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Authors:
Miguel Mascarenhas Saraiva, Miguel Mascarenhas Saraiva

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A case-control study demonstrating improved visualization when capsule endoscopy is performed after preparation with polyethylene glycol and ascorbic acid

Mascarenhas-Saraiva, Miguel José; Mascarenhas-Saraiva, Miguel

ManopH Gastroenterology Clinic. CUF Hospital. Porto. Portugal.

Contact Information: Miguel Mascarenhas-Saraiva, ManopH, CUF Hospital, Porto (Portugal). e-mail: miguelmascarenhassaraiva@gmail.com;

ABSTRACT

Background: Capsule endoscopy is used increasingly to obtain images of the gastrointestinal tract, yet it still remains unclear what is the best preparation for this type of exploration.

Aims: The aim of this study was to compare the results of capsule endoscopy explorations performed after a basic preparation with a clear liquid diet, reduced iron intake and fasting or following preparation with a PEG/ascorbate solution.

Methods: The results obtained from a prospective intervention group that used a PEG/ascorbate solution to prepare for capsule endoscopy were compared with those from a retrospective group of patients who followed the more basic preparation. The quality of visualization was assessed with the Park score, assessing visualization of the mucosal surface and the cleanliness of the intestinal lumen. The capsule transit time in different segments of the gastrointestinal tract was also evaluated.

Results: A significant improvement in the quality of small intestine visualization was observed in individuals prepared with the PEG/ascorbate solution as opposed to the basic preparation. Indeed, there were significant differences in the two separate components that contribute to the overall visualization score, with better mucosa visualization and lumen content scores in the intervention group, reflecting improved performance. The presence of diabetes appears to affect the results of these explorations, at least when employing the

PEG/ascorbate preparation.

Conclusions: Preparation with a PEG/ascorbate solution improves the results of capsule endoscopy when compared to a basic preparation, without the inconvenience of the more stringent preparations used for colonoscopies.

Keywords: Capsule Endoscopy, PEG/ascorbate, Bowel preparation, Mucosa visualization, Gastric transit

Abbreviations: CE, Capsule endoscopy; PEG, polyethylene glycol; CLS, cleansing score; S.D., standard deviation; OBG, obscure gastrointestinal bleeding; GI, gastrointestinal.

INTRODUCTION

Capsule endoscopy (CE) is a procedure used to study conditions that mainly affect the small intestine. However, the use of CE generally produces much better image quality in the proximal small intestine than in the distal ileum, which is mainly due to the presence of residual material, such as air bubbles, food residues and bile pigments in the latter (1). Less frequently, the battery life of the capsule may also become an issue as it may be insufficient for the capsule to reach the cecum if the transit time becomes too long.

There remains some controversy as to the ideal preparation necessary to perform CE, with some favoring a less aggressive approach while others recommend more stringent preparations, such as those used for colonoscopies (2–5). The usual preparation for CE involves ceasing oral iron supplementation over the preceding 3 days, light meals and a liquid diet on the day prior to intervention, as well as fasting for the 10 hours prior to performing CE on the day of examination. However, other bowel preparations have also been tested, such as those involving the intake of solutions of polyethylene glycol (PEG: (6–9), alone or in conjunction with ascorbate (10), sodium phosphate (11–15) or magnesium citrate. The effect of the use of simethicone is controversial, although a combination of PEG and simethicone has been proposed as a good approach to small bowel preparation for CE (16). Prokinetics, have also been considered as another option, although this approach is not generally recommended (16,17).

In order to shed further light on this issue, the aim of this study was to evaluate the potential benefits of a simple and reliable cleansing regimen that involves the use of a PEG and ascorbate preparation. The main measures used to evaluate the effectiveness of this preparation were CE image quality and transit time, while other parameters such as the completion rate and the quality of mucosa visualization were also assessed.

METHODS

Study design

In order to optimize resources and minimize patient inconvenience, we used here a group of patients recruited retrospectively as a control for a comparative analysis, with patients recruited prospectively who prepared for a CE procedure using a PEG/ascorbate protocol. As such, this was a non-randomized study onto which patients with various clinical indications that required CE were enrolled, in the case of the control group after the exploration took place, or before the study took place in the case of the PEG/ascorbate (intervention) group. The patients in the control group were prepared for CE using a basic protocol that involved following a diet of light meals and then of clear liquid, reduced iron intake due to the suspension of iron supplementation for 3 days prior to the procedure when necessary, and 10 hour fasting prior to the exploration. By contrast, the patients in the intervention group were prepared following a similar protocol but with the additional consumption of 2 liters of a PEG/ascorbic acid solution. All patients recruited prospectively provided their informed consent (or that of their legal guardians) to participate in this study, which was carried out in accordance with the guidelines laid down in the Helsinki declaration and with the approval of the hospital's local ethical committee.

Participants

The patients that participated in this study were referred to undergo a CE for a variety of clinical indications between May 2016 and May 2017. The procedures were carried out at the Manoph and iCUF centers, and all the subjects were aged between 17 and 83 years of age (mean age=55 years old; SD=±17), 43 % of patients were male (n=49) and 57 % were female (n=64; table 1). As described previously, the participants were considered in two groups: the intervention group (prospective) and the control group (retrospective). The

intervention group included patients who were referred for only one examination. The exclusion criteria included non-compliance with the prescribed preparation, making it impossible to follow the protocol, and the use of a different model of capsule from the one established (see below).

Patients in the intervention group drank one liter of a PEG/ascorbic acid solution the evening prior to the CE intervention and another liter the morning before ingesting the capsule. The preparation used is a colon preparation commercialized as Moviprep®, a lemon flavored powder provided as 4 sachets: 2 sachets "A", each containing PEG (referred to as Macrogol; 100 g), anhydrous sodium sulfate (7.5 g), sodium chloride (2.7 g) and potassium chloride (1 g); and 2 sachets "B", each containing ascorbic acid (4.7 g) and sodium ascorbate (5.9 g). The product is prepared by diluting one sachet "A" and one sachet "B" in one liter of water, as indicated in the package leaflet of the product.

All CE examinations were carried out using the Given SB3 CE system. In the absence of a more universally accepted standard, small-intestine cleanliness was assessed in accordance with a scale devised previously by Park et al (1). This scale contemplates a cleansing score (CLS) of 0 to 3, where 3 is better and 0 is worse. This scoring system selects one frame taken every 5 min (1 frame/5 min) to reduce the time over which small intestine cleansing is graded and it evaluates two independent parameters: the proportion of the mucosa visualized; and the degree of obscuration by bubbles, debris, bile or other material. Small intestine cleanliness may also be graded objectively by scoring the images according to the percentage of the area visible. As a rule, the accepted cut-off score for adequate small intestine preparation for CE is 2.25, defined as the mean of the two individual cleansing parameters. In addition, when complete small intestine visualization was possible, gastric, orocecal and small intestine transit times were also compared.

Outcomes

The main evaluation parameters were the quality of visualization of the mucosal surface, as well as the presence of material in the intestinal lumen, measured as indicated above (1). In addition, the time required for the capsule to reach the cecum was assessed, considered to indicate complete transit through the gastrointestinal (GI) tract and a complete exploration. In addition, the differences in capsule transit time in different GI tract segments were also

evaluated.

Statistical analysis

The results of bowel preparation were compared using a Mann-Whitney U-test, having first established the data followed a normal distribution using a Kolmogorov-Smirnov test. Categorical data were compared using a Chi-squared test, and the Fisher-exact and Student T-tests were also employed where appropriate. P-values less than 0.05 were considered statistically significant and all statistical analyses were carried out with the SPSS software (IBM Corp.).

RESULTS

This study analyzed data obtained from 113 CEs carried out on 113 patients, 57 explorations carried out on patients in the intervention group and 56 in the control group. Various medical conditions led to the need to perform a CE exploration and they included: obscure gastrointestinal bleeding (OBG, 51 %), suspicion of Crohn's disease (20 %), abdominal pain (11 %), diarrhea (6 %), suspicion of small bowel tumors (5 %), Crohn's disease follow-up (4 %) familial polyposis follow-up (2 %), and other less common reasons (2 % - Table 1). When considering other relevant morbidities in the patient cohort, 13 % of patients had diabetes, 5 % were obese, 11 % had previously been subjected to digestive system surgery, 35 % had been subjected to abdominal surgery not involving the digestive system and 1 % had undergone radiotherapy. These characteristics of the patient cohort and the specific features of the control and intervention group can be seen in Table 1. When these two study groups were compared, the only statistically significant difference between the two was related to the proportion of diabetic patients, who constituted 21 % of the intervention group (n=12) and only 5 % of the control group (n=3, p = 0.014). In addition, the difference in digestive system surgery undergone by patients in the two groups was close to significance, with 5 % of the intervention group (n=3) having undergone such surgery, as opposed to 16 % (n=9) of the control group (p = 0.062). No other relevant differences were observed between the two groups of patients. When the specific baseline characteristics of the control and intervention group of the diabetic patients were compared, no significant

differences were observed (Supplementary Table 1).

Efficacy analysis

The main parameters of the exploration that were evaluated were the proportion of cases in which visualization of the cecum was achieved (a complete examination) and the quality of the images of the small bowel obtained. In 92 % of explorations it was possible to view the small intestine in its entirety and conversely, in only 8 % of cases there was no visualization of the last part of the small bowel and of the entrance of the colon (Table 2). The median score for visualization of the small bowel was 2.40, which could be broken down into the visualization of the mucosa, with a median score of 2.70, and the presence of material in the intestinal lumen that gave a median score of 2.20. The mean gastric transit time (GTT) was 25 minutes and 7 seconds, while the mean small bowel transit time (SBTT) was 4 hours and 19 minutes.

When the results of cecum visualization were compared between the two groups, there were no significant differences in the overall score obtained for the control and intervention group (5 % vs 11 %, p = 0.321: Table 2). However, significant differences were detected in the scores for the quality of small bowel visualization (2.45 vs 2.35, p = 0.003: see Figure 1 and Table 2). In the cases where the exploration was considered to be incomplete (with no cecum visualization), the quality of small bowel visualization was scored as 2.20, and there was no significant difference between the intervention (2.35) and control group (2.00, p = 0.298: Table 2). Relative to the control group (2.35), a significantly higher score was apparent for this parameter in the intervention group when the exploration was considered to be complete (2.45, p = 0.007). Significant differences were also noted when the two individual parameters that made up the total quality score were evaluated independently, with a higher mucosa visualization score (2.70 vs 2.60, p = 0.004) and lumen content score in the intervention group (2.30 vs 2.10, p = 0.003), representing improved performance. In terms of gastric transit time, the difference between the intervention group (27’02’’) and the control groups (16’48’’) was close to statistical significance (p = 0.060), while no significant differences were found in the median CBTT and CE battery life (Table 2).

Confounding adjustment analysis

Since the incidence of diabetes differed between the two study groups (80 % of the diabetic patients were in the intervention group, n=12), a confounding adjustment analysis was carried out for this variable (Table 2). Regarding the parameters of the exploration considered, there were no significant differences in cecum visualization between the intervention group and the control group of patients with or without diabetes (Table 2). The capsule reached the cecum in all patients with diabetes in which the exploration was performed, while in only 93 % of patients without diabetes did the capsule fully pass through the entire small bowel. While the proportion of these latter patients in which the exploration was concluded completely appeared to be higher in the intervention group than in the control group (93 % vs. 89 %), this difference was not statistically significant (p = 0.501).

There were significant differences in the quality of small bowel visualization in the patients without diabetes, in which the median quality of visualization score was higher in the intervention group (2.45) than in the control group (2.35, p = 0.010). Segmenting these patients relative to the completeness of the exploration, the median score in the intervention group was higher than in the control group (2.50 vs. 2.35 with cecum visualization, and 2.35 vs. 2.00 with no cecum visualization). Nonetheless, this difference was only statistically significant in those patients in whom the capsule reached the cecum (p = 0.021). In diabetic patients, this tendency was also notable and again, the patients in the intervention group apparently achieved a higher quality of visualization score (2.50) than those in the control group (2.25), although this did not reach statistical significance probably due to the small sample size (p = 0.082). A similar trend was consistently observed for the two individual parameters that made up the overall quality of visualization score (proportion of the mucosa visualized and lumen content). The GTT and SBTT were not significantly different between the intervention and control groups, both among patients with and without diabetes (Table 2).

Completeness cofactors analysis

Bearing in mind that completing the exploration in its entirety is an important factor when validating the examination, as analysis was carried out to compare the two groups: uncomplete and complete explorations. The characteristics of these two groups were similar at baseline (Table 3) but as expected, there were differences in the quality of visualization with lower scores associated with the incomplete examinations (2.20) rather than the complete ones (2.45, p = 0.019). There were also differences in the scores obtained for the individual parameters of quality, with a lower score for the visualization of the mucosa (2.50: p = 0.031) and for lumen content (1.90, p = 0.014), and higher scores for the complete explorations (2.70 and 2.20, respectively: see Table 3). By contrast, there were no differences in GTT between these two groups.

DISCUSSION

In this study we have assessed how a preparative protocol involving the use of a PEG/ascorbate solution might improve the quality of the results obtained in CE explorations. When compared to a more basic protocol based on fasting, the preparation with the PEG/ascorbate solution produced markedly better results in all the main parameters assessed, visualization and cleansing, as well as a possible improvement in transit time. These results confirm previous suggestions that the use of PEG solutions combined with other components may improve the success rates and the clinical information obtained from CE examinations

Several studies have been published regarding the effectiveness of different bowel preparations for CE explorations. In 2010, an initial pioneering study of bowel preparation with PEG was carried out on a sample of 68 patients considered for CE who received either 2 or 4 liters of a PEG solution (1). As a result, it became clear that image quality improved when patients were prepared for CE using PEG than in those who followed a protocol that essentially involved fasting alone (18). Indeed, when compared to no bowel preparation, bowel preparation with PEG results in adequate visualization in significantly more patients subject to CE. Subsequently, evidence was presented that supported the use of a PEG solution in conjunction with oral simethicone as the preparation of choice for CE (19), and it was later proposed that the PEG/simethicone combination might be the best preparation for small bowel CE (20).

Although it has become clear that patient preparation with PEG is associated with better visualization of the intestine, as can be measured using the scoring system defined in Park et al (1), a consensus regarding the need for intestinal preparation for CE is still lacking (2, 21). Similarly, the stringency of such preparations has yet to be defined. Hence, in this study we assessed the use of a smaller volume of a PEG solution for bowel preparation, which might be more convenient and comfortable for the patient, while still providing optimal visualization of the small intestine. The use of a relatively small volume PEG/ascorbate preparative solution led to higher quality small intestine visualization, producing better scores in both of the individual components that made up that score, the quality of mucosa visualization and lumen content. Similarly, there appeared to be a close to significant improvement in GTT in these patients. This latter parameter may not only reduce patient discomfort by shortening the explorations but perhaps, and importantly, it will reduce the possibility of incomplete explorations due to the loss of battery power during the intervention.

Defining the least stressful protocol for the patient to prepare for a CE endoscopy is likely to lead to greater compliance and therefore, produce better results. Indeed, compliance with a PEG/ascorbate protocol proved to be better than when PEG was combined with simethicone, the former preparation apparently producing less nausea and vomiting (22). This higher compliance is likely to lead to a more optimal success rate in terms of the completion of such explorations and as such, enhance the rate of correct diagnosis while reducing the need for repeat tests. Both these factors will not only enhance patient satisfaction but they are also likely to reduce healthcare costs, not least by achieving more accurate and earlier diagnosis of GI conditions, which are therefore likely to be resolved more easily and rapidly. It is also important to note that better visualization scores were associated with completion of the explorations, even though this parameter did not appear to be associated with any difference in the transit times. Thus, when assessing the benefits of new protocols it will be important to ensure that they do not have a negative effect on the proportion of complete explorations.

Although diagnostic yield was not determined here, according to the guidelines for bowel preparation by the Korean Gut Image Study Group (23) bowel preparation with PEG is thought to enhance diagnostic yield when compared with fasting alone or a clear liquid diet,

as well as improving small bowel visualization quality, without affecting the cecal completion rate. Furthermore, previous studies have shown that bowel preparation with a 2 litre PEG solution results in similar diagnostic yield, small bowel visualization quality and cecal completion rate in CE as that achieved after preparation with a 4 litre PEG solution (24,25).

In our study, the only significant difference between the baseline characteristics of the intervention and control group that might have affected the results was a higher proportion of diabetic patients in the intervention group. However, when the data obtained was considered in relation to diabetes, the median quality of small bowel visualization was still higher in the intervention group. As such, diabetes does not appear to explain the differences observed in the total sample between the control and intervention groups, nor does it appear to have a negative effect on the results of the explorations, although in this case the small sample size may potentially have masked any effects of diabetes. Thus, it would appear not to be necessary to have to adapt the protocol specifically to patients with diabetes, and perhaps other morbidities.

In summary, this study confirms that low volume PEG preparations represent a good way to obtain high quality images of the small intestine through CE. However, more studies using these protocols will still be necessary to confirm these results and to explore further adaptations that may provide additional advantages to patients.

DISCLOSURES

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REFERENCES

1. Park SC, Keum B, Hyun JJ, *et al.* A novel cleansing score system for capsule endoscopy. World Journal of Gastroenterology 2010;16:875–880.

2. Yung DE, Rondonotti E, Sykes C, *et al.* Systematic review and meta-analysis: is bowel preparation still necessary in small bowel capsule endoscopy? Expert Rev Gastroenterol

Hepatol 2017;11:979–993.

3. Hookey L, Louw J, Wiepjes M, *et al.* Lack of benefit of active preparation compared with a clear fluid-only diet in small-bowel visualization for video capsule endoscopy: results of a randomized, blinded, controlled trial. Gastrointest. Endosc. 2017;85:187–193.

4. Bahar R, Gupta A, Mann SK. Clear Liquids versus Polyethylene Glycol Preparation for Video Capsule Endoscopy of the Small Bowel: A Randomized Controlled Trial. Digestion 2019;99:213–218.

5. Yang L, Wang X, Gan T, *et al.* Polyethylene Glycol for Small Bowel Capsule Endoscopy. Gastroenterol Res Pract 2017;2017:7468728.

6. Shiotani A, Opekun AR, Graham DY. Visualization of the small intestine using capsule endoscopy in healthy subjects. Digestive Diseases and Sciences 2007;52:1019–1025.

7. Niv Y, Niv G. Capsule endoscopy: Role of bowel preparation in successful visualization. Scandinavian Journal of Gastroenterology 2004;39:1005–1009.

8. Fireman Z, Paz D, Kopelman Y. Capsule endoscopy: Improving transit time and image view. World Journal of Gastroenterology 2005;11:5863–5866.

9. Ben-Soussan E, Savoye G, Antonietti M, *et al.* Is a 2-liter PEG preparation useful before capsule endoscopy? Journal of Clinical Gastroenterology 2005;39:381–384.

10. Xavier S, Rosa B, Monteiro S, *et al.* Bowel preparation for small bowel capsule endoscopy - The later, the better! Dig Liver Dis 2019;51:1388–1391.

11. Ell C, Remke S, May A, *et al.* The first prospective controlled trial comparing wireless capsule endoscopy with push enteroscopy in chronic gastrointestinal bleeding. Endoscopy 2002;34:685–689.

12. Villa F, Signorelli C, Rondonotti E, *et al.* Preparations and Prokinetics. Gastrointestinal Endoscopy Clinics of North America 2006;16:211–220.

13. Ge ZZ, Chen HY, Goa YJ, *et al.* The role of simeticone in small-bowel preparation for capsule endoscopy. Endoscopy 2006;38:836–840.

14. Dai N, Gubler C, Hengstler P, *et al.* Improved capsule endoscopy after bowel preparation. Gastrointestinal Endoscopy 2005;61:28–31.

15. Albert J, Göbel CM, Leßke J, *et al.* Simethicone for small bowel preparation for capsule endoscopy: A systematic, single-blinded, controlled study. Gastrointestinal Endoscopy 2004;59:487–491.

16. Kotwal VS, Attar BM, Gupta S, *et al.* Should bowel preparation, antifoaming agents, or prokinetics be used before video capsule endoscopy? A systematic review and meta-analysis. Eur J Gastroenterol Hepatol 2014;26:137–145.

17. Song HJ, Moon JS, Shim K-N. Optimal Bowel Preparation for Video Capsule Endoscopy. Gastroenterol Res Pract 2016;2016:6802810.

18. Rondonotti E, Spada C, Adler S, *et al.* Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Technical Review. Endoscopy 2018;50:423–446.

19. Oliva S, Cucchiara S, Spada C, *et al.* Small bowel cleansing for capsule endoscopy in paediatric patients: A prospective randomized single-blind study. Digestive and Liver Disease 2014;46:51–55.

20. Kotwal VS, Attar BM, Gupta S, *et al.* Should bowel preparation, antifoaming agents, or prokinetics be used before video capsule endoscopy? A systematic review and meta-analysis. European Journal of Gastroenterology and Hepatology 2014;26:137–145.

21. Ponte A, Pinho R, Rodrigues A, *et al.* Review of small-bowel cleansing scales in capsule endoscopy: A panoply of choices. World journal of gastrointestinal endoscopy 2016;8:600–9.

22. Pontone S, Angelini R, Standoli M, *et al.* Low-volume plus ascorbic acid vs high-volume plus simethicone bowel preparation before colonoscopy. World J Gastroenterol 2011;17:4689–4695.

23. Song HJ, Moon JS, Do JH, *et al.* Guidelines for Bowel Preparation before Video Capsule Endoscopy. Clin Endosc 2013;46:147–154.

24. Kantianis A, Karagiannis S, Liatsos C, *et al.* Comparison of two schemes of small bowel preparation for capsule endoscopy with polyethylene glycol: a prospective, randomized single-blind study. Eur J Gastroenterol Hepatol 2009;21:1140–1144.

25. Park SC, Keum B, Seo YS, *et al.* Effect of bowel preparation with polyethylene glycol on quality of capsule endoscopy. Dig. Dis. Sci. 2011;56:1769–1775.

Table 1. Baseline characteristics of the patient cohort

	All patients			
	Intervention	**Control**	**p value**	**Total**

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	group	group		
Patients, n (%)	57 (50)	56 (50)	-	113 (100)
Age, mean (SD)	53 (18)	57 (16)	0.214*	55 (17)
Gender, n (%)				
male	27 (47)	22 (39)	0.386+	49 (43)
female	30 (53)	34 (61)		64 (57)
Indication, n (%)				
OGB	28 (49)	29 (52)	0.777+	57 (51)
Abdominal pain	4 (7)	8 (14)	0.210+	12 (11)
Diarrhea	3 (5)	4 (7)	0.716-	7 (6)
Crohn's disease	11 (19)	11 (20)	0.963+	22 (20)
Crohn's disease surveillance	3 (5)	2 (4)	1.000-	5 (4)
Polyposis syndrome surveillance	2 (4)	0 (0)	-	2 (2)
Suspected Tumor	4 (7)	2 (4)	0.679-	6 (5)
Other	2 (4)	0 (0)	-	2 (2)
Diabetes, n (%)	12 (21)	3 (5)	0.014+	15 (13)
Obese, n (%)	5 (9)	1 (2)	0.206-	6 (5)
Prior abdominal surgery, n (%)	3 (5)	9 (16)	0.062+	12 (11)
Prior, non-digestive, abdominal surgery, n (%)	19 (33)	20 (36)	0.790+	39 (35)
Radiotherapy, n (%)	1 (2)	0 (0)	1.000-	1 (1)

*Student T-test, 2 independent samples; +Chi-squared; -Fisher's exact test; OGB, obscure gastrointestinal bleeding.

Supplementary table 1. Baseline characteristics of the Diabetic Patients

	Diabetic patients		
	Intervention group	**Control group**	**p value**
Patients, n (%)	12 (80)	3 (20)	-
Age, mean (SD)	64 (13)	66 (8)	0.790*
Gender, n (%)			
male	4 (33)	1 (33)	1.000-
female	8 (67)	2 (67)	
Indication, n (%)			
OGB	10 (83)	3 (100)	
Abdominal pain	1 (8)	0 (0)	1.000-
Diarrhea	0 (0)	0 (0)	
Crohn's disease	0 (0)	0 (0)	

Crohn's disease surveillance	0 (0)	0 (0)	
Polyposis syndrome surveillance	0 (0)	0 (0)	
Suspected Tumor	1 (8)	0 (0)	
Other	0 (0)	0 (0)	
Diabetes, n (%)			
Obese, n (%)	2 (17)	0 (0)	1.000[-]
Prior abdominal surgery, n (%)	0 (0)	0 (0)	-
Prior, non-digestive, abdominal surgery, n (%)	3 (25)	1 (33)	0.976[+]
Radiotherapy, n (%)	0 (0)	0 (0)	-

*Student T-test, 2 independent samples; [+] Chi-squared; [-]Fisher's exact test; OGB, obscure gastrointestinal bleeding.

Table 2. Results of the exploration in the whole cohort, as well as in diabetic and non-diabetic patients

	All patients			Diabetic patients			Non-Diabetic patients			
	Intervention group	Control group	p value	Intervention group	Control group	p value	Intervention group	Control group	p value	Total
Cecum visualization, n (%)										
Yes	54 (95)	50 (89)	0.321[-]	12 (100)	3 (100)	1.000[-]	42 (93)	47 (89)	0.501[-]	104 (92)
No	3 (5)	6 (11)		0 (0)	0 (0)		3 (7)	6 (11)		9 (8)
Visualization quality score, median (25%:75%)	2.45 (2.35:2.75)	2.35 (1.91:2.55)	0.003[#]	2.50 (2.33:2.75)	2.25 (1.85:2.33)	0.082[#]	2.45 (2.35:2.75)	2.35 (1.95:2.55)	0.010[#]	2.40 (2.10:2.70)
Mucosa visualization score (25%:75%)	2.70 (2.50:2.90)	2.60 (2.20:2.775)	0.004[#]	2.70 (2.55:2.90)	2.50 (2.10:2.60)	0.144[#]	2.70 (2.50:2.90)	2.60 (2.20:2.80)	0.012[#]	2.70 (2.40:2.90)
Lumen content score (25%:75%)	2.30 (2.10:2.60)	2.10 (1.63:2.38)	0.003[#]	2.30 (2.10:2.60)	2.00 (1.60:2.05)	0.050[#]	2.30 (2.10:2.60)	2.10 (1.63:2.38)	0.013[#]	2.20 (1.85:2.50)
Visualization quality score according to completeness of exploration, median (25%:75%)										
With cecum visualization	2.50 (2.35:2.75)	2.35 (2.00:2.60)	0.007[#]	2.50 (2.33:2.75)	2.25 (1.85:2.33)	0.082[#]	2.50 (2.35:2.75)	2.35 (2.00:2.60)	0.021[#]	2.45 (2.21:2.70)
With no cecum visualization	2.35 (2.23:2.40)	2.00 (1.20:2.35)	0.298[#]	-	-	-	2.35 (2.23:2.40)	2.00 (1.20:2.35)	0.298[#]	2.20 (1.50:2.40)
Median GTT (25%:75%)	27’02s’’ (15’47’’:60’06’’)	16’48’’ (10’54’’:41’26’’)	0.060[#]	31’22’’ (20’26’’:52’10’’)	16’13’’ (8’19’’:20’51’’)	0.112[#]	26’50’’ (14’45’’:60’14’’)	16’56’’ (10’54’’:43’02’’)	0.116[#]	25’07’’ (13’39’’:52’10’’)
Median SB transit time, min (25%:75%)	238 (184: 343)	281 (215:344)	0.153[#]	246 (200:302)	208 (117:236)	0.386[#]	238 (185: 351)	291 (225:345)	0.119[#]	259 (199:343)
Median CE battery life, min (25%:75%)	252 (157:316)	227 (159: 285)	0.493[*]	250 (197:320)	316 (293:414)	0.248[#]	252 (150:287)	224 (216:277)	0.277[#]	235 (160:296)

*Student T-test, 2 independent samples; [-]Fisher’s exact test; [#]Mann-Whitney U-test; GTT, Gastric transit time; SB, small bowel; CE, Capsule endoscopy.

Table 3. Baseline characteristics and results of the exploration according to completeness of the examinations

	Uncomplete examinations	Complete examinations	p value	total
Baseline characteristics				
Patients, n (%)	9 (8)	104 (92)		113 (100)
Interventional	3 (33)	54 (52)	0.321-	57 (50)
Control	6 (67)	50 (48)		56 (50)
Age, mean (SD)	53 (20)	55 (17)	0.214 *	55 (17)
Gender, n (%)				
male	4 (44)	45 (43)	1.000-	49 (43)
female	5 (56)	59 (57)		64 (57)
Indication, n (%)				
OGB	2 (22)	55 (53)	0.094-	57 (51)
Abdominal pain	2 (22)	10 (10)	0.244-	12 (11)
Diarrhea	0 (0)	7 (7)	1.000-	7 (6)
Crohn's disease	4 (44)	18 (17)	0.070-	22 (20)
Crohn's disease surveillance	1 (11)	4 (4)	0.345	5 (4)
Polyposis syndrome surveillance	0 (0)	2 (2)	1.000-	2 (2)
Suspected Tumor	0(0)	6 (6)	1.000-	6 (5)
Other	0 (0)	2 (2)	1.000-	2 (2)
Diabetes, n (%)	0 (0)	15 (14)	0.605-	15 (13)
Obese, n (%)	1 (11)	5 (5)	0.399-	6 (5)
Prior abdominal surgery, n (%)	1 (11)	11 (11)	0.271-	12 (11)
Prior, non-digestive, abdominal surgery, n (%)	5 (56)	34 (33)	0.271-	39 (35)
Radiotherapy, n (%)	0 (0)	1 (1)	1.000-	1 (1)
Parameters of the exploration				
Visualization quality score, median (25%:75%)	2.20 (1.80:2.35)	2.45 (2.23:2.70)	0.019#	2.40 (2.10:2.70)
Mucosa visualization score, median (25%:75%)	2.50 (1.70:2.70)	2.70 (2.43:2.90)	0.031#	2.70 (2.40:2.90)
Lumen content score, median (25%:75%)	1.90 (1.30:2.20)	2.20 (1.93:2.50)	0.014#	2.20 (1.85:2.50)
Median GTT (25%:75%)	32'22'' (13'41'':51'13'')	22'17'' (13'37'':52'22'')	0.504#	25'07'' (13'39'':52'10'')

*Student T-test, 2 independent samples; -Fisher's exact test; #Mann-Whitney U-test; OGB,

obscure gastrointestinal bleeding; GTT, Gastric transit time.