

# Utility, Performance and Safety of Single Balloon Enteroscopy in Patients with Hereditary Polyposis Syndromes

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## ABSTRACT

**Background & Aims:** Patients with hereditary polyposis syndromes are at high risk of developing small bowel polyps. We aimed to investigate the effectiveness of single balloon enteroscopy (SBE) in detecting and removing such polyps and to compare its diagnostic yield to videocapsule endoscopy (VCE).

**Methods:** We retrospectively recruited patients undergoing SBE and VCE in our center for familial adenomatous polyposis (FAP), Peutz-Jeghers syndrome (PJS), Cowden syndrome (CS) and juvenile polyposis syndrome (JPS). K Cohen concordance index and sensitivity, specificity, positive/negative predictive value (PPV-NPV) and odds ratio (OR) were calculated.

**Results:** We recruited 17 patients (9 females, 8 males, age range 29-82), undergoing 35 SBE procedures (7 JPS, 2 LS, 7 PJS, 4 CS, 15 FAP). Small bowel polyps were found in 19 cases (54%), in 6 JPS, 4 PJS, 2 CS and 7 FAP, with size ranging 3 mm-3 cm. The risk of small bowel polyps was not linked to the presence of gastric (OR=1.12, p=1), nor duodenal polyps (OR=0.89, p=1). Compared to VCE, the k index was 0.33±0.16, with sensitivity 79%, specificity 53%, PPV=68%, NPV=67%. Agreement was higher for polyps >1 cm (k=0.53) than for small ones (k =0.35). Thirteen polypectomy sessions were performed in polyps >1 cm, removing median 3 polyps/session (range 1-6). We observed only one early bleeding, treated with clips, and two cases of post-procedural abdominal pain.

**Conclusions:** Small bowel polyps may be commonly found in the polyposis syndrome. Concordance VCE-SBE is only fair. Polypectomy may be easily performed during SBE, with a low complication rate.

**Key words:** enteroscopy – videocapsule endoscopy – small bowel – polyps – Peutz Jeghers – familial adenomatous polyposis.

**Abbreviations:** CS: Cowden syndrome; DAE: device-assisted enteroscopy; FAP: adenomatous polyposis; JPS: juvenile polyposis syndrome; LS: Lynch syndrome; NPV: negative predictive value; OR: odds ratio; PJS: Peutz-Jeghers syndrome; PPV: positive predictive value; SBE: single balloon enteroscopy; VCE: videocapsule endoscopy.

## INTRODUCTION

Hereditary polyposis syndromes are a group of diseases or syndromes caused by mutations in specific genes with peculiar clinical phenotypes, carrying a high risk of developing hereditary colorectal cancer. In such context, hereditary colorectal cancer can occur at an early age, often associated with other cancer types; therefore, surveillance and prevention strategies need to be

implemented and established at appropriate times to decrease the associated mortality rate in these familial scenarios. Around the 30% of colorectal cancer has a genetic component. In particular, hereditary colorectal cancer represents about 5% of this subset. An inheritance pattern of transmission regarding specific gene mutations leading to development of hereditary colorectal cancer characterizes Lynch syndrome (LS), familial adenomatous polyposis (FAP), MUTYH-associated polyposis syndromes, juvenile polyposis syndromes (JPS), Cowden syndrome (CS) and polymerase proofreading-associated polyposis. After Lynch syndrome, FAP is the second most common hereditary colorectal cancer syndrome and is responsible for about 1% of all colorectal cancer cases [1]. Of interest, all the above mentioned syndromes carry a variable risk of developing polypoid lesions in the small bowel; their

detection and subsequent treatment is entirely based on specific risk factors and clinical conditions.

Familial adenomatous polyposis is an autosomal dominant disorder caused by germline mutations in the APC gene resulting in the formation of hundreds of colo-rectal adenomatous polyps. In FAP, small bowel surveillance is not routinely indicated, but if the patient undergoes duodenal surgery, as in the case of advanced duodenal or ampullary lesions (high grade ampullary adenoma or invasive duodenal cancer), small bowel examination should be performed before surgery through capsule endoscopy and if positive, proper diagnosis and treatment with enteroscopy [2]. Jejunal adenomas can be found in up to 75% of cases, while ileal adenomas in 20% of cases. In both cases their prevalence is lower than duodenal adenomas [3].

Peutz-Jeghers syndrome (PJS) is an autosomal dominant hereditary syndrome, diagnosed in the presence of a pathogenic germline mutation in the serine-threonine kinase 11 tumor suppressor gene associated with the presence of characteristic mucocutaneous pigmentation and a positive family history. Peutz-Jeghers syndrome is predominantly characterized by small bowel polyposis (60%-90%) especially in the jejunum, with the histological type of hamartomas, that have been reported to cause major acute complications, such as obscure bleeding and intussusception, or, occasionally, abdominal pain. The cumulative risk of cancer in PJS is lower than 60% by the age of 70 years [4]. Surveillance according to ESGE includes a baseline colonoscopy at 8 years of age, then routinely by the age of 18 years, every 1-3 years; instead, gastric and small bowel surveillance should be performed through esophagogastroduodenoscopy following the same intervals as for colonoscopy completed by investigations with MRI or videocapsule endoscopy (VCE) starting by the age of 8 years and repeated at 1-3 years intervals. Elective polypectomy should be performed eventually in the case of detection of small bowel polyps larger than 15-20 mm, by means of device-assisted enteroscopy [4, 5].

Another hamartomatous inherited polyposis is represented by the Cowden syndrome or phosphatase and tensin homolog (PTEN) -hamartoma syndrome, characterized by macrocephaly and multiple benign hamartomatous lesions in different organs. Gastrointestinal polyps can develop in the small bowel, although more rarely than they develop in the esophagus, stomach and large bowel. In those cases, more frequent locations could be the duodenum and the proximal segments of the jejunum [6]. Cancer risk is greater for breast and thyroid gland. Gastrointestinal surveillance includes only colonoscopy, by the age of 35 years and repeated every 5 years [7, 8].

Juvenile polyposis syndrome is a rare autosomal dominant polyposis syndrome characterized by a germline mutation in SMAD4 or BMPR1A carrying a variable gastrointestinal cancer risk (up to 68%). In JPS the development of large bowel polyps occurs in the first two decades of life. Most frequently these are found in the large bowel and in the stomach, where they can lead to maldigestion and malabsorptive conditions, such as protein-losing enteropathy [7]. Small bowel surveillance is currently not recommended according to the rare occurrence of small bowel involvement [4]. However, SMAD4 mutation

seems more frequently associated to the occurrence of small bowel polyps, specifically to the duodenum; therefore, a duodenoscopy appears to be appropriate [5].

Lynch syndrome is an autosomal dominant disorder caused by mutations in the mismatch repair genes, namely MLH1, MSH2, MSH6, PMS2 or EPCAM. Lynch syndrome is primarily associated with colorectal cancer and endometrial cancer, but also with an increased predisposition to ovarian cancer, stomach, small intestine, hepatobiliary system, pancreas, renal and brain neoplasms [9]. The estimated lifetime risk of developing small bowel cancer in Lynch syndrome is < 5% [10]. Small bowel surveillance is currently not recommended in Lynch syndrome.

Therefore, small bowel polyps vary greatly in distribution and frequency in this heterogeneous group of inherited polyposis disorders; thus, an univocal strategy and treatment is not addressable.

Enteroscopic techniques have evolved significantly in the past 20 years, encompassing a wide range of indications: obscure gastrointestinal bleeding evaluation and control, small bowel tumors and polyps evaluation. The appropriate selection of the technique should be based on local expertise of the endoscopist and on instrument availability in the unit and the approach (anterograde or retrograde) should be based on the videocapsule endoscopy (VCE) study to identify the bowel segments through the transit time [11]. Videocapsule endoscopy still represents the best technique to screen for small bowel polyps, except for PJS, as stated by ESGE guidelines [4], and for FAP patients, where the score of Spiegelman may address the choice to perform a more detailed small bowel study through enteroscopy. Indeed, FAP patients with more severe duodenal polyposis are at higher risk of small bowel lesions and thus may benefit from device-assisted enteroscopy (DAE) for therapeutic purpose [12]. Device-assisted enteroscopy namely double-balloon enteroscopy (DBE) and single-balloon enteroscopy (SBE), are based on different techniques having in common a device helping the progression of the scope. Double-balloon enteroscopy, also known as push-and-pull enteroscopy was introduced in 2001; it utilizes an endoscope with an inflatable balloon on the tip, plus a soft flexible overtube, has also with an inflatable balloon to its distal end; both balloons can be inflated and deflated separately, thus allowing the overtube to act as an anchor during progression. Single-balloon enteroscopy was introduced in 2007, following the same basic insertion technique as DBE, but lacking the balloon on the scope; therefore anchoring is obtained through the angulation of the tip and the deflation of the balloon after a deep insertion movement [13].

On this base, we performed the present study with the aim to evaluate the efficacy of SBE in detecting and then removing small bowel polyps in patients with hereditary polyposis syndromes, and, at the same time, to compare the diagnostic yield of SBE with video-capsule endoscopy (VCE) in this group of patients. Secondary objectives included the assessment of the safety profile concerning this diagnostic-interventional technique in terms of complications, and finally to examine the hypothesis of a possible risk of correlation between small bowel polyps and the presence of gastro-duodenal polyps.

## METHODS

### Study Design and Patient Enrollment

We conducted a retrospective cohort study which included all consecutive patients with PJS, FAP, CS and JPS who underwent single-balloon enteroscopy (SBE) and videocapsule endoscopy (VCE) between the 2016 and 2023 at the Section of Gastroenterology and Digestive Endoscopy, Department of Precision and Regenerative Medicine-Jonian Area of the Azienda Ospedaliero- Universitaria Consorziata Policlinico di Bari, Italy.

The patients enrolled in our study were diagnosed on the basis of proven specific genetic mutations. Patient-related information and follow-up were retrieved by endoscopy and clinical databases. For each patient included in the study, the following data were collected: biographical data (gender, age, date of birth); type of hereditary polyposis syndrome; year of enteroscopy performance; type of enteroscopy (anterograde, retrograde or bidirectional); number of polyps found and/or removed; polyp size; any complications of the SBE procedure; date and report of the VCE that was performed more closely in time to the enteroscopic examination (within 3 months); finding of gastric polyps in the patient history at EGDS; finding of duodenal polyps in patient history at EGDS; patient oncological history; history of previous surgery. In particular, all these data were retrieved by checking medical records at the Rare Diseases Outpatient Clinic and reports of VCE present in paper or digital at the Digestive Endoscopy Outpatient Clinic.

The study was conducted in agreement with the indications of the Declaration of Helsinki. Given the retrospective nature of the study, an approval from the local Ethics committee was not required. However, when the patients signed the informed consent to undergo endoscopic procedures, they agreed to the anonymous handling of disease-related data for research purposes.

### Enteroscopic Procedure and Treatment

Single-balloon enteroscopy procedures were performed using the Olympus SIF-Q180 Enteroscope with overtube (Olympus America Inc.) under general anesthesia and endotracheal intubation. The endoscopist who performed all the procedures was a gastroenterologist specifically dedicated to this field. Written informed consent to undergo the procedure was obtained from each patient in the morning of the scheduled procedure. The entry route was guided by VCE reports: anterograde for polyps detected in the first 60% of a VCE study obtained by considering at what time the lesion was detected, relatively to the total small bowel transit time; retrograde in the last 40%. In the case of anterograde procedures, the patient was fasting overnight. In patients undergoing retrograde procedures, the standard bowel preparation entailed the administration of 3 liters of polyethyleneglycol 4000 on the evening before the procedure, followed by an additional 1 litre on the morning of the procedure, 3 hours prior to the beginning of the procedure.

To assess depth of insertion, ink tattooing was performed to the most distal point reached. During SBE, the polyp size was visually estimated comparing the diameter of the polypectomy snare used. Techniques of choice were piecemeal

or en-bloc EMR and hot snare polypectomy. The polypectomy technique was chosen at the discretion of the endoscopist, as well as submucosal saline/diluted-adrenaline injection and post-polypectomy prophylactic clipping, all based on specific polyp morphological characteristics. Polyps were routinely retrieved for pathological examination and sent to the Pathology Department of the same hospital. Any enteroscopy-related complications (e.g. hemorrhage, perforation, and acute pancreatitis) were systematically evaluated and recorded in medical charts. The complications were defined as intra-procedural (occurring during the procedure) and post-procedural (occurring subsequently to the procedure) subclassified in early ( $\leq 24$  hours) or delayed (2-30 days). Bleeding was classified as minor when it presented as self-limiting or when hemostasis was achieved during the index procedure. Immediate complications were evaluated during the hospital stay, while delayed ones were recorded by a phone call at one month after the index procedure. For each patient undergoing SBE, reports of antecedently performed VCEs were retrieved and the reports of the two examinations were compared to assess their concordance and diagnostic yield.

### Video Capsule Endoscopy Procedure

Video capsule examinations were performed with Pillcam SB2 and SB3 (Medtronic, Dublin, Ireland). All patients gave their informed consent. Capsule endoscopy was performed after a 12-hour fast. Polyethylene glycol was administered in a split manner: 3 L the evening before and 1 L the same morning of the procedure. Fluid and light meals were allowed 2 and 4 hours after capsule ingestion, respectively. The data recorder was removed after 12 hours of recording and the digital information was downloaded and analyzed using Rapid software. The capsule endoscopy findings were assessed. The small bowel area was divided into three tertiles (proximal, middle, and distal) based on recording time duration. In the report, the small bowel polypoid lesions were approximately characterized in number and maximum diameter.

### Statistical Analysis

Continuous variables were expressed as mean  $\pm$  standard deviation, discrete variables as proportions/percentages. Cohen's  $k$  concordance index was calculated in order to assess the agreement between SBE and VCE in evaluating a finding. Sensitivity, specificity, positive and negative predictive value (PPV-NPV) of SBE, in comparison with VCE as gold standard, were calculated. Moreover, in order to correlate the presence of gastric/duodenal polyps with those of the small bowel, the odd ratios (ORs) with their respective confidence intervals (CIs) at 95% according to Mantel-Haenszel were analyzed. All statistical analyses were 2-sided. A  $p$  value  $< 0.05$  was considered statistically significant. Data handling and statistical analysis were performed with Graphpad Prism 5 software (La Jolla, California, USA).

## RESULTS

### Patient Characteristics

Between January 2016 and January 2023, seventeen patients with PJS, FAP, CS, Lynch Syndrome and JPS were enrolled [8

males; 9 females; mean age  $55 \pm 19$  years (range 29-82 years)], specifically 4 with JPS, 4 with PJS, 3 with CS, 5 with FAP and 1 with LS. Two female patients were affected by juvenile polyposis/hereditary hemorrhagic telangiectasia syndrome and received pulmonary embolization for an artero-venous malformation. Among other relevant comorbidities, 10 patients had previous history of cancers, in some cases multiple: we recorded 7 cases of papillary thyroid carcinoma (all in FAP patients), 3 breast cancers and 3 pancreatic adenocarcinomas. Among previous surgery, 13 patients had at least one abdominal surgery: 2 had a right colectomy, one left colectomy and 6 proctocolectomy. Finally, 4 small bowel resections, 2 partial gastric resections and one Whipple procedure were recorded. Clinical characteristics are presented in Table I.

**Table I.** Patient characteristics

Total no. of patients	17
Age	$55 \pm 19$
Gender, no. (%)	
Female	9 (53)
Male	8 (47)
Hereditary Polyposis Syndrome, no. (%)	
JPS	2 (12)
JPS + HHT	2 (12)
PJS	4 (24)
CS	3 (18)
FAP	5 (30)
LS	1 (5)
Mean age at first SBE, years (range)	
JPS	35.5 (26-42)
PJS	31.2 (25-39)
CS	58.7 (53-62)
FAP	58.2 (34-71)
LS	68 (-)
History of abdominal surgery, no. (%)	13 (76)
Small-bowel resection, no. (%)	4 (23)
History of malignancies, no. (%)	10 (59)

JPS: juvenile polyposis syndrome; HHT: hemorrhagic hereditary telangiectasia; PJS: Peutz-Jeghers syndrome; CS: Cowden syndrome; FAP: familial adenomatous polyposis; LS: Lynch syndrome.

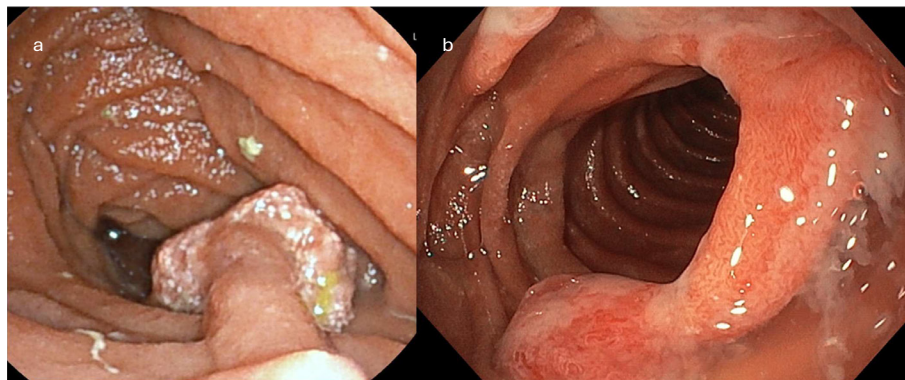
**Procedural Parameters**

A total number of 35 SBE procedures were performed in these patients, in particular: 7 in patients with JPS; 2 in patients with LS; 4 in patients with CS; 7 in patients with PJS; and 15 in patients with FAP. The procedure parameters are summarized in Table II. Twenty-seven SBE procedures were performed via an antegrade approach, 7 via a retrograde approach, 1 with a bidirectional approach. Polyps were found in 19 procedures (54.28%), of which 6 in patients with JPS, 4 in patients with PJS (Fig. 1), 2 in patients with CS, 7 in patients with FAP. No polyps resulted from both the antegrade and retrograde enteroscopy of the single patient with LS. The size of the polyps ranged from 3 mm to 30 mm. Thirteen polypectomy sessions were performed for polyps > 10 mm, with a median of

**Table II.** SBE procedural parameters

Total no. of procedures	35
Number of SBEs per disease, no. (%)	
JPS	7 (20)
LS	2 (6)
CS	4 (11)
PJS	7 (20)
FAP	15 (43)
Route of SBE, no. (%)	
Antegrade	27 (77)
Retrograde	7 (20)
Bidirectional	1 (3)
Number of SBEs with polyp finding, no. (%)	19 (54)
JPS	6 (32)
PJS	4 (21)
CS	2 (11)
FAP	7 (37)
LS	0
Polyp size, range (mm)	2-30
Total no. of polypectomies	13
Number of resected polyps per SBE (no.), median (range)	3 (1-6)
Number of SBEs related to complications, total no. (%)	3 (9)

SBE: single balloon enteroscopy; JPS: juvenile polyposis syndrome; HHT: hemorrhagic hereditary telangiectasia. For the rest of abbreviations see Table I.



**Fig. 1.** Endoscopic view of two hamartomatous polyps in Peutz-Jeghers Syndrome (a and b).

3 polyps removed per session (range 1-6). All polyps resected in JPS had histological features of juvenile polyps. In PJS all polyps were hamartomatous. In FAP, all removed polyps were adenomatous.

Gastric polyps were found in 12/17 patients (70.59%). The risk of having small bowel polyps when gastric polyps were present was not significant, OR = 1.3 (95% CI 0.23-7.8),  $p = 1$ . Duodenal polyps were found in 10/17 patients (58.82%). The risk of having small bowel polyps when duodenal polyps were present was also not significant, OR = 1.7 (95% CI 0.40-7.1),  $p = 0.71$ .

Regarding the diagnostic performance for polyp detection compared to VCE, the  $k$ -index was  $0.516 \pm 0.148$  with sensitivity 76.2%, specificity 72.7%, PPV 84.2%, NPV 61.5%. The likelihood ratio was 2.79.

The level of agreement was  $k = 0.458 \pm 0.157$  for polyps < 1 cm in size, while for polyps > 1 cm in size was:  $k = 0.507 \pm 0.208$ .

We observed 6 cases (one JPS, one CS and 4 FAP), in which enteroscopy detected polyps in the proximal jejunum which were missed by SBCE. In all cases, they were small in size, ranging from 2 to 7 mm, and this could explain the missed visualization at capsule endoscopy. Finally, in no cases polyps located at Ampulla of Vater were detected.

### Complications

In terms of complications related to the enteroscopic examination, only one case of intra-procedural early bleeding had occurred, which was treated with clips. Two patients experienced post-procedural abdominal pain.

## DISCUSSION

Patients affected by inherited polyposis syndromes have an increased risk of developing small bowel polyps. Enteroscopy may be critical for the removal of these lesions to prevent the development of small bowel cancer or other complications such as small bowel obstruction and intussusception, in the case of PJS. Not long ago, the management of small bowel polyps was primarily surgical and often required several interventions with consequent multiple resections over time, potentially leading to short bowel syndrome. The development of advanced enteroscopy systems (including SBE), which combine a thorough evaluation of the small bowel with the removal of any polyps, has provided the opportunity for non-surgical management of small bowel polyps, making it the most effective treatment. In a comparative study, Koh et al. [14] showed that the maximum insertion time for SBE was shorter than for DBE using the antegrade approach (40 min vs 50 min, respectively), with the same therapeutic yield and low rate of adverse events after diagnostic or therapeutic enteroscopy for both procedures. Similar results were found in a retrospective study and a meta-analysis of large comparative studies [15].

In the current study, SBE was effective in detecting and subsequently removing small bowel polyps in patients with hereditary polyposis syndromes. The study showed that, out of a total of 35 SBE procedures performed, polyps were detected in 19 cases (54.28%) and 13 polypectomy sessions were performed for polyps > 1 cm in size, with a median of 3 polyps removed per session (range 1-6).

This evaluation might show some limitations. First, the small number of recruited patients ( $n = 17$ ) and, consequently, the number of performed SBEs ( $n = 35$ ), although the timespan of considered SBEs was sufficiently large (up to 7 years). Nevertheless, we emphasize that the small number is consistent with the rarity of the syndromes and the relative novelty of the enteroscopic approach compared to previous management strategies. Furthermore, the study highlighted the safety of this diagnostic-interventional technique in terms of complications. Indeed, the study reports a low number of minor complications (three, including two cases of post-procedural abdominal pain and only one case of early intra-procedural bleeding treated with endoclips) and a zero rate of major complications. Despite the favorable results in terms of complications, it is worth noting that this is an invasive procedure, so its burden is significant and the time needed for performance is not negligible. For this reason, we attempted to test the hypothesis of selecting only those patients who can really benefit from enteroscopy, so that the risk/benefit ratio could be reduced. The data from the aforementioned studies suggest that such patients could be those with PJS and JPS. In fact, 4 out of 7 patients with PJS and 6 out of 7 JPS patients who underwent SBE benefited from polypectomy. In agreement with this, current studies only confirm clear evidence in favour of PJS and a screening strategy for small bowel polyps is currently only recommended for this syndrome [4]. Guidelines suggest the use of magnetic resonance imaging (MRI) or VCE every 1-3 years, depending on the disease phenotype. In this context, balloon enteroscopy plays a central role in the removal of polyps, especially those that cause symptoms of subocclusion or intussusception despite their small size. In these circumstances, both SBE and DBE have been shown to be indicated and capable of removing polyps up to 6-10 cm in size [16, 17].

Recently, for instance, polypectomy procedures were described in 102 patients with resection of polyps larger than 10 mm, achieving complete treatment in the 98% of patients, with a complication rate of 7.7% (mainly bleeding, perforation, or pancreatitis) [18].

The guidelines do not recommend other indications for regular small bowel screening by SBE for hereditary polyposis except PJS. For the other syndromes, VCE is still the best technique for small bowel polyp screening in order to avoid unnecessary invasive procedures. From the results of this study, regarding the diagnostic performance for polyps compared to VCE, the  $k$ -index is  $0.516 \pm 0.148$  (with sensitivity of 76.2%, specificity of 72.7%, VPP of 84.2%, VPN of 61.5%). The level of agreement was higher for polyps > 1 cm ( $k = 0.458 \pm 0.157$ ), compared with those < 1 cm in size ( $k = 0.507 \pm 0.208$ ). The limitation of VCE is not allowing any operative maneuvers. Therefore, for other syndromes, it is more indicated to perform SBE only in cases of positive finding of polyposis lesions recorded at VCE. These two procedures are, therefore, complementary in the diagnostic work-up. Initial diagnostic imaging with VCE could be followed by therapeutic and interventional DAE. The time indication of VCE, defined as the location of the lesion as a percentage of the total transit time along the entire GI tract (mouth-cecum), can be used to select the best approach (antegrade or retrograde) for subsequent enteroscopic examination.

Even for FAP, guidelines lack a clear protocol for small bowel surveillance. Although oncological risk does not seem to imply the need to look for polyps in the small bowel, it has been suggested that patients with FAP with a more severe Spigelman score have an increased risk of developing polyps in the small bowel [12]. Therefore, the ASGE guidelines limited the indications for small bowel enteroscopy to patients with FAP with Spigelman score grade IV; in addition, enteroscopy could be considered for therapeutic purposes in patients with positive VCE or MRI who are symptomatic, or in the context of preoperative surveillance in patients awaiting duodenal surgery [19]. Considering that most small bowel polyps occur in the proximal jejunum rather than the ileum, total enteroscopy is not always necessary [20].

On the other hand, in Lynch syndrome (LS), even VCE has shown several cases of false positives (approximately 11%) leading to unnecessary enteroscopy [21] as well as a false negative rate of 1.5% leading to several cases of undiagnosed cancer [22]. Therefore, VCE may require further evaluation in this patient population and one possible area of interest is the implementation of artificial intelligence in VCE.

Exploration of the small intestine is a fascinating field of interest in gastroenterological and endoscopic practice. However, it should be noted that enteroscopy is an invasive procedure, so its burden is significant. For this reason, it could be useful to select only those patients who could really benefit from it. Finally, among the disadvantages of device-assisted enteroscopy, the long procedure time is of relevance. Despite these limitations, we believe that these data may be a resource for establishing management of patients with PJS in the future. Conversely, small bowel polyps, which may be commonly found in polyposis syndromes, are commonly detected by VCE and subsequently treated by SBE.

## CONCLUSIONS

However, in the present study, the concordance between VCE and SBE is only fair, thus suggesting the need of improving current procedures. Finally, polypectomy can be easily performed during SBE, with a low complication rate.

**Conflicts of interest:** None to declare.

**Authors' contributions:** G.L., A.D.L. and S.R. conceived the study. G.L., A.I. and S.R. performed enteroscopy. M.P. performed videocapsules. R.R., A.C.M., F.C. and M.B. collected the data. G.L., R.R. and E.I. performed statistical analysis. R.R., A.C.M., F.C. wrote manuscript draft. G.L., E.I., M.B., M.P. and A.D.L. revised the draft. All authors read and approved the final version.

## REFERENCES

- Kim HM, Kim TI. Screening and surveillance for hereditary colorectal cancer. *Intest Res* 2024;22:119-130. doi:10.5217/ir.2023.00112
- Pennazio M, Venezia L, Cortegoso Valdivia P, Rondonotti E. Device-assisted enteroscopy: An update on techniques, clinical indications and safety. *Dig Liver Dis* 2019;51:934-943. doi:10.1016/j.dld.2019.04.015
- Fukushi G, Yamada M, Kakugawa Y, et al. Genotype-phenotype correlation of small-intestinal polyps on small-bowel capsule endoscopy in familial adenomatous polyposis. *Gastrointest Endosc* 2023;97:59-68.e7. doi:10.1016/j.gie.2022.08.042
- van Leerdam ME, Roos VH, van Hooft JE, et al. Endoscopic management of polyposis syndromes: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2019;51:877-895. doi:10.1055/a-0965-0605
- Pennazio M, Rondonotti E, Despott EJ, et al. Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2022. *Endoscopy* 2023;55:58-95. doi:10.1055/a-1973-3796
- Saito K, Nomura F, Sasaki Y et al. Characteristics of Small Bowel Polyps Detected in Cowden Syndrome by Capsule Endoscopy. *Case Rep Gastrointest Med* 2015;2015: 475705. doi:10.1155/2015/475705
- Rosty C, Brosens LAA. Pathology of Gastrointestinal Polyposis Disorders. *Gastroenterol Clin North Am* 2024;53:179-200. doi:10.1016/j.gtc.2023.09.006
- Piazzolla M, Borraccino AV, Rizzi S, Losurdo G, Di Leo A. Jejunal venous malformations in Cowden syndrome: a case report. *J Gastrointest Liver Dis* 2022;31:480-481. doi:10.15403/jgld-4655
- Kastrinos F, Samadder NJ, Burt RW. Use of Family History and Genetic Testing to Determine Risk of Colorectal Cancer. *Gastroenterology* 2020;158:389-403. doi:10.1053/j.gastro.2019.11.029
- Losurdo G, Di Leo M, Rizzi S, et al. Familial Intestinal Polyposis and device assisted enteroscopy: where do we stand? *Expert Rev Gastroenterol Hepatol* 2023;17:811-816. doi:10.1080/17474124.2023.2242240
- Serrano M, Mão-de-Ferro S, Pinho R, et al. Double-balloon enteroscopy in the management of patients with Peutz-Jeghers syndrome: a retrospective cohort multicenter study. *Rev Esp Enferm Dig* 2013;105:594-599. doi:10.4321/s1130-01082013001000004
- Papagni S, Rizzi S, Principi M, et al. Familial adenomatous polyposis small bowel surveillance: could indicators for video-capsule endoscopy be ascertained? *Minerva Gastroenterol Dietol* 2016;62:272-273.
- Muniraj T, Lee LS. Enteroscopy for GI Fellows. In: Adler DG. (Eds). *Upper endoscopy for GI fellows*. Springer, Cham. 2017. doi:10.1007/978-3-319-49041-0\_13
- Koh JTE, Kim Wei L, Francisco CP, et al. Double balloon enteroscopy versus single balloon enteroscopy: A comparative study. *Medicine (Baltimore)* 2024;103:e38119. doi:10.1097/MD.00000000000038119
- Kim TJ, Kim ER, Chang DK, Kim YH, Hong SN. Comparison of the Efficacy and Safety of Single- versus Double-Balloon Enteroscopy Performed by Endoscopist Experts in Single-Balloon Enteroscopy: A Single-Center Experience and Meta-Analysis. *Gut Liver* 2017;11:520-527. doi:10.5009/gnl16330
- Bizzarri B, Borrelli O, de'Angelis N, et al. Management of duodenal jejunal polyps in children with Peutz-Jeghers syndrome with single balloon enteroscopy. *J Pediatr Gastroenterol Nutr* 2014;59:49-53. doi:10.1097/MPG.0000000000000351
- Akarsu M, Ugur Kantar F, Akpinar H. Double-balloon endoscopy in patients with Peutz-Jeghers syndrome. *Turkish J Gastroenterol* 2012;23:496-502. doi:10.4318/tjg.2012.0356
- Cao Z, Jin W, Wu X, Pan W. Endoscopic Therapy of Small Bowel Polyps by Single-Balloon Enteroscopy in Patients with Peutz-Jeghers Syndrome. *Int J Clin Pract* 2022;2022:7849055. doi:10.1155/2022/7849055
- Yang J, Gurudu SR, Koptiuch C, et al. American Society for Gastrointestinal Endoscopy guideline on the role of endoscopy in familial adenomatous polyposis syndromes. *Gastrointest Endosc* 2020;91:963-982.e2. doi:10.1016/j.gie.2020.01.028

20. Katsinelos P, Kountouras J, Chatzimavroudis G, et al. Wireless capsule endoscopy in detecting small-intestinal polyps in familial adenomatous polyposis. *World J Gastroenterol* 2009;15:6075-6079. doi:[10.3748/wjg.15.6075](https://doi.org/10.3748/wjg.15.6075)
21. Monahan KJ, Bradshaw N, Dolwani S, et al. Guidelines for the management of hereditary colorectal cancer from the British Society of Gastroenterology (BSG)/Association of Coloproctology of Great Britain and Ireland (ACPGBI)/United Kingdom Cancer Genetics Group (UKCGG). *Gut* 2020;69:411-444. doi:[10.1136/gutjnl-2019-319915](https://doi.org/10.1136/gutjnl-2019-319915)
22. Haanstra JF, Al-Toma A, Dekker E, et al. Prevalence of small-bowel neoplasia in Lynch syndrome assessed by video capsule endoscopy. *Gut* 2015;64:1578-1583. doi:[10.1136/gutjnl-2014-307348](https://doi.org/10.1136/gutjnl-2014-307348)