Esophageal lesions detected during small bowel capsule endoscopy : incidence, diagnostic and therapeutic impact

J.F. Juanmartiñena Fernández[1], I. Fernández-Urién Sainz[1], C. Saldaña Dueñas[1], A. Elosua González[1], M. Montañés Guimera[1], B. Zabalza Ollo[2], S. Pardo González[3], J.J. Vila Costas[1]

(1) Department of Gastroenterology and (2) Clinical Analysis, Complejo Hospitalario de Navarra, Pamplona (Spain) ; (3) Department of Anesthesiology and Reanimation. Hospital Universitario Marqués de Valdecilla, Santander (Spain).

Abstract

Background : **Nowadays, capsule endoscopy is the first-line procedure for the visualization of the small bowel. Although it was primarily designed with this goal, it may also identify other segments of the gastrointestinal tract. The aim of the current study is to evaluate the incidence of esophageal abnormalities detected in patients undergoing small bowel capsule endoscopy and its impact on patient management.**

Patients and Methods : **This study is a retrospective analysis of data from 2217 consecutive capsule endoscopy procedures performed at a single tertiary-care centre between January 2008 and February 2016. Patient baseline characteristics, esophageal lesions, diagnosis and management before and after capsule endoscopy were recorded and a descriptive analysis was then performed.**

Results : **2217 patients were finally included in the analysis. 1070 were male (48.2%) and the mean age was 56.1 ± 19.5 years (12-93). Obscure gastrointestinal bleeding (52.3%) and inflammatory bowel disease (18.3%) were the main procedure indications. Esophageal abnormalities were detected in 105 out of 2217 patients (4.7%). The most common lesions detected were peptic esophagitis (58.1%) and esophageal varices (17.1%). This information had a clinical/ diagnostic impact of 3.3% and a therapeutic impact of 3.2%.**

Conclusion : **Capsule endoscopy detects not only small bowel lesions, but also significant esophageal lesions that may be overlooked during initial gastroscopy. Therefore, all images of the esophagus should be read during small bowel capsule endoscopy, since it could provide relevant information that may result in changes on patient´s management.** (Acta gastroenterol. belg., **2017**, 80, **499-504**).

Key words : capsule endoscopy,small bowel, esophageal lesions, gastroscopy.

Abbreviations : Small Bowel Capsule Endoscopy (SBCE) ; Obscure Gastrointestinal Bleeding (OGIB) ; Esophageal Lesions (EL).

Introduction

To date, small bowel capsule endoscopy (SBCE) is considered as the first-line procedure for the visualization of the small bowel (SB) (1-3). Since its development over a decade ago, SBCE has become a widely accepted tool. It has revolutionized the approach to SB diseases investigation and management, as it is a minimally invasive technique that directly visualizes the mucosal surface of the SB, usually inaccessible to conventional endoscopy (4-7). Designed primarily to provide diagnostic imaging of the small intestine, SBCE has been used predominantly for obscure gastrointestinal bleeding (OGIB) and suspected Crohn's disease (8,9). However, due to its excellent safety profile, numerous other indications have been established in the last years including the assessment of celiac disease, investigation of SB tumors and the surveillance of hereditary polyposis syndromes (10,11). Unlike OGIB, where small intestine exploration was typically indicated when no source of bleeding was identified in conventional endoscopies (12,13), to date prior conventional endoscopy (gastroscopy and ileocolonoscopy) is not always mandatory regarding new capsule indications. However, in all the cases, SBCE gives the opportunity to examine other areas of the GI tract such as esophagus, stomach or colon (14,15). Furthermore, it could detect lesions in proximal and distal segments of the GI tract that may have been overlooked by conventional endoscopy (16,17). It is well known that both upper and lower GI endoscopic procedures have false negatives (18-20). However, the incidence and impact of these lesions on patient management has not been well documented. As a result, it is not clear whether all images of a video capsule procedure should be reviewed. The aim of the current study is to evaluate the incidence of esophageal lesions (EL) in patients undergoing SBCE and its impact on patient management.

Patients and methods

This study is a retrospective analysis of data from 2217 consecutive SBCE undergoing in a single tertiary-care centre (Complejo Hospitalario de Navarra) between January 2008 and February 2016. All patient with incomplete data recorded were excluded from the study. Variables included in the analysis were: patients´ demographics, procedure indications, presence and type of EL during SBCE, performance of gastroscopy before and after SBCE, patient diagnosis and management before and after SBCE and patient outcome.

Correspondence to : José Francisco Juanmartiñena Fernández, Department of Gastroenterology, Complejo Hospitalario de Navarra, Irunlarrea 3, CP 31008, Pamplona Navarra (Spain). Phone : (+34) 658426309.
Email : jf.juanmartinena@gmail.com

Submission date : 24/01/2017
Acceptance date : 03/10/2017

Definitions

- *Gastroscopy pre-SBCE* : were considered only those gastroscopies performed 30 months before SBCE procedure.
- *Additional findings*: refer to those EL different from those findings detected by previous gastroscopy.
- *New findings*: were considered those EL detected in patients with no previous findings in the endoscopy (ie: negative gastroscopy).
- *Clinical impact*: was defined as the proportion (%) of patients with changes in their pre-SBCE procedure diagnosis.
- *Therapeutic impact*: was defined as the proportion (%) of patients with changes in their pre-SBCE procedure treatment.

CE procedure

All SBCE examinations were performed using the PillCam®SB2 (January 2008-November 2012) and PillCam®SB3 (December 2012-February 2016), Given Imaging, Yoqneam, Israel. Patients were usually presented for SBCE in an outpatient setting without any bowel preparation or prokinetics and after fasting for 8 hours. The device was then administered. A light breakfast after 2 hours and a light meal after 5 hours were permitted. At the end of the recording period, patients returned to the endoscopy unit where data recorder was removed and images were downloaded on the computer. SBCE recordings were reviewed by experienced readers at 12 frames per second using the Rapid® Reader software. The capsule was swallowed in right supine (42.4%), supine (32.8%) or orthostatic (24.8%) positions.

Statistical analysis

The statistical analysis was performed using the 15.0 version of the SPSS software (IBM Corporation, New York, USA). For normally distributed quantitative data, all results are shown as mean (SD, range) within the given values. For not normally distributed quantitative data, all results are presented as median and interquartile range. Qualitative variables are presented as simple proportions. For qualitative data comparison, a chi-square test was used considering p values under 0.05 as statistically significant.

Ethics considerations

An informed consent form was obtained from all patients before the SBCE procedure and the Institutional Review Board from our Institution approved data collection and their use for the present study purpose.

Results

Patients´ demographics

During the study period, 2224 SBCE procedures were performed. Seven capsule explorations were excluded from the analysis because of missed data. Therefore, 2217 procedures were finally included in the analysis. One thousand seventy were male (48,2%) and the mean age was 56.1 ± 19.5 years (12-93). Patients were referred for SBCE due to: OGIB in 1160 cases (52.3%), known or suspected Crohn´s disease in 406 cases (18.3%), abdominal pain in 184 cases (8.3%), chronic diarrhoea in 144 cases (6.5%) and other indications in 323 cases (14.6%). SBCE was normal in 886 patients (40%) and SB abnormalities were noted in 1301 patients (58.6%). These SB findings were: 36.2% erosions/ulcers (n = 471), 32.0% angiodysplasias (n = 416), 16.3% inflammatory bowel mucosa (n = 212), 5.0% tumors (n = 65), 4.6 % active bleeding (n = 60) and 5.9% other lesions (n = 77). In 30 patients (1.4%), SB was not explored because SBCE was retained in the stomach and did not pass through the pylorus during all the battery life-period.

Esophageal findings

Esophageal abnormalities were detected in 105 out of 2217 patients (4.7%). Among them, the Z line was identified in 61.9% (n = 65) and more than 80% of the gastroesophageal junction was seen in two thirds of cases (n = 52). The mean time spent to explore the esophagus was 248.4 ± 730.3 (1-6000) seconds. The esophageal findings noted by SBCE were: 58.1% peptic esophagitis (n = 61), 17.1% esophageal varices (n = 18), 11.4% Barrett esophagus (n = 12), 3.8% eosinophilic esophagitis (n = 4), 3.8% esophageal polyps (n = 4), 2.9% esophageal stenosis (n = 3), 1.9% esophageal diverticula (n = 2), and 1% Schatzki ring (n = 1).

In 65 of 105 patients (61.9%) undergoing SBCE, findings were identified simultaneously in SB and esophagus. Up to 78 patients (74.3%) had a previous gastroscopy. The mean number of gastroscopies was 1.08 ± 1.08 (1-7) while the mean waiting-time between gastroscopy and SBCE was 233.3 ± 462.9 days (0-2900). Taking into account only those patients with an upper endoscopy in the last 30 months before SBCE (n = 74, 70.5%), EL were found in 43 (58.1%) patients in whom EL were overlooked during gastroscopy: in 3 patients (7.0%) there were new findings different from those detected by the previous gastroscopy (i.e: additional findings) while in 40 patients (93.0%) there were new findings after a negative upper endoscopy. These esophageal findings were: 60.5% peptic esophagitis (n = 26), 16.4% Barrett esophagus (n = 7), 7.0% esophageal varices (n = 3), 4.6% esophageal stenosis (n = 2), 4.6% polyps (n = 2), 2.3% diverticula (n = 1), 2.3% suspected eosinophilic esophagitis (n = 1) and 2.3% Schatzki ring (n = 1). On the other hand, esophageal findings were identified by both procedures in 31 patients (41.9%): 51.7% peptic esophagitis (n = 16), 38.7% esophageal varices (n = 12), 3.2% Barrett esophagus (n = 1), 3.2% esophageal stenosis (n = 1) and 3.2% polyps (n = 1). EL were also found in 31 patients (29.5%) with no previous gastroscopy, and they were: 61.3% peptic esophagitis (n

Table 1. — **Type of esophageal findings during small bowel capsule endoscopy**

Overall (n = 105)		**Overlooked lesions* (n = 43)**	
Type of lesion	**n (%)**	**Type of lesion**	**n (%)**
Peptic Esophagitis	61 (58.1%)	Peptic Esophagitis	26 (60.5%)
Esophageal Varices	18 (17.1%)	Barrett Esophagus	7 (16.4%)
Barrett Esophagus	12 (11.4%)	Esophageal Varices	3 (7.0%)
Esophageal Polyps	4 (3.8%)	Esophageal Stenosis	2 (4.6%)
Suspected Eosinophilic Esophagitis	4 (3.8%)	Esophageal Polyps	2 (4.6)
Esophageal Stenosis	3 (2.9%)	Esophageal Diverticula	1 (2.3%)
Esophageal Diverticula	2 (1.9%)	Suspected Eosinophilic Esophagitis	1 (2.3%)
Schatzki Ring	1 (1%)	Schatzki Ring	1 (2.3%)

* Esophageal lesions (EL) missed by gastroscopy.

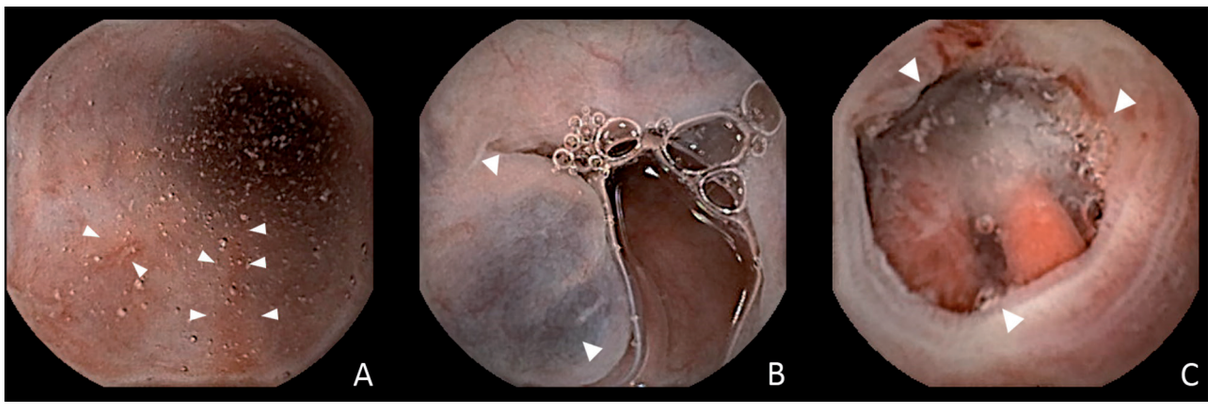


Figure 1. — Esophageal findings during small bowel capsule endoscopy (SBCE) : A) Peptic esophagitis ; B) Esophageal varices ; C) Esophageal peptic stenosis.

= 19), 12.9% Barrett esophagus (n = 4), 9.7% suspected eosinophilic esophagitis (n = 3), 9.7% esophageal varices (n = 3), 3.2% esophageal diverticula (n = 1) and 3.2% polyps (n = 1).

Table 1 and Figure 1 show lesions and type of lesions detected in the esophagus during small bowel CE.

Clinical and therapeutic impact

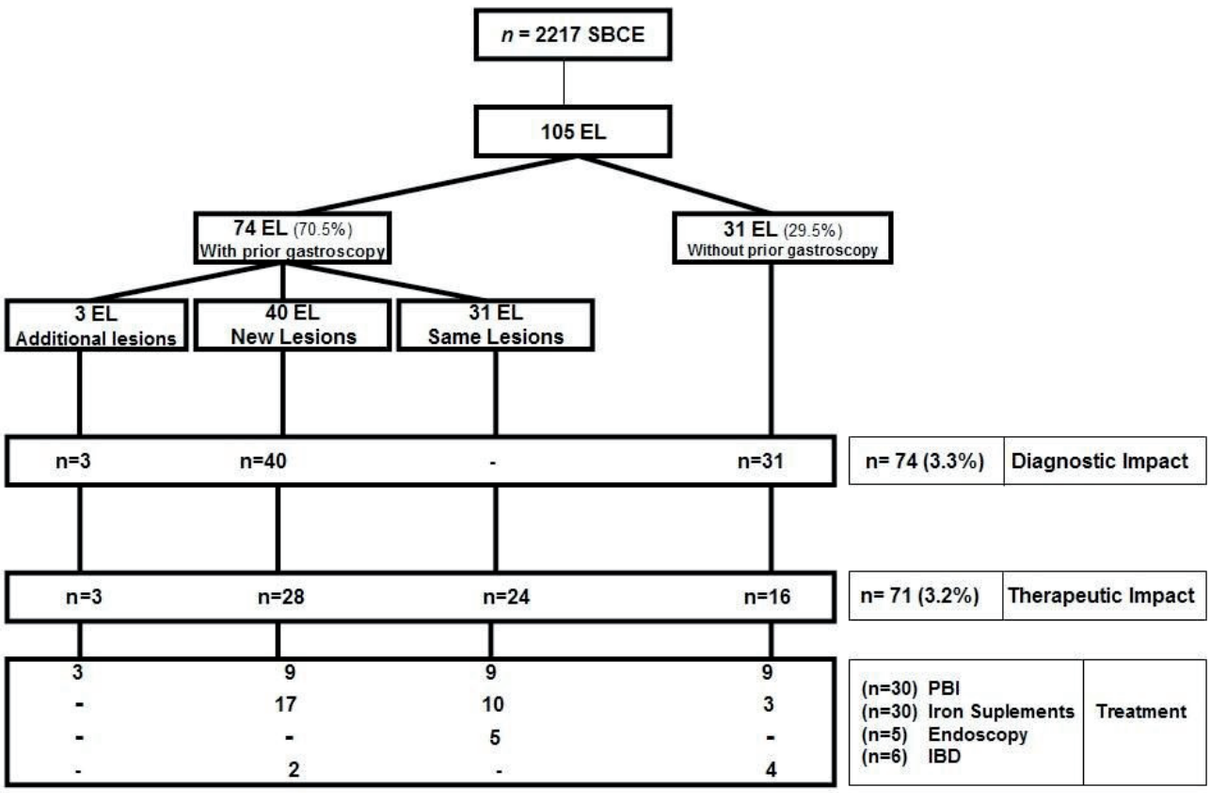
Esophageal findings during SBCE led to a diagnostic change in 74 out of 105 patients (70.5%) resulting in an overall clinical impact of 3.3%. The frequency of diagnostic changes was significantly higher among those patients who had not undergone a previous gastroscopy (100% versus 60.2%, p<0.01). Although 74 of them (70.5%) had a previous upper endoscopy, a second gastroscopy was needed in 13 patients (12.4%). On the other hand, due to the presence of esophageal findings during SBCE, seventy-one patients (67.6%) experienced changes on their initial therapeutic strategy resulting in an overall therapeutic impact of 3.2%. The frequency of therapeutic changes was significantly greater among those patients who had undergone a previous gastroscopy (73.7% versus 55%, p<0.01). Pharmacological therapy was the treatment of choice in 66 patients (92.9%), followed by therapeutic endoscopy in 5 patients (7.1%). Iron supplements (n = 30) and proton pump inhibitors (n = 30) in the pharmacological group and Argon Beam (n = 5) for vascular lesions (angiodyslplasia) in the endoscopic group were the most common treatment changes seen in the study after SBCE performance.

Table 2 Summarizes the study results.

Discussion

CE has been developed to examine the SB in a simple and non-invasive way (4-7). Its ability to visualize SB lesions has been demonstrated in a high number of

Table 2. — **Summary of the results from the study: Clinical and therapeutic impact**



EL : Esophageal lesions ; SBCE : Small Bowel Capsule Endoscopy ; PBI : Proton-pump inhibitor; IBD: inflammatory bowel disease.

studies (1-3). In 2001, SBCE was firstly accepted for the study of the small intestine in patients with OGIB when no source of bleeding was identified after negative conventional endoscopies (gastroscopy and colonoscopy) (8,9). However, due to its excellent safety profile and because it is well accepted by patients, numerous other indications have been established in the last years (10,11). Nowadays, regarding new capsule indications, schedules for the investigation of the SB have also evolved, so that a prior conventional endoscopy (gastroscopy and ileocolonoscopy) is no longer mandatory as it was over a decade ago. However, in all the cases, the technology of CE gives the opportunity to examine not only the small intestine, but also other areas of the GI tract where CE passes throughout until battery-life expiration (14,15). Furthermore, it may detect lesions proximal to small intestine that could have been overlooked at previous gastroscopy (16,17). Over the last years some studies have reported the ability of CE to detect lesions outside the small intestine, and sometimes, within the reach of conventional gastroscopy (21). *Kitiyakara et al* in 2005, *Rana et al* in 2011 and *Lipileur et al* in 2012 were the first authors to identify esophagogastric lesions missed at initial gastroscopy in patients undergoing SBCE (22-24). In all of them, OGIB was the principal indication for performing SBCE. In contrast, although OGIB still is the principal indication in the current study (52.3%), other indications like Crohn´s or celiac disease have also been included. Up to 4.7% of non-small bowel lesions were identified. They were commonly distributed in the distal esophagus, being peptic disease the most common lesion found. However, some studies suggested the rapid passage of capsule through the esophagus may limit esophageal exploration to a few single pictures and therefore, may reduce the visualization of the Z line (25). Nevertheless, in our series, esophageal exploration and visualization of the gastroesophageal junction have been possible in two third of cases, being these values higher than those presented in the literature. The explanation could be that most of the patients with EL (60.8%) swallowed SBCE in the right lateral decubitus position, as it seems the position of capsule administration may improve the visualization of the esophagus (26,27). To date, it is thought new capsule devices could allow better visualization of the lower esophagus than SBCE (PillCam®ESO2 and PillCam®COLON2, Given Yoqneam Israel) as they have two cameras, each one at both ends, that may improve the exploration. However, its use is limited, not recommending these procedures alone for the visualization of the esophagus in clinical practice, but as a complement to gastroscopy (28-30). To date, it is not clear why these lesions revealed

by CE are missed at initial upper endoscopy, although some possible explanations in patients with OGIB may be related to lesions characteristics (size of the lesion, unusual location) or to endoscopic procedures (quality of exploration, complete examination rates or endoscopist experience) (15,31).

As we have shown above, CE could be considered a complementary tool for the exploration of the esophagus in patients with negative gastroscopy or when the esophagus has not been visualized, as up to 4.7% of lesions are identified during SB explorations (32,33). Therefore, we recommend a careful review of the esophagogastric images during SBCE explorations, even more in those patients without initial upper endoscopy (34). However, as we can observe, not all EL detected by CE were considered significant, as only two third of cases turned into new treatment indications, changing the management in 3.2% of the overall patients. Like with PillCam®ESO2, peptic esophagitis, esophageal varices or Barrett esophagus were some of the lesions identified by SBCE in our study (28,30). There is no doubt that CE may identify EL and that is better accepted and preferred by patients over standard video upper GI endoscopy. However it should not replace gastroscopy as it still is the gold-standard for the study of esophagus, allowing also to take biopsy specimens during the procedure if needed (35-37).

We faced certain limitations in the current study : 1) A retrospective study design. 2) A prospective long term follow-up is mandatory for confirming that the so-called potentially significant lesions are not really incidental findings. 3) Heterogeneity of SBCE indications makes unnecessary, on some occasions, a previous conventional endoscopy. Unlike OGIB, where conventional endoscopy should always precede capsule exploration, initial gastroscopy is not essential in some other cases such as known Crohn´s disease, in which evaluation of the SB mucosa is only needed to assess treatment response (34).

Probably, in these cases, EL had previously been identified if initial gastroscopy would have been indicated. Anyway, in most cases, these lesions were probably incidental findings with a doubtful clinical meaning. 4) Low rate of second-look gastroscopies that may confirm capsule findings, probably related to benign nature of EL and to its easiest treatment with pharmacologic approach. 5) Heterogeneity in SBCE administration among patients, resulting in high esophagus transit time differences among studies (29). 6) There is a lack of information regarding the maximum period of time between conventional endoscopic procedures and SBCE. We have chosen 30 months as an arbitrary date, although in this sense, it is well known endoscopic procedures should be repeated if prior endoscopy was not reliable. Otherwise, SBCE should be performed as soon as possible after a negative colonoscopy (8,9).

In conclusion: this study demonstrates that once SBCE is indicated, a careful review of the images obtained of the esophagus should be done because some lesions may be overlooked during conventional gastroscopy resulting in new diagnoses and changes in patient management.

References

1. IDDAN G., MERON G., GLUKHOVSKY A., SWAIN P. Wireless capsule endoscopy. *Nature*, 2000, **405** : 417.
2. MERON G.D. The development of the swallowable video capsule (M2A). *Gastrointest. Endosc.*, 2000, **52** : 817-9.
3. LEWIS B.S., SWAIN P. Capsule endoscopy in the evaluation of patients with suspected small intestinal bleeding : Results of a pilot study. *Gastrointest. Endosc.*, 2002, **56** : 349-53.
4. SCAPA E., JACOB H., LEWCOWICZ S., MIGDAL M., GAT D., GLUCKHOVSKI A., *et al.* Initial experience of wireless-capsule endoscopy for evaluating occult gastrointestinal bleeding and suspected small bowel pathology. *Am. J. Gastroenterol.*, 2002, **97** : 2776-9.
5. MATAS J.L., ASTEINZA M., LOSCOS J.M., FERNÁNDEZ S., RAMIREZ-ARMENGOL J.A., DÍAZ-RUBIO M. Diagnostic yield and safety of capsule endoscopy. *Rev. Esp. Enferm. Dig.*, 2006, **98** : 666-73.
6. CARRETERO C., FERNÁNDEZ-URIÉN I., BETES M., MUÑOZ-NAVAS M. Role of videocapsule endoscopy for gastrointestinal bleeding. *World J. Gastroenterol.*, 2008, **14** : 5261-4.
7. FIREMAN Z., KOPELMAN Y. Small Bowell Capsule Endoscopy : Have we conquered the last Frontier? *Isr. Med. Assoc. J.*, 2008, **10** : 298-301.
8. SHIM K.N., MOON J.S., CHANG D.K., DO J.H., KIM J.H., MIN B.H, *et al.* Guideline for capsule endoscopy : obscure gastrointestinal bleeding. *Clin. Endosc*., 2013, **46** : 45-53.
9. GERSON L.B., FIDLER J.L., CAVE D.R., LEIGHTON J.A. ACG clinical guideline : Diagnosis and Management of Small Bowel Bleeding. *Am. J. Gastroenterol.*,. 2015, **110** : 1265-87.
10. LADAS S.D., TRIANTAFYLLOU K., SPADA C., RICCIONI M.E., REY J.F., NIV Y., *et al.* European Society of Gastrointestinal Endoscopy (ESGE): recommendations on clinical use of video capsule endoscopy to investigate small-bowel, esophageal and colonic diseases. *Endoscopy*, 2010, **42** : 220-7.
11. PENNAZIO M., SPADA C., ELIAKIM R., KEUCHEL M., MAY A., MULDER C.J., *et al.* Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders : European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy*, 2015, **47** : 352-76.
12. TAE C.H., SHIM K.N. Should Capsule Endoscopy Be the First Test for Every Obscure Gastrointestinal Bleeding? *Clin. Endosc*., 2014, **47** : 409-14.
13. MARTÍNEZ-GONZÁLEZ J., TÉLLEZ VILLAJOS L., AICART-RAMOS M., CRESPO PÉREZ L., GRAUS MORALES J., BOIXEDA MIGUEL D., *et al*. Capsule endoscopy and obscure gastrointestinal bleeding: does the form of presentation matter? *Gastroenterol. Hepatol.,* 2015, **38** : 47-53.
14. ELIJAH D., DAAS A., BRADY P. Capsule endoscopy for obscure GI bleeding yields a high incidence of significant treatable lesions within reach of standard upper endoscopy. *Clin. Gastroenterol.,* 2008, **42** : 962-3.
15. TACHECI I., DEVIÈRE J., KOPACOVA M., DOUDA T., BURES J., VAN GOSSUM A. The importance of upper gastrointestinal lesions detected with capsule endoscopy in patients with obscure digestive bleeding. *Acta Gastroenterol. Belg*., 2011, **74** : 395-9.
16. SIDHU R., SANDER D.S., MCALINDON M.E. Does capsule endoscopy recognise gastric antral vascular ectasia most frequently than conventional endoscopy? *J. Gastrointestin. Liver Dis.,* 2006, **15** : 375-7.
17. GILBERT D., O´MALLEY S., SELBY W. Are repeat upper gastrointestinal endoscopy and colonoscopy necessary within six months of capsule endoscopy in patients with obscure gastrointestinal bleeding? J. *Gastroenterol. Hepatol*., 2008, **23** : 1806-9.
18. FRY L.C., BELLUTTI M., NEUMANN H., MALFERTHEINER P., MONKEMULLER K. Incidence of bleeding lesions within reach of conventional upper and lower endoscopes in patients undergoing double-balloon enteroscopy for obscure gastrointestinal bleeding. *Aliment. Pharmacol. Ther*., 2009, **29** : 342-9.
19. SCHÖNFELD J., HAUSER D., HARTMANN C.A., SCHROUDER J. Adenomas and Carcinomas Missed in Routine Colonoscopy: A Prospective Study in resected Colon Segments. *Z. Gastroenterol.* 2014, **52** : 1153-6.
20. RICCIONI M.E., URGESI R., CIANCI R., MARMO C., GALASSO D., COSTAMAGNA G. Obscure recurrent gastrointestinal bleeding: a revealed mystery? *Scand. J. Gastroenterol.,* 2014, **49** : 1020-6.
21. FIREMAN Z., KOPELMAN Y. Small Bowell Capsule Endoscopy: Have we conquered the last Frontier? *Isr. Med. Assoc. J.*, 2008, **10** : 298-301.
22. KITIYAKARA T., SELBY W. Non-small-bowel lesions detected by capsule endoscopy in patients with obscure GI bleeding. *Gastrointest. Endosc.*, 2005, **62** : 234-8.

23. RANA S.S., BHASIN D.K., SINGH K. Colonic lesions in patients undergoing small bowell capsule endoscopy. *Int. J. Colorectal. Dis*., 2011, **26** : 699-702.
24. LEPILEUR L., DRAY X., ANTONIETTI M., IWANICKI-CARON I., GRIGIONI S., CHAPUT U., *et al.* Factors Associated With Diagnosis of Obscure Gastrointestinal Bleeding. *Clin. Gastroenterol. and Hepatol*., 2012, **10** : 1376-80.
25. CHEN W.S., ZHU L.H., LI D.Z., CHEN L., WU Y.L., WANG G. String esophageal capsule endoscopy with real-time viewing improves visualization of the distal esophageal Z-line : a prospective, comparative study. *Eur. J. Gastroenterol. Hepatol*., 2014, **26** : 309-12.
26. FERNÁNDEZ-URIEN I., BOROBIO E., ELIZALDE I., IRISARRI R., VILA J.J. Z-line examination by the PillCam SB: prospective comparison of three ingestion protocols. *World J. Gastroenterol.*, 2010, **16** : 63-8.
27. FERNÁNDEZ-URIEN I., JIMÉNEZ-PÉREZ F.J. Is string esophageal capsule endoscopy really better than esophageal capsule endoscopy in the right supine position for Z-line examination? *Eur. J. Gastroenterol. Hepatol*., 2014, **26** : 685.
28. SCHOOFS N., DEVIÈRE J., VAN GOSSUM A. PillCam colon capsule endoscopy compared with colonoscopy for colorectal tumor diagnosis: a prospective pilot study. *Endoscopy*, 2006, **38** : 971-7.
29. GOSSNER L. Potential contribution of novel imaging modalities in nonerosive reflux disease. *Best Pract. Res. Clin. Gastroenterol*., 2008, **22** : 617-24.
30. GRALNEK I.M., ADLER S.N., YASSIN K., KOSLOWSKY B., METZGER Y., ELIAKIM R. Detecting esophageal disease with second-generation capsule endoscopy: initial evaluation of the PillCam ESO 2. *Endoscopy*, 2008, **40** : 275-9.
31. SELBY W. Can clinical features predict the likelihood of finding abnormalities when using capsule endoscopy in patients with GI bleeding of obscure origin? *Gastrointest. Endosc.*, 2004, **59** : 782-7.
32. LIAO Z., GAO R., XU C., LI Z.S. Indications and detection, completion and retention rates of small-bowel capsule endoscopy: a systematic review. *Gastrointest. Endosc.*, 2010, **71** : 280-6.
33. LIU K., KAFFES A.J. Review article: the diagnosis and investigation of obscure gastrointestinal bleeding. *Aliment. Pharmacol. Ther.*, 2011, **34** : 416-23.
34. KIM M., JANG H.J.The role of small bowel endoscopy in small bowel Crohn's disease: when and how? *Intest. Res*., 2016, **14** : 211-7.
35. MEVES V., BEHRENS A., POHL J. Diagnostics and Early Diagnosis of Esophageal Cancer. *Viszeralmedizin*, 2015, **31** : 315-8.
36. MACÍAS-GARCÍA F., DOMÍNGUEZ-MUÑOZ J.E. Update on management of Barrett's esophagus. *World J. Gastrointest. Pharmacol. Ther*., 2016, **7** : 227-34.
37. MAURICE J., BRODKIN E., ARNOLD F., NAVARATNAM A., PAINE H., KHAWAR S., *et al.* Validation of the Baveno Vi Criteria to Identify Low Risk Cirrhotic Patients not Requiring Endoscopic Surveillance for Varices. *J. Hepatol*., 2016, **65** : 899-905.