Retrospective Study

Essential role of small bowel capsule endoscopy in reclassification of colonic inflammatory bowel disease type unclassified

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Abstract

AIM
To evaluate the role of small bowel capsule endoscopy (SBCE) on the reclassification of colonic inflammatory bowel disease type unclassified (IBDU).

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INTRODUCTION

The differential diagnosis of Crohn’s disease (CD) and ulcerative colitis (UC) relies on a combination of clinical, analytical, imaging, endoscopic and histologic data[1,2]. In 5% of patients with inflammatory bowel disease limited to the colon is not possible to establish a definitive diagnosis into CD or UC[3]. In 1978, Price introduced the concept of indeterminate colitis to describe cases in which colonic resections had been undertaken for chronic inflammatory bowel disease but a definitive diagnosis of either of UC and CD was not possible[4]. In 2005, the Montreal Working Party proposed that the term “indeterminate colitis” should be reserved for patients in whom surgical specimen is available and the term “colonic IBD type unclassified” (IBDU) for patients with no surgical specimen available and for whom the endoscopy is inconclusive and histology reveals chronic inflammation with absence of definite diagnostic features of either CD or UC[5]. Actually, for most patients, IBDU represents a temporary diagnosis, as it has been estimated that 80% of them will be reclassified to either CD or UC within 8 years[6].

The correct diagnosis of inflammatory bowel disease is extremely important to define prognosis, therapeutic orientation and surgical intervention[7,8]. Since Small Bowel Capsule Endoscopy (SBCE) enables a direct endoscopic visualization of throughout the small intestine with higher diagnostic yield compared to conventional endoscopy or imaging studies[9,10], it may be expected to contribute for the reclassification of IBDU. We report a multicenter study that aimed to evaluate the role of SBCE to reclassify patients with IBDU.

MATERIALS AND METHODS

We performed a multicenter study including consecutive patients undergoing SBCE between 2002 and 2014 for IBDU, ASCA negative/pANCA negative.

All patients had undergone an ileocolonoscopy prior to SBCE. Inclusion criteria were as follows: Patients with clinical features of chronic IBD, without previously known small bowel involvement, in whom endoscopic type and/or distribution of lesions did not allow a definite diagnosis of CD or UC, microscopy indicating active and patchy transmucosal chronic inflammation with minimal or moderate architectural distortion and absence of unequivocal diagnostic features for either CD or UC, after exclusion of infectious colitis[5]. Subjects were excluded from entering the study if they had nonsteroidal anti-inflammatory drugs intake within 4 wk prior to capsule endoscopy[11], clinical or imaging evidence of bowel stenosis or occlusion, or a follow-up of less than 12 mo.

Patients underwent SBCE with PillCam® SB1/SB2/
RESULTS

A total of 36 consecutive patients with IBDU underwent SBCE procedures between October 2002 and August 2014, with a mean follow-up before the exam of 30 mo (1-108 mo).

The mean age of patients at the time of diagnosis of IBDU and at time of SBCE was 33 years and 36 years, respectively, with 58% being of female gender.

Table 1 summarizes the demographic and clinical characteristics of the study population. The capsule was ingested without difficulty by all of the 36 subjects. There were no cases of capsule retention or reported adverse events in any of the subjects included in this study.

A complete small-bowel examination was achieved in 97.2% of studies. The mean follow-up after SBCE was 52 mo (12-156 mo).

At the moment of SBCE thirty four patients had clinically active disease and received anti-inflammatory treatment, as summarized in Tables 2 and 3. SBCE revealed small bowel lesions in 13 of patients (36.1%) and 23 (63.9%) patients had no lesions detected on SBCE. The distribution of the lesions in the small intestine were as follows: Two patients had multiple ulcersations (n ≥ 8) throughout the entire small bowel, 1 patients had ulcerations in first and second tertiles, 1 patient had ulcerations only in the second tertile, 5 patients had multiples ulcerations in the third tertile. In 4 patients the capsule revealed subtle findings of focal edema in a single short segment of the small bowel (Table 2).

Nine patients (25%) had inflammatory lesions considered significant (LS ≥ 135) and consistent with a diagnosis of CD (Table 2). In 4 of those patients (44.4%) a subsequent ileocolonoscopy showed, by this occasion, lesions compatible with CD in the terminal ileum and histology of colonic lesions was unspecific. In the remaining 5 patients (55.6%), the histology of colonic lesions was unspecific and ileoscopy detected no lesions.

In 27 patients (75%), the SBCE revealed no significant inflammatory activity (LS < 135). Among these patients, no lesion was detected in 23 patients and subtle lesions were found in 4 cases (Tables 2 and 3).

One patient (4.3%) with no lesions at SBCE had on follow-up a subsequent ileoscopy which revealed lesions compatible with CD (Table 3).

In 12 of 23 patients (52.2%) with no lesions at SBCE, a diagnosis of UC was established on follow-up, on average 38.3 mo after SBCE (Table 3). Four patients (25%) with a final diagnosis of UC had subtle lesions (focal edema) on SBCE (Table 2). In all of these patients the endoscopic and histological findings were consistent with the diagnosis of UC, which remained in clinical and analytical remission on follow-up.

Ten patients (27.8%) remained with a diagnosis of IBDU after an mean follow-up of 42 mo (Table 3). Considering the endoscopic criterion of significant inflammatory activity to predict a diagnosis of CD, using a cut-off for LS ≥ 135 [13], it would result in no false positive and only one false negative examinations, corresponding to a sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 90%, 100%, 100% and 94%, respectively.

In 6 of 9 patients (66.7%) with significant inflammatory activity detected in SBCE, the treatment during the follow-up was escalated to immunosuppressive drugs or biological therapy (Table 2). In 3 of 16 (18.8%) patients with a definitive diagnosis of UC and in 4 of 10 (40%) patients who remained with a diagnosis of IBDU on follow-up, a new IBD medication was introduced during the follow-up.

The start of treatment with thiopurines and/or biologics in patients who were previously naive to those medications

| Table 1 Demographics and clinical characteristics of the inflammatory bowel disease type unclassified patients |
|-------------------------------------------------|
| No. of patients, n (%) | Gender | Age (yr) (mean ± SD) at diagnosis | Age (yr) (mean ± SD) at SBCE | Device (no. patients), n (%) | PillCam® SB1 | PillCam® SB2 | PillCam® SB3 | Mirocam® | Endocapsule® | Gastric transit time (min) | Small bowel transit time (min) | Capsule retention | Follow-up (mo) before SBCE | Follow-up (mo) after SBCE |
|-------------------------|--------|---------------------------------|-----------------------------|--------------------------------|-------------|-------------|-------------|----------|-------------|--------------------------|-----------------------------|-------------------|--------------------------|--------------------------|
| 36 (100)                | Male   | 33.2 ± 13.1 (15-64)             | 35.9 ± 13.3 (18-64)         | 13 (36.1)                      | 16 (44.4)  | 1 (2.8)     | 5 (13.9)    | 1 (2.8)  | 30.2 ± 29.9 (1-108) | 290.4 ± 101.5 (52-480) | 0                  | 32.0 ± 29.9 (1-108) | 51.9 ± 40.5 (12-156) |
| 21 (58.3)               | Female | 30.2 ± 13.3 (18-64)             | 33.2 ± 13.1 (15-64)         | 16 (44.4)                      | 33.2 ± 13.1 (15-64) | 1.25 (2.8) | 5 (13.9)    | 1 (2.8)  | 36 (100)        | 36 (100)                  | 0                  | 32.0 ± 29.9 (1-108) | 51.9 ± 40.5 (12-156) |

IBDU: Inflammatory bowel disease type unclassified; SB: Small bowel; SBCE: Small bowel capsule endoscopy.
occurred in 6/9 (66.7%) vs 5/27 (18.5%) patients with or without significant inflammatory activity detected at the SBCE, respectively ($P = 0.012$).

**DISCUSSION**

Ileocolonoscopy remains the first line exam to achieve the diagnosis in patients with suspected IBD.[14] Nonetheless, ileocolonoscopy can miss CD and result in false negative results due to skip lesions throughout the terminal ileum.[15]

Upper endoscopy, SBCE, computed tomography enterography (CTE) and magnetic resonance enterography (MRE) can provide important information and may be useful to establish a definitive diagnosis.[9,10]

In patients with suspected CD and negative ileocolonoscopy findings, recent European guidelines recommends SBCE as the next diagnostic exam for small bowel investigation, in the absence of obstructive symptoms or known stenosis.[11]

SBCE has proven its superiority in identifying inflammatory lesions consistent with the diagnosis of CD in the small intestine when compared to CTE[9,16] or MRE[10], thus it has assumed an important role on the evaluation of patients with suspected CD[13,17-19], having a high negative predictive value for the absence of significant

### Table 2 Clinical characteristics and outcome of the patients with positive small bowel capsule

| Case | Sex | Age | SBCE Findings | LS  | Treatment pre-SBCE | Treatment post-SBCE | Diagnostic at follow-up |
|------|-----|-----|---------------|-----|-------------------|---------------------|------------------------|
| 1    | F   | 38  | Multiple jejuno-ileal ulcerations | 1404 | 5ASA | 5 ASA + AZT | CD |
| 2    | F   | 18  | Ulcer ($n = 1$) and edema of 3° tertile | 143  | AZT | Anti-TNF | CD |
| 3    | M   | 23  | Ulcer ($n = 1$) and edema of 3° tertile | 143  | 5ASA | 5ASA | CD |
| 4    | F   | 20  | Ulcerations ($n = 2$) and edema of 3° tertile | 233  | 5ASA | 5ASA | CD |
| 5    | F   | 33  | Ulcer ($n = 3$) of 2° tertile | 225  | 5ASA | 5ASA | CD |
| 6    | F   | 19  | Multiple ulcerations and edema of 3° tertile | 908  | 5ASA | AZT | CD |
| 7    | M   | 60  | Focal edema of 1° tertile | 8    | No treatment | 5ASA | UC |
| 8    | M   | 22  | Multiple jejuno-ileal ulcerations | 2880 | 5ASA | 5ASA + AZT | CD |
| 9    | F   | 32  | Multiple ulcerations and edema of 3° tertile | 908  | 5ASA | AZT | CD |
| 10   | F   | 27  | Focal edema of 3° tertile | 8    | Prednisolone | anti-TNF | UC |
| 11   | F   | 47  | Focal edema of 2° tertile | 8    | 5ASA | 5ASA | UC |
| 12   | F   | 31  | Ulceration and edema of 1° ($n = 5$) and 2° tertile ($n = 6$) | 879  | 5ASA + Prednisolone | AZT | CD |
| 13   | M   | 44  | Focal edema of 3° tertile | 8    | 5ASA | 5ASA | UC |

5ASA: Mesalamine; anti-TNF: Anti-tumor necrosis factor drug; AZT: Azathioprine; CD: Crohn’s disease; SBCE: Small bowel capsule endoscopy; LS: Lewis score; UC: Ulcerative colitis.

### Table 3 Clinical characteristics and outcome of the patients with negative small bowel capsule

| Case | Sex | Age | Treatment pre-SBCE | Treatment post-SBCE | Diagnostic at follow-up |
|------|-----|-----|-------------------|---------------------|------------------------|
| 1    | M   | 45  | 5ASA | 5ASA | IBDU |
| 2    | F   | 15  | Prednisolone, 5ASA | 5ASA | UC |
| 3    | F   | 27  | AZT, 5ASA | AZT | UC |
| 4    | F   | 26  | 5ASA | 5ASA | UC |
| 5    | M   | 31  | 5ASA | 5ASA | IBDU |
| 6    | F   | 34  | 5ASA | 5ASA | IBDU |
| 7    | M   | 21  | 5ASA | 5ASA | IBDU |
| 8    | F   | 22  | 5ASA | 5ASA, AZT | IBDU |
| 9    | F   | 56  | 5ASA | 5ASA | UC |
| 10   | F   | 27  | AZT, anti-TNF | AZT, anti-TNF | UC |
| 11   | F   | 30  | 5ASA | 5ASA | UC |
| 12   | M   | 24  | 5ASA | 5ASA | CD |
| 13   | M   | 49  | 5ASA | 5ASA | UC |
| 14   | M   | 43  | 5ASA | 5ASA | UC |
| 15   | F   | 30  | 5ASA + AZT | Anti-TNF | IBDU |
| 16   | M   | 24  | 5ASA | 5ASA | UC |
| 17   | F   | 20  | 5ASA | 5ASA | UC |
| 18   | M   | 55  | 5ASA | 5ASA | IBDU |
| 19   | F   | 31  | 5ASA | 5ASA, AZT, Anti-TNF | UC |
| 20   | F   | 48  | 5ASA | 5ASA, AZT | IBDU |
| 21   | M   | 64  | 5ASA | 5ASA | UC |
| 22   | M   | 44  | No treatment | 5ASA | IBDU |
| 23   | M   | 53  | 5ASA | 5ASA | IBDU |

5ASA: Mesalamine; anti-TNF: Anti-tumor necrosis factor drug; AZT: Azathioprine; CD: Crohn’s disease; SBCE: Small bowel capsule endoscopy; UC: Ulcerative colitis.
inflammatory activity\(^{13}\). However, there is still limited evidence for the role of SBCE in patients with IBDU\(^{13}\).

Most studies\(^{20-22}\) used the non-validated diagnostic criteria for small-bowel CD proposed by Mow et al\(^{23}\) (presence of more than three ulcerations). Meanwhile, two scoring systems have been developed to standardize the quantification of inflammatory activity in the small bowel. The Capsule Endoscopy Crohn’s Disease Activity Index (CECDAI) is based on evaluation of the following parameters: Inflammation, extent of disease and presence of a stricture, while the LS evaluates villous appearance, ulcers and strictures\(^{12}\). The LS has shown a better performance than the CECDAI at describing small-bowel inflammation\(^{24}\).

Indeed, LS has been shown a strong interobserver agreement for the determination of the inflammatory activity, and it is validated for the reporting small-bowel inflammatory activity\(^{25,26}\).

In our study, the findings revealed by SBCE were consistent with a diagnosis of CD, based upon LS ≥ 135, in 9 of 36 (25%) of the subjects with IBDU, which is in line with the 16%-50% range described in other previous series\(^{20,22,27-29}\). An even higher percentage has been reported in pediatric patients\(^{14}\).

In the present study, 4 patients (25%) with final diagnosis of UC had subtle small bowel lesions, such as focal edema, without a significant inflammatory activity, LS < 135, and with clinical and analytical remission during follow-up. Indeed, previous studies already reported a significantly higher frequency of small-bowel lesions in UC patients as compared with that in the control healthy volunteers\(^{30}\). The significance of the presence of these lesions and the possible risk of misdiagnosis is still indeterminate\(^{31}\).

Although a negative SBCE study did not allow to definitely exclude a future diagnosis of small bowel CD, as further investigation and biopsies on follow-up led to a diagnosis of CD in one patient, the absence of significant inflammatory activity (LS < 135) in the small intestine actually allowed exclusion of CD in 94% of cases.

Based on our findings, SBCE may lead to reclassification of disease from suspected IBDU to definitive CD in 25% of cases. Furthermore, treatment with thiopurines and/or biologics was initiated more often in patients with significant inflammatory activity detected on SBCE (66.7% vs 18.5%, P = 0.012). This association suggests that capsule findings may be helpful in the clinical management of these patients, as already been proven in other series\(^{28,32-34}\).

There are some limitations of this study, including its retrospective design, a limited number of subjects, and no direct comparison of SBCE with alternative small-bowel diagnostic imaging; however, the last was not an aim of this study.

Nevertheless, to our knowledge this is one of the studies with larger number of patients included to evaluate this particular issue\(^{20,22,27-29}\).

There are no definite diagnostic criteria for IBDU, as it must be considered a provisional diagnosis until more information (clinical, endoscopic, radiologic or pathologic) or data on follow-up enable a definitive reclassification\(^{35}\). Mucosal biopsy samples before treatment can be useful to distinguish UC from CD, but this distinction is based primarily on the pattern, type and location (distribution) of the disease, rather than specific histological features, for which there is much overlap between the two diseases\(^{36}\). Therefore, SBCE has a valuable role in the reclassification of patients with IBDU, may also contribute to establish the strategy for clinical management, and should be performed in the undefined diagnosis, which IBDU represents, in order to contribute to a definite diagnosis.

**COMMENTS**

**Background**

Colonic inflammatory bowel disease type unclassified (IBDU) is defined as a chronic idiopathic inflammatory bowel disease limited to the colon, whose combination of clinical, analytical, imaging, endoscopic and histological elements does not allow a differential diagnosis between Crohn’s disease (CD) and ulcerative colitis.

**Research frontiers**

In patients with suspected CD and negative ileocolonoscopy findings, small-bowel capsule endoscopy (SBCE) is the next diagnostic exam for small-bowel investigation, in the absence of obstructive symptoms or known stenosis. Since SBCE enables a direct endoscopic visualization of throughout the small intestine, it may be expected to contribute for the reclassification of IBDU. However, the role of SBCE in IBDU has not been clearly established. In this study, the authors evaluate the role of SBCE on the reclassification of IBDU.

**Innovations and breakthroughs**

In this study, inflammatory activity on SBCE was objectively assessed by determining the Lewis score (LS). SBCE lead to reclassification of disease from IBDU to definitive CD in 25% of cases. Although a negative SBCE study did not allow to definitely exclude a future diagnosis of small bowel CD, as further investigation and biopsies on follow-up led to a diagnosis of CD in one patient, the absence of significant inflammatory activity (LS < 135) in the small intestine actually allowed exclusion of CD in 94% of cases.

**Applications**

This study suggests that SBCE is useful in the reclassification of patients with IBDU. Facing a patient with IBDU, a SBCE should be performed in order to diagnosis or exclude a CD.

**Peer-review**

This manuscript “Essential role of small bowel capsule endoscopy in reclassification of colonic inflammatory bowel disease type unclassified” is well written.

**REFERENCES**

1. Van Assele G, Dignass A, Panes J, Beaujargi J, Karagiannis J, Alie M, Ochsenkühn T, Orchard T, Rogler G, Lois E, Kupecinakas L, Mantzaris G, Travis S, Stange E. The second European evidence-based Consensus on the diagnosis and management of Crohn’s disease: Definitions and diagnosis. J Crohns Colitis 2010; 4: 7-27 [PMID: 21122488 DOI: 10.1016/j.crohns.2009.12.003]

2. Dignass A, Eliakim R, Magro F, Maasser C, Chowers Y, Geboes K, Mantzaris G, Reinisch W, Colombel JF, Vermeire S, Travis S, Lindsay JO, Van Assele G. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 1: definitions and diagnosis. J Crohns Colitis 2012; 6: 965-990 [PMID: 23040452 DOI: 10.1016/j.crohns.2012.04.011].
Monteiro S et al. Small bowel capsule endoscopy in IBDU patients

10.1016/j.crohns.2012.09.003

3 Odze R. Diagnostic problems and advances in inflammatory bowel disease. Mod Pathol 2003; 16: 347-358 [PMID: 12692200 DOI: 10.1097/01.mp.0000074647.8204.d1]

4 Price AB. Capsule endoscopy: the spectrum of non-specific inflammatory bowel disease--‘colitis indeterminate’. J Clin Pathol 1978; 31: 567-577 [PMID: 670413 DOI: 10.1136/jcp.31.6.567]

5 Silverman MS, Satsangi J, Ahmad T, Arroyo ID, Bernstein CN, Brandt CD, Burket ML, Caprilli R, Colombel JF, Gasche C, Ghebresaw K, Jewell DP, Karban A, Lotus EV, Peña AS, Riddell RH, Sachar DB, Schreiber S, Steinhardt AH, Targan SR, Vermeire S, Warren B. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol 2005; 19 Suppl A: 5A-36A [PMID: 16151544]

6 Meucci G, Bortoli A, Riccioli FA, Girelli CM, Radadli F, Rivolta R, Tarearella M. Frequency and clinical evolution of indeterminate colitis: a retrospective multi-center study in northern Italy. Gismii (Gruppo di Studio per le Malattie Infiammatorie Intestinali). Eur J Gastroenterol Hepatol 1999; 11: 909-913 [PMID: 10514127 DOI: 10.1002/ejgh.2009.12.002]

7 Dignass A, Van Assche G, Lindsay JO, Lémann M, Söderholm J, Colombel JF, Danese S, D’Hoore A, Gasull M, Gomollon F, Hommes DW, Michetti P, O’Morain C, Oresland T, Windsor A, Stange EF, Travis SP. The second European evidence-based consensus on the diagnosis and management of Crohn’s disease: Current management. J Crohns Colitis 2010; 4: 28-62 [PMID: 21122489 DOI: 10.1016/j.jcjc.2009.12.002]

8 Dignass A, Lindsay JO, Stamm A, Windsor A, Colombel JF, Alles M, D’Hares G, D’Hoore A, Mantzaris G, Novack G, Oresland T, Reimisch W, Sars M, Stange E, Vermeire S, Travis S, Van Assche G. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 2: current management. J Crohns Colitis 2012; 6: 991-1030 [PMID: 23040451 DOI: 10.1016/j.jcjc.2012.09.002]

9 Dionisio GM, Gurudu SR, Leighton JA, Leontiadis GI, Fleischer DE, Hara AK, Heigh RI, Shiff AD, Sharma VK. Capsule endoscopy has a significantly higher diagnostic yield in patients with suspected Crohn’s disease—diagnostic value and complications. Diagn Ther Endosc 2010; 2010: 101284 [PMID: 20811612 DOI: 10.1155/2010/101284]

10 Maunoury V, Savoye G, Bouracile A, Boulhnik Y, Jarry M, Sacher-Huvelin S, Ben Soussan E, Lerebours E, Galmiche JF, Colombel JF. Value of wireless capsule endoscopy in patients with indeterminate colitis (inflammatory bowel disease type unclassified). Inflamm Bowel Dis 2007; 13: 152-155 [PMID: 17206697 DOI: 10.1002/ibd.20060]

11 Lopes S, Figueiredo P, Fertello F, Freire P, Almeida N, Léria C, Gouveia H, Leitão MC. Capsule endoscopy in inflammatory bowel disease type unclassified and indeterminate colitis serologically negative. Inflamm Bowel Dis 2010; 16: 1663-1668 [PMID: 20848457 DOI: 10.1002/ibd.21249]

12 Mehdizadeh S, Chen G, Enayati PJ, Cheng DW, Han NJ, Shaye OA, Ippoliti A, Vasiliakas EA, Lo S, Papidakis KA. Diagnostic yield of capsule endoscopy in ulcerative colitis and inflammatory bowel disease of unclassified type (IBDU). Endoscopy 2008; 40: 30-35 [PMID: 18055645 DOI: 10.1055/s-2007-995359]

13 Mow WS, Lo SK, Targan SR, Dubinsky MC, Treyzon L, Abreu- Martin MT, Papidakis KA, Vasiliakas EA. Initial experience with wireless capsule enteroscopy in the diagnosis and management of inflammatory bowel disease. Clin Gastroenterol Hepatol 2004; 2: 31-40 [PMID: 15017630 DOI: 10.1016/s1543-5662(03)00289-1]

14 Koulouzidou A, Douglas S, Plevis JS. Lewis score correlates more closely with faecal calprotectin than Capsule Endoscopy Crohn’s Disease Activity Index. Dig Dis Sci 2007; 52: 987-993 [PMID: 22057284 DOI: 10.1007/s10620-011-1956-8]

15 Cotter J, Dias de Castro F, Magalhães J, Moreira MJ, Rosa B. Validation of the Lewis score for the evaluation of small-bowel Crohn’s disease activity. Endoscopy 2015; 47: 330-335 [PMID: 25412092 DOI: 10.1055/s-0034-1390894]

16 Rosa B, Moreira MJ, Rebelo A, Cotter J. Lewis score: a useful clinical tool for patients with suspected Crohn’s Disease submitted to capsule endoscopy. J Crohns Colitis 2012; 6: 692-697 [PMID: 22380899 DOI: 10.1016/j.crohns.2011.12.002]

17 Viazis N, Karanamios DG. Indeterminate colitis—the role of wireless capsule endoscopy. Aliment Pharmacol Ther 2007; 25: 859; author reply 860 [PMID: 17373927 DOI: 10.1111/j.1365-2036.2006.03527.x]

18 Kalla R, Mcalinden ME, Drew K, Sidhu R. Clinical utility of capsule endoscopy in patients with Crohn’s disease and inflammatory bowel disease unclassified. Eur J Gastroenterol Hepatol 2013; 25: 706-713 [PMID: 23325280 DOI: 10.1111/ejh.12230 DOI: 10.1097/MEG.0b013e32835d58b5]

19 Grañack IM, Cohen SA, Ephrah M, Najeri P, Gobin T, Sherrod L, Lewis J. Small bowel capsule endoscopy impacts diagnosis and management of pediatric inflammatory bowel disease: a prospective study. Dig Dis Sci 2012; 57: 465-471 [PMID: 21901253 DOI: 10.1007/s10620-011-1984-5]

20 Higurashi T, Endo H, Yoneda M, Hoso T, Sakai K, Takahashi H, Inamori M, Uchiyama S, Kojima T, Kawanaka K, Natsume Y, Nagase H, Nakajima A. Capsule-endoscopic findings of ulcerative
Monteiro S et al. Small bowel capsule endoscopy in IBDU patients

colitis patients. *Digestion* 2011; 84: 306-314 [PMID: 22041924 DOI: 10.1159/000333086]
31 Kopylov U, Seidman EG. Role of capsule endoscopy in inflammatory bowel disease. *World J Gastroenterol* 2014; 20: 1155-1164 [PMID: 24574702 DOI: 10.3748/wjg.v20.i5.1155]
32 Lorenzo-Zúñiga V, de Vega VM, Domènech E, Cabré E, Mañosa M, Boix J. Impact of capsule endoscopy findings in the management of Crohn’s Disease. *Dig Dis Sci* 2010; 55: 411-414 [PMID: 19255845 DOI: 10.1007/s10620-009-0758-8]
33 Cotter J, Dias de Castro F, Moreira MJ, Rosa B. Tailoring Crohn’s disease treatment: the impact of small bowel capsule endoscopy. *J Crohns Colitis* 2014; 8: 1610-1615 [PMID: 24631311 DOI: 10.1016/j.crohns.2014.02.018]
34 Kopylov U, Nemeth A, Koulaouzidis A, Makins R, Wild G, Afif W, Britton A, Johansson GW, Bessissow T, Eliakim R, Toth E, Seidman EG. Small bowel capsule endoscopy in the management of established Crohn’s disease: clinical impact, safety, and correlation with inflammatory biomarkers. *Inflamm Bowel Dis* 2015; 21: 93-100 [PMID: 25517597 DOI: 10.1097/mib.0000000000000255]
35 Odze RD. A contemporary and critical appraisal of ‘indeterminate colitis’. *Mod Pathol* 2015; 28 Suppl 1: S30-S46 [PMID: 25560598 DOI: 10.1038/modpathol.2014.131]
36 Odze RD. IBD: role of the pathologist in the diagnosis and management of IBD. *Nat Rev Gastroenterol Hepatol* 2013; 10: 625-626 [PMID: 24126560 DOI: 10.1038/nrgastro.2013.198]

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