph nodes and mesenteric tissue could not be represented by endoscopy. Compared with computed tomography and magnetic resonance imaging, SICUS provides a dynamical real-time visualization of small-bowel lesions, and the amount of oral contrast agent taken by the patients for SICUS is far less. Therefore, it is worthwhile to recommend SICUS in clinical application of CD assessment.

There are still some limitations of our study. Firstly, the proper application of SICUS is to a high degree user-dependent which relies on the personal expertise of operators, but the introduction of the oral contrast seems to increase the accuracy of diagnosis. Secondly, more large-sampled, multicentered researches are still expected in the future to confirm our results.

To sum up, SICUS is not only accurate enough but also informative enough to make a complete assessment about the location, extent, number, and almost all kinds of complications in CD small-bowel lesions. What is more, considering the non-invasiveness, radiation-free, well-tolerance, and relatively low cost characteristics of SICUS, SICUS is also the most suitable choice in frequent CD follow-up.

References

[1] Maconi G, Carsana L, Fociani P, et al. Small bowel stenosis in Crohn’s disease: clinical, biochemical and ultrasonographic evaluation of histological features. Aliment Pharmacol Ther 2003;18:749–56.
[2] Calabrese E, Zorzi F, Onali S, et al. Accuracy of small-intestine contrast ultrasonography, compared with computed tomography enteroclysis, in characterizing lesions in patients with Crohn’s disease. Clin Gastroenterol Hepatol 2013;11:950–5.
[3] Cosnes J, Cattan S, Blain A, et al. Long-term evolution of disease behavior of Crohn’s disease. Inflamm Bowel Dis 2002;8:244–50.
[4] Panis J, Bouzas R, Chaparro M, et al. Systematic review: the use of ultrasonography, computed tomography and magnetic resonance imaging for the diagnosis, assessment of activity and abdominal complications of Crohn’s disease. Aliment Pharmacol Ther 2011;34:125–45.
[5] Parente F, Maconi G, Bollani S, et al. Bowel ultrasound in assessment of Crohn’s disease and detection of related small bowel strictures: a prospective comparative study versus x ray and intraoperative findings. Gut 2002;50:490–5.
[6] Petruzziello C, Calabrese E, Onali S, et al. Small bowel capsule endoscopy vs conventional techniques in patients with symptoms highly compatible with Crohn’s disease. J Crohns Colitis 2011;5:139–47.
[7] Chiorean L, Schreiber-Dietrich D, Braden B, et al. Transabdominal ultrasound for standardized measurement of bowel wall thickness in normal children and those with Crohn’s disease. Med Ultrason 2014; 16:319–24.

[8] Mos, Holt G, Iuthas S, et al. The sensitivity of transabdominal ultrasound in the diagnosis of ureterolithiasis. Med Ultrason 2010;12: 188–97.

[9] Calabrese E, La Seta F, Buccellato A, et al. Crohn’s disease: a comparative prospective study of transabdominal ultrasonography, small intestine contrast ultrasonography, and small bowel enema. Inflamm Bowel Dis 2005;11:139–45.

[10] Rodgers PM, Verma R. Transabdominal ultrasound for bowel evaluation. Radiol Clin North Am 2013;51:133–48.

[11] Pallotta N, Civitelli F, Di NG, et al. Small intestine contrast ultrasonography (SICUS) in the diagnosis of small intestine lesions. Ultrasound Med Biol 2012;38:74–84.

[12] Pallotta N, Baccini F, Montesani G, et al. Small intestine contrast ultrasonography (SICUS) for the detection of small bowel complications in crohn’s disease: a prospective comparative study versus intraoperative findings. Inflamm Bowel Dis 2012;18:74–84.

[13] Pallotta N, Tomes E, Viscido A, et al. Small intestine contrast ultrasonography: an alternative to radiology in the assessment of small bowel disease. Inflamm Bowel Dis 2005;11:146–53.

[14] Pallotta N, Baccini F, Corazzari E. Small intestine contrast ultrasonography (SICUS) in the diagnosis of small intestine lesions. Ultrasound Med Biol 2001;27:335–41.

[15] Hashash JG, Regueiro MD. The evolving management of postoperative Crohn’s disease. Expert Rev Gastroenterol Hepatol 2012;6:637–48.

[16] Pelouquin JM, Pardi DS, Sandborn WJ, et al. Diagnostic ionizing radiation exposure in a population-based cohort of patients with inflammatory bowel disease. Am J Gastroenterol 2008;103:2015–22.

[17] Macconi G, Bolzioni E, Giussani A, et al. Accuracy and cost of diagnostic strategies for patients with suspected Crohn’s disease. J Crohns Colitis 2014;8:1684–92.

[18] Dinnis J, Deeks J, Kirby J, et al. A methodological review of how heterogeneity has been examined in systematic reviews of diagnostic test accuracy. Health Technol Assess 2005;9:1–13, iii.

[19] Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst 1959;22:719–48.

[20] Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. J Clin Epidemiol 2005;58:882–93.

[21] Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529–36.

[22] Onali S, Calabrese E, Petruzziello C, et al. Small intestine contrast ultrasonography vs computed tomography enteroclysis for assessing ileal Crohn’s disease. World J Gastroenterol 2012;18:6088–95.

[23] Kumar S, Hakim A, Alexakis C, et al. Small intestinal contrast ultrasonography for the detection of small bowel complications in Crohn’s disease: correlation with intraoperative findings and magnetic resonance enterography. J Gastroenterol Hepatol 2015; 30:86–91.

[24] Alois M, Di NG, Romano G, et al. Magnetic resonance enterography, small-intestine contrast US, and capsule endoscopy to evaluate the small bowel in pediatric Crohn’s disease: a prospective, blinded, comparison study. Gastrointest Endosc 2015;81:420–7.

[25] Chatu S, Pilcher J, Saxena SK, et al. Diagnostic accuracy of small intestine ultrasonography using an oral contrast agent in Crohn’s disease: comparative study from the UK. Clin Radiol 2012;67:553–9.

[26] Parente F, Greco S, Molteni M, et al. Oral contrast enhanced bowel ultrasonography in the assessment of small intestine Crohn’s disease. A prospective comparison with conventional ultrasound, x ray studies, and ileocolonoscopy. Gut 2004;53:1652–7.

[27] Calabrese E, Petruzziello C, Onali S, et al. Severity of postoperative recurrence in Crohn’s disease: correlation between endoscopic and sonographic findings. Inflamm Bowel Dis 2009;15:1635–42.

[28] Cittadini G, Giasotto V, Garlaschi G, et al. Transabdominal ultrasonography of the small bowel after oral administration of a non-absorbable anechic solution: comparison with barium enteroclysis. Clin Radiol 2001;56:225–30.

[29] Biancone L, Calabrese E, Petruzziello C, et al. Wireless capsule endoscopy and small intestine contrast ultrasonography in recurrence of Crohn’s disease. Inflamm Bowel Dis 2007;13:1256–65.

[30] Castiglione F,ucci L, Pesce G, et al. Oral contrast-enhanced sonography for the diagnosis and grading of postsurgical recurrence of Crohn’s disease. Inflamm Bowel Dis 2008;14:1240–5.

[31] Rutgeerts P, Geboes K, Vantrappen G, et al. Natural history of recurrent Crohn’s disease at the ileocolonic anastomosis after curative surgery. Gut 1984;25:665–72.

[32] Rutgeerts P, Geboes K, Vantrappen G, et al. Predictability of the postoperative course of Crohn’s disease. Gastroenterology 1990;99: 956–63.

[33] Nyahanga C, Kochhar G, Costa G, et al. Management of Crohn’s disease in the new era of gut rehabilitation and intestinal transplantation. Inflamm Bowel Dis 2016;22:1763–76.

[34] D’Inca R, Caccaro R. Measuring disease activity in Crohn’s disease: what is currently available to the clinician. Clin Exp Gastroenterol 2014; 7:151–61.

[35] Waterland P, Athanasiou T, Patel H. Post-operative abdominal complications in Crohn’s disease in the biological era: Systematic review and meta-analysis. World J Gastrointest Surg 2016;8:274–83.

[36] Mosli M, Al BM, Al-Judabhi B, et al. Advances in the diagnosis and management of inflammatory bowel disease: challenges and uncertainties. Saudi J Gastroenterol 2014;20:81–101.

[37] Lightner AL, Pemberton JH, Loftus EJ. Crohn’s disease of the ileoanal pouch. Inflamm Bowel Dis 2016.

[38] El-Assmar K, El-Shafei E, Abdel-Latif M, et al. Surgical aspects of inflammatory bowel disease. Inflamm Bowel Dis 2005;11:139–46.

[39] Bennett JL, Ha CY, Efron JE, et al. Optimizing perioperative Crohn’s disease management: role of coordinated medical and surgical care. World J Gastroenterol 2015;21:1182–8.

[40] Goetz M, Neurath MF. Imaging techniques in inflammatory bowel disease: recent trends, questions and answers. Gastroenterology 2009;137(suppl 3):S174–82.

[41] Born C, Nagel B, Leinsinger G, et al. MRI with oral filling in patients with chronic inflammatory bowel diseases. Radiologie 2003;43:34–42.

[42] Maccioni F, Ali AN, Mazzamurro F, et al. Detection of Crohn disease lesions of the small and large bowel in pediatric patients: diagnostic value of MR enterography versus reference examinations. AJR Am J Roentgenol 2014;203:W335–42.