Total motorized spiral enteroscopy: first prospective clinical feasibility trial

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Background and Aims: Motorized spiral enteroscopy (MSE) was recently introduced into clinical practice and shown to be safe and effective for antegrade enteroscopy. The aim of the current trial was to prospectively study the efficacy and safety of MSE for visualization of the entire small bowel.

Methods: All consecutive patients with indications for complete enteroscopy meeting the inclusion criteria were enrolled in a prospective observational bicentric trial, starting with antegrade MSE; a retrograde approach was performed if MSE remained incomplete from antegrade. The primary objective was to ascertain the total enteroscopy rate (TER); secondary objectives were diagnostic yield, procedural success, time, depth of maximum insertion (DMI), therapeutic yield, and adverse events (AEs).

Results: Thirty patients (16 women, 14 men; median age 64 years [range, 37-100]) were enrolled. Technical success rate of antegrade MSE (advancement beyond the ligament of Treitz) and retrograde MSE (advancement beyond the ileocecal valve [ICV]) were 100% and 100%, respectively. Overall TER was 70%: 16.6% antegrade approach alone and 53.4% bidirectional approach. Median antegrade DMI distal from the ligament of Treitz was 490 cm (range, 160-600); median insertion time 26 minutes (range, 15-110). The median retrograde DMI beyond the ICV was 120 cm (range, 40-600), and median insertion time was 17 minutes (range, 1-68). Overall diagnostic and therapeutic yields were 80% and 86.7%, respectively. Overall AE rate was 16.7%. No serious AEs occurred.

Conclusions: This prospective study showed that complete enteroscopy is feasible with MSE, either from antegrade alone or bidirectionally, with high success rates and short procedural duration. These results justify further evaluation of MSE in a large prospective multicenter study, preferably with inclusion of a control group. (Clinical trial registration number: NCT03438695.) (Gastrointest Endosc 2021;93:1362-70.)

The first step in the clinical approach to small-bowel disorders usually includes a noninvasive imaging technique such as video capsule endoscopy or magnetic resonance imaging for visualization of any abnormal findings in the small intestine.[1-6] Enteroscopy allows for direct endoscopic visual access to the small bowel with the option for tissue acquisition and therapeutic procedures.[1-3,6,7] However, deep enteroscopy is a challenging and time-consuming procedure, and, in particular, visualization of the entire small intestine is usually only achieved by experts in enteroscopy using device-assisted enteroscopy (DAE) techniques.[8-12] The role of the different available techniques,

Abbreviations: AE, adverse event; DAE, device-assisted enteroscopy; DBE, double-balloon enteroscopy; DMI, depth of maximum insertion; ICV, ileocecal valve; MSE, motorized spiral enteroscopy; PSE, PowerSpiral enteroscopy; SBE, single-balloon enteroscopy; SE, spiral enteroscopy; TER, total enteroscopy rate; TSR, technical success rate.

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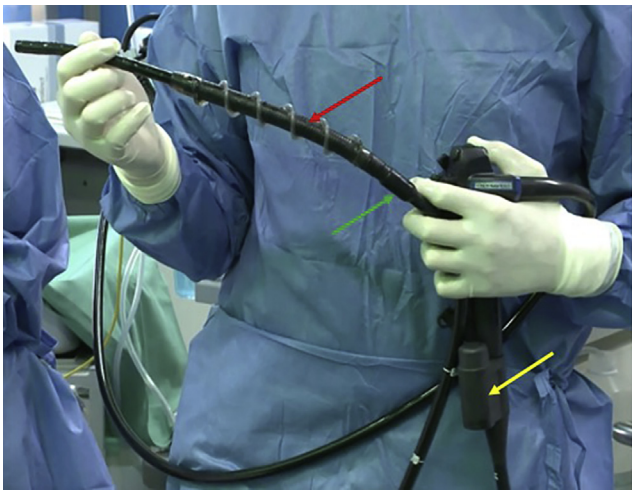

Figure 1. Motorized Spiral Enteroscope PSF-1 (PowerSpiral; Olympus Medical Systems Corporation, Tokyo, Japan) is a reusable endoscope, similar to a pediatric colonoscope of 1680 mm in length, with an outer diameter of 11.3 mm at the insertion portion. An integrated electric motor is used to rotate a short disposable spiral overtube (*red arrow*, 240 mm length, 31.1 mm outer diameter of the soft spiral fins) that is attached to a rotation coupler (*green arrow*) located 40 cm proximal to the endoscope's tip. Direction and speed of motorized rotation of the spiral section is controlled by a foot pedal switch (not shown). Clockwise and counterclockwise rotation is used to traverse the small bowel by "pleating" or "unpleating" the small bowel onto or from the insertion tube, respectively. The direction and force that is applied to the tissue by spiral rotation is continuously monitored by the system and shown on the display (spiral rotation force indicator, see Fig. 2A and C). An integrated safety mechanism stops spiral rotation automatically if a certain threshold is exceeded.

including double-balloon enteroscopy (DBE), single-balloon enteroscopy (SBE), and manual spiral enteroscopy (SE), was addressed by guidelines.[1-3,6] Although balloon-assisted enteroscopy uses 1 or 2 balloons, 1 each on the outside of a long overtube and the endoscope for DBE and only 1 on the overtube for SBE, and a push-and-pull technique to traverse the small bowel,[13,14] the principle of SE is the conversion of rotational energy of a spiral located on the outside of a long overtube into linear force to pleat the intestine onto or from the enteroscope.[15]

Motorized SE (MSE), using the novel PSF-1 PowerSpiral Enteroscope (Olympus Medical Systems Corporation, Tokyo, Japan), was introduced into clinical practice and represents a new technology, namely "self-propelling enteroscopy," that is a technical refinement of the principle of SE.[16] An integrated electric motor is used to rotate a short spiral overtube at the distal part of the insertion section of the enteroscope (Fig. 1). PowerSpiral enteroscopy (PSE) was recently shown to be effective for antegrade deep enteroscopy in terms of diagnostic success rates, procedural duration, and depth of maximum insertion (DMI) in an initial prospective pilot study by our group.[17] The diagnostic yield of antegrade PSE was 74.2%, which is not inferior in comparison with pooled data from meta-analyses using standard DAE techniques.[8-10,12,18] However, because in the trial almost 90% of the PSE procedures remained incomplete, important clinical findings may have been missed.

In general, total enteroscopic examination of the small intestine is achieved in a bidirectional approach in most cases, combining antegrade and retrograde DAE. However, at the time of conducting the trial, no data existed about the use of PSE from a retrograde approach and therefore about its true efficacy with respect to the capability of visualization of the entire small bowel. In a prospective feasibility trial, our group recently showed that PSE was effective and safe for colonoscopy and provided successful access to the small bowel with an ileum intubation rate of 96.7%.[19] The aim of the current prospective trial was to evaluate the feasibility and success rate of complete enteroscopy using MSE.

METHODS

Study design

This prospective, investigator-initiated, noncontrolled clinical trial (Total Motorized Spiral Enteroscopy Trial [TMSET]) was conducted at 2 European endoscopic tertiary referral centers. The study protocol was approved by the institutional review board at each center before initiation of the trial. The study was registered at the U.S. National Library of Medicine database (published February 19, 2018; clinicaltrials.gov, identifier: NCT03438695).

Inclusion and exclusion criteria

Patients with suspected small-bowel disease with a positive or suggestive finding on prior small-bowel imaging (capsule endoscopy, radiology) or other clinical indication for total enteroscopy were enrolled after obtaining informed consent. Exclusion criteria are shown in Table 1.

Study device

The study device (PowerSpiral Enteroscope; Olympus Medical Systems) was first described by our group.[16,17,19] Details are described in Figure 1.

MSE and periprocedural management

All procedures were performed by 1 of 4 endoscopists at the 2 study centers (H.N., T.B., J.D., M.A.) with experience of more than 20 cases of antegrade PSE. All antegrade procedures were performed with the patient under general anesthesia as per protocol. Retrograde PSE procedures were done with the patient under deep sedation conditions using propofol alone or with additional midazolam.

Routinely, a wire-guided bougienage of the upper esophageal sphincter with a standard 18- to 20-mm Savary bougie was performed before peroral PSE. Bowel preparation was only administered for retrograde PSE. For antegrade PSE, the study device was inserted through the

TABLE 1. Exclusion criteria

Patients under age 18 years
Health status ≥4 according to American Society of Anesthesiologists' classification
Pregnancy
Known coagulopathy (international normalized ratio ≥2.0, platelets <70/ nL)
Intake of antiplatelet agents or anticoagulants (other than aspirin) within the last 7 days
Any medical contraindication to standard enteroscopy
Presence of any intraluminal or extraluminal foreign body in the abdominal cavity
Any prior gastric, small-bowel, or colonic surgery or implantable devices in these locations
Known or suspected bowel obstruction or stenosis or history of bowel obstruction
Known or suspected esophageal stricture or Schatzki ring
Known gastric or esophageal varices
Known or suspected stricture of the colon or ileocecal valve
Suspected perforation of the GI tract
Inability to tolerate sedation or general anesthesia for any reason
Inability to tolerate endotracheal intubation
Absence of signed informed consent

mouth and advanced with the assistance of motorized clockwise spiral rotation. For the retrograde approach, the study device was inserted transanally. All procedures were performed using CO_2 insufflation. If at any point a stricture was observed or excessive resistance was encountered, further advancement of the endoscope was ceased and the reason for procedure termination was documented.

During the antegrade procedure, at the deepest point, an ink dye injection into the submucosal space was performed using a 23-gauge needle for documentation of the DMI (first creating a saline solution bleb, followed by injection of India ink) (Fig. 2). After reaching the cecum from the antegrade direction, the procedure was recorded as a total enteroscopy, and no additional retrograde PSE was performed. If the antegrade approach remained incomplete, retrograde PSE was performed on the following day. If during the retrograde PSE procedure the previously placed ink dye marker was observed, the procedure was counted as a total enteroscopy (further advancement of the endoscope was possible, if clinically indicated, at the discretion of the endoscopist) (Fig. 2). If not, the procedure was incomplete. After reaching DMI or the cecum from the antegrade direction, the ink dye marker from the retrograde approach, or if in any case no further advancement of the endoscope could be achieved, the endoscope was withdrawn using motorized counterclockwise spiral rotation. Therapeutic interventions and/or tissue sampling was usually performed during the withdrawal phase as clinically appropriate and at the discretion of the endoscopist (Fig. 3).

Postprocedural measures

Clinical investigations and determination of blood cell counts and serum levels of C-reactive protein were done 24 hours after the last PSE procedure. Thirty days after the procedure, patients were interviewed by telephone for evaluation of complaints or delayed adverse events (AEs).

Study aim, endpoints, and definitions

The aim of the study was to evaluate the efficacy and safety of PSE for visualization of the entire small bowel ("total enteroscopy") in patients with suspected small-bowel disease and indication for a complete enteroscopy (1 or more positive findings on prior small-bowel imaging or other clinical indication for a total enteroscopy). The primary endpoint was the total enteroscopy rate (TER) for PSE (percentage of subjects in whom PSE could achieve visualization of the entire small bowel). The group of subjects in whom the primary endpoint was achieved could be subdivided into 2 clinical situations: antegrade approach alone, which was total antegrade enteroscopy from mouth to cecum, or bidirectional approach, which was incomplete antegrade enteroscopy with visualization of the ink dye marker during the retrograde PSE procedure. Secondary endpoints are shown in Table 2.

Data management, statistical analysis, and sample size calculation

Study data were collected and analyzed at the coordinating study center in Düsseldorf, Germany. Case report forms were completed at both centers by physicians and trained study nurses. The database was created with Microsoft Excel (Microsoft, Redmond, Wash, USA), and data entry was done by trained study nurses at the Department of Gastroenterology, Evangelisches Krankenhaus Düsseldorf. Data entry was verified by a physician. Statistical analyses were carried out using SAS version 9.3 or higher (SAS Institute, Cary, NC, USA).

Continuous measures are summarized by sample size, mean, median, standard deviation, minimum, and maximum. Categorical measures are presented as the counts and percentages of subjects in each category. The exact binomial test was used to compare qualitative data. $P < .05$ was considered statistically significant.

All authors had access to the study data and reviewed and approved the final manuscript. The study was conceived as a proof-of-concept feasibility trial with a fixed number of 30 patients to be enrolled without a statistical case number calculation or inclusion of a control group.

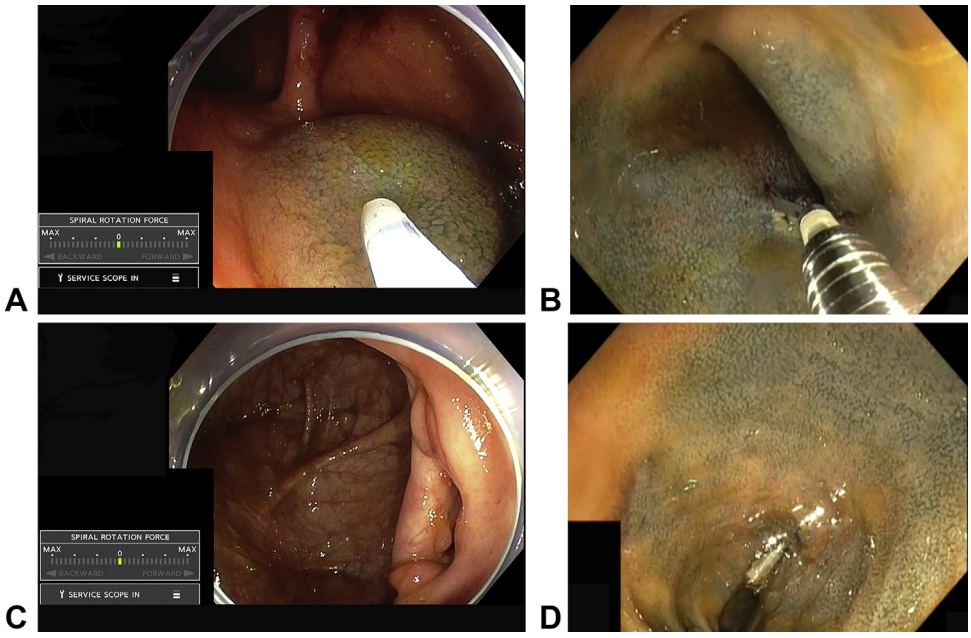

Figure 2. Endoscopic view of the ileum during antegrade PowerSpiral enteroscopy (PSE). **A,** The rotation force indicator shows no movement of the spiral overtube. Submucosal injection of India ink for marking of depth of maximum insertion. **B,** Additional application of a through-the-scope clip. **C,** Retrograde PSE with approach to the ileocecal valve. **D,** Retrograde visualization of submucosal tattoo and clip, proof of total bidirectional enteroscopy.

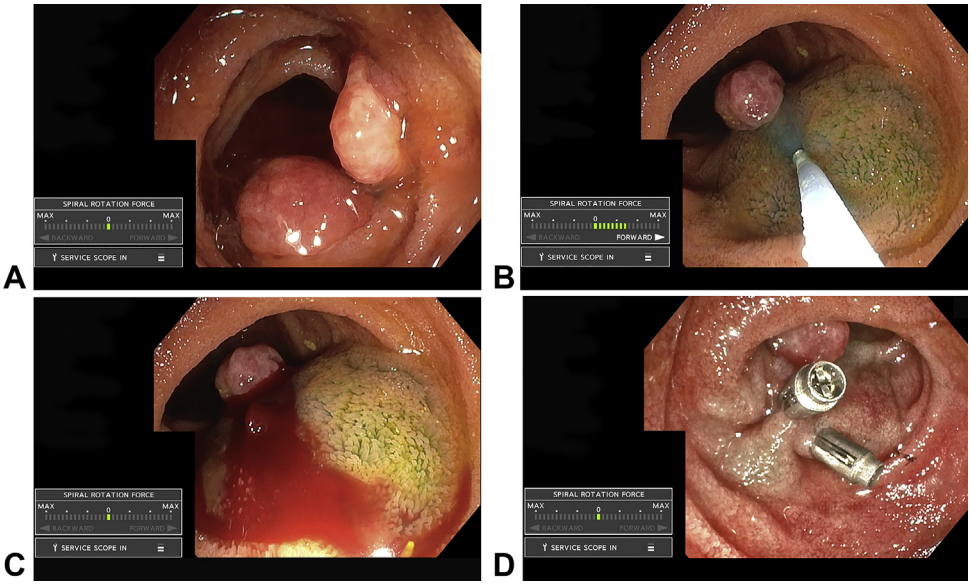

Figure 3. A, Visualization of multiple polyps in the ileum. **B,** Submucosal injection for EMR. **C,** Pulsating bleeding. **D,** Successfully treated with 2 through the scope clips.

Recruitment of patients

All consecutive patients with an indication for a complete enteroscopy were registered at both centers and screened for enrollment. Patients who did not meet the inclusion criteria or refused to sign the informed consent form were excluded from the study.

RESULTS

Patient characteristics and indications for enteroscopy

Between April and October 2018, 38 patients with indication for total enteroscopy were screened for eligibility. Details are listed in Table 3 and Figure 4.

TABLE 2. Secondary endpoints

Technical success rate of antegrade PSE (defined as successful insertion of the endoscope at least to the ligament of Treitz) and of retrograde PSE (defined as successful insertion of the endoscope at least beyond the ileocecal valve)
DMI, measured in cm beyond the ligament of Treitz during antegrade and beyond the ileocecal valve during retrograde on withdrawal of the endoscope according to current European Society of Gastrointestinal Endoscopy technical guideline for device-assisted enteroscopy[3,29]
Procedure time until DMI was reached and total procedural time for each route
User feedback (ease of use; 1-5 numeric rating scale, 1 = very good)
Diagnostic yield, defined as the percentage of procedures with a definitive endoscopic diagnosis (this enteroscopic diagnosis either confirmed a diagnosis from previous small-bowel studies or established a new definitive diagnosis at the anatomic location identified in previous imaging studies or novel findings that could explain the clinical symptoms)
Rate of therapeutic interventions (for calculation of the therapeutic yield, biopsy sampling or India ink injections done for marking of DMI were not counted)
Adverse events during and after the procedure within a follow-up interval of 30 days

PSE, PowerSpiral enteroscopy; *DMI*, depth of maximum insertion.

Procedural data

The antegrade PSE procedure was performed in all 30 patients, of which 5 procedures (16.6%) were complete as the cecum was reached. One patient refused to undergo retrograde PSE after an incomplete antegrade procedure with successful treatment of multiple arteriovenous malformation. Thus, 24 patients underwent an additional retrograde PSE procedure. The technical success rates for antegrade PSE, with advancement at least to the ligament of Treitz, and retrograde PSE, with advancement at least beyond the ileocecal valve (ICV), were both 100% (30/30 and 24/24, respectively).

Procedural times for antegrade PSE, defined as the median insertion time from the mouth to the ligament of Treitz, was 2 minutes (range, 1-14). The median procedural duration from the ligament of Treitz to DMI was 26 minutes (range, 15-110). The median withdrawal time was 12 minutes (range, 6-25). The median total procedure time was 51 minutes (range, 32-133).

Procedure times for retrograde PSE, defined as the median insertion time from anus to cecum, was 5 minutes (range, 1-17). The median time for successful intubation of the ICV was 2 minutes (range, 1-24). The median procedural duration from ICV to the ink dye marker or DMI was 17 minutes (range, 1-68). The median withdrawal time was 5 minutes (range, 2-27). The median total procedure time was 40 minutes (range, 8-90). For ease of use, the median overall rating was 2 on a numeric rating scale from 1 to 5 (1 = very good) for antegrade and retrograde PSE procedures.

Insertion depth and TER

For antegrade PSE, the median DMI beyond the ligament of Treitz was 490 cm (range, 160-600). In 5 patients (16.7%), a total antegrade enteroscopy that reached the cecum was achieved. Reasons for incomplete antegrade PSE were no further advancement of the endoscope possible despite spiral rotation and abdominal manipulation from outside (n = 20) and high torqueing resistance during spiral rotation with multiple automatic motor stops in the same endoscope position (n = 5). Median body mass indices of patients with complete and incomplete antegrade procedures were identical at 27 kg/m^2 (range complete, 23.3-30.9; range incomplete, 19.5-36.8). The median DMI from the retrograde approach was 120 cm (range, 40-600). In 16 patients (66.7%), of all attempted 24 retrograde procedures, the ink dye marker could be visualized, resulting in a complete enteroscopy in a bidirectional approach. Reasons for incomplete enteroscopy were no further advancement despite spiral rotation and abdominal manipulation (n = 5), high resistance during spiral rotation with multiple automatic motor stops in the same endoscope position (n = 2), and a severe inflammatory stricture (n = 1). Overall, total enteroscopy using PSE could be achieved in 21 cases, resulting in a TER of 72.4% (21/29, per protocol) and 70% (21/30, intention to treat).

Diagnostic yield

The overall diagnostic yield was 80% (24/30). The diagnostic yield for antegrade PSE alone was 73.3% (22/30). In 2 patients, the diagnosis could only be made in the retrograde approach, resulting in an additional diagnostic yield of retrograde PSE of 6.7% (2/30). Diagnoses are listed in Table 4.

Yield of interventional PSE

In total, 43 endoscopic interventions were performed in 76.7% (23/30) of all antegrade and 41.7% (10/24) of all retrograde procedures, resulting in an overall yield (per patient) of 86.7% (26/30). Interventions are listed in Table 5. In 3 patients, therapeutic interventions were performed during retrograde PSE only (10%). A median of 1 type (range, 0-2) of intervention was performed during antegrade PSE procedures and 0 (range, 0-2) during retrograde PSE.

All interventions and therapies attempted were successful. The median time for interventions per procedure was 6 minutes (range, 1-20) for antegrade and 3 minutes (range, 1-10) for retrograde PSE procedures.

TABLE 3. Patient characteristics and indication for total enteroscopy (n = 132)

Characteristics	Value
Male	14
Female	16
Age, y	
Range	37-100
Median	64
American Society of Anesthesiologists class	
I	3 (10)
II	14 (46.7)
III	13 (43.3)
Body mass index, kg/m^2	
Range	19.5-36.8
Median	27
Clinical indication	
Suspected mid-GI bleeding*	23 (76.7)
Pure iron deficiency anemia†	1 (3.3)
Other	6 (20)
Positive imaging modality before PSE	
Video capsule endoscopy	25 (83.3)
Other modality‡	4 (13.3)
None	1 (3.3)
Suspected diagnosis before PSE	
Arteriovenous malformation	20 (66.7)
Inflammatory lesion	5 (16.7)
Polyp/neoplasia	3 (10)
Other	2 (6.7)

Values are n (%) unless otherwise defined. Thirteen of 30 patients (43%) had severe comorbidities according to the American Society of Anesthesiologists' class III.
PSE, PowerSpiral enteroscopy.
*Suspected mid-GI bleeding and positive small-bowel imaging modality, for example, video capsule endoscopy for detecting a potential bleeding source.
†Pure iron deficiency anemia defined with negative EGD, colonoscopy, and small-bowel imaging for bleeding source.
‡Magnetic resonance imaging (n = 1), CT (n = 1), US (n = 1), and double-balloon enteroscopy (n = 1).

AEs and follow-up

Procedure-related AEs were observed in 5 patients (16.7%). In 3 patients (10%) deep mucosal tears were observed (1 in the ileum during antegrade PSE, 2 at the ICV during retrograde PSE), all of which were clinically asymptomatic. In 1 patient, a hematoma of the jejunal wall was observed during withdrawal of the endoscope during antegrade PSE. This was also not clinically symptomatic. During follow-up, 1 patient had mild, rapidly resolving swallowing discomfort. No serious AEs, nonanticipated AEs, or device AEs occurred. No further delayed AEs occurred later during the 30-day follow-up period.

DISCUSSION

Motorized PSE has recently been shown to provide a high diagnostic yield of 74% in a preliminary prospective multicenter trial.[17] However, this trial was limited to an antegrade approach only and did not primarily aim for evaluation of insertion depth and TER. Despite achieving a high DMI of median 450 cm and complete antegrade enteroscopy in 10.6% of the cases, almost 90% of the procedures remained incomplete. Therefore, there were outstanding questions regarding how deep one can really go into the small bowel using PSE and what its true efficacy is for achieving a complete enteroscopy. Generally, results of trials reporting the insertion depths achieved with the different enteroscopy techniques should always be interpreted with caution because measurement is not an objective parameter and is susceptible to bias.[20] The only objective parameter is the rate of complete enteroscopy. Rates of complete enteroscopy using conventional SE are very low. This is mainly because of the use of an ineffective retrograde approach with limited insertion depth proximal to the ICV.[21,22] However, independent from the DAE technique used, in most cases a combined, bidirectional approach is needed to achieve total enteroscopy.

In this context, this first prospective trial, with the primary aim of evaluating TER, demonstrated that PSE was able to achieve a high rate of complete enteroscopy of 70% in a cohort of patients without previous abdominal surgery. The rate of complete enteroscopy using DBE was 44% in the currently largest meta-analysis by Xin et al[18] that included 12,823 DBE procedures from 66 trials. Of note, only 1.6% of these were achieved from the antegrade approach alone. In the current trial, TER using only antegrade PSE was 16.7%, more than 10-fold higher. Depending on the endoscopist's level of experience, TERs using DBE of up to 66% have been reported in single trials from expert centers.[23] Another large meta-analysis by Lenz and Domagk[9] that included 68 trials found a pooled complete enteroscopy rate for DBE of 33.9%. TER for SBE is substantially lower (12.4%) and is almost nonexistent for SE (2.9%). Remarkably, the current trial demonstrated that, as a clear difference from manual SE, first retrograde PSE was feasible with a technical success rate of 100% and second retrograde PSE was able to achieve total enteroscopy in a bidirectional approach in 53.3% of all cases. The results of the current trial were confirmed by a recent retrospective study on PSE in 61 patients, achieving a TER of 60.6%, of which 31.1% were complete from the antegrade approach alone and 29.5% were done in a bidirectional approach.[24]

From a more technical perspective, the question remains as to why in the current trial in 1 (large) group of patients PSE works very well with smooth and easy passage of the small bowel, whereas in another group of patients

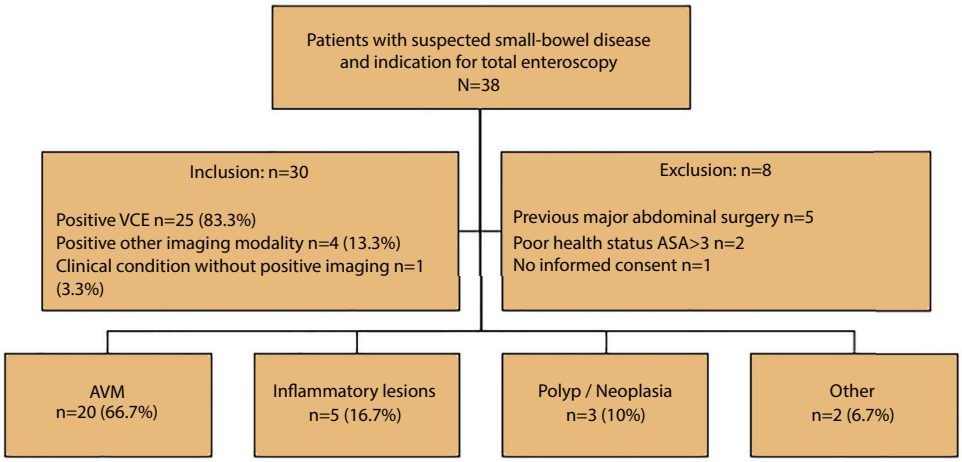

Figure 4. Flowchart of inclusion and exclusion of patients and suspected diagnoses before direct enteroscopy. Eight patients were not included because of previous major abdominal surgery (n = 5), poor health status (ASA class >III, n = 2), or refusal to sign informed consent (n = 1). Thirty patients (14 men, 16 women) met the inclusion criteria and were enrolled. *ASA*, American Society of Anesthesiologists; *AVM*, arteriovenous malformations; *VCE*, video capsule endoscopy.

TABLE 4. Diagnoses during enteroscopy and diagnostic yield

Diagnoses	No. of cases (n = 30)	Percentage
Arteriovenous malformation	16	53.4
Polyps/neoplastic lesions	4	13.3
Inflammatory lesions (ie, ulcers, erosions)	6	20
Large epiphrenic diverticulum	1	3.3
Blue bleb rubber nevus syndrome	1	3.3
Tissue sampling performed	14	46.7
Diagnostic yield overall	24	80

deep enteroscopy remains cumbersome or even impossible. Reasons for a more or less favorable outcome of PSE in general and in particular in terms of an antegrade approach may be associated with patient- or procedure-related factors. In the current trial, no obvious demographic or procedural differences were identified between patients with successful complete antegrade, complete bidirectional, and incomplete PSE procedures. However, the case number in our trial is too small to perform reliable post-hoc subgroup analyses. Out trial showed that in 16.6% of cases total antegrade enteroscopy with reaching the cecum could be achieved. Although this appears to be a substantial improvement compared with the standard DAE technique, the question remains as to why the remaining 83.4% failed. The insertion phase during antegrade PSE was stopped when either high resistance during spiral rotation was encountered (several automatic motor stops in the same position) or no further advancement was visible despite continued rotation of the spiral segment in the same endoscope position. At this point, on the basis of available limited data, one can only speculate about the reasons for impeding further pleating of the small bowel in these 2 aforementioned situations. First, the small bowel may be fixed by adhesions (in particular relevant for further studies in patients after abdominal surgery who were not included in the current trial), and second, the small bowel might be simply too long or the endoscope too short to allow the small intestine to be completely pleated onto the insertion tube portion. Although in a recently published retrospective trial in 61 patients from an Indian population a higher total antegrade enteroscopy rate of 31.1% could be achieved, the overall TER was lower with only 60.6% compared with our results.[24] Variation in the TER compared with our trial may occur because of inclusion of demographically different populations (Western Europe and India). However, current available data still leave room for further refinement of the MSE procedure, but the mechanisms are not yet fully understood. In this context, future comparative trials should be adjusted to demographic characteristics (ie, patient's body mass index), indication (ie, bleeding, suspected neoplasia, or inflammatory

TABLE 5. Interventions performed during antegrade and retrograde enteroscopy

Intervention	Direction of PowerSpiral enteroscopy	
	Antegrade (n = 30)	Retrograde (n = 24)
Argon plasma coagulation	15 (50.0)	6 (25.0)
Application of one or more clips	11 (36.7)	3 (12.5)
EMR	3 (10.0)	0 (0)
Injection (for hemostasis or marking of tumor location)	3 (10.0)	2 (8.3)

Values are n (%).

lesions), previous surgery and type of altered anatomy, and type of anesthesia used to identify factors that may influence efficacy of MSE. Furthermore, a different sequence of MSE starting with a retrograde approach may be evaluated as well.

The main advantage of conventional SE over balloon-assisted techniques is a shorter procedural duration, as shown in a meta-analysis.[8] Because the total procedure time, among other factors, depends on the therapeutic procedures performed, it seems that this is not an ideal surrogate parameter for the speed of the enteroscopy technique itself. However, in the current trial, the total procedure time for antegrade PSE was 51 minutes and 40 minutes for retrograde PSE. Procedure times are difficult to extract from the available meta-analyses. In 2 randomized controlled trials comparing DBE and SBE, mean procedure times for the combined antegrade and retrograde approach were 161 minutes and 105 minutes using DBE and 186 minutes and 96 minutes using SBE, respectively.[25,26]

The overall diagnostic yield of PSE in the current trial was 80%. In 22 cases (73.3%), a diagnosis could be made from the anterograde approach alone. Remarkably, the additional value of retrograde PSE was only 6.7% (2/30). This means that in most patients the diagnosis could be made without complete enteroscopy. However, finding a diagnosis is one thing but determining the extension of a known disease or the number of lesions is another, and in this context insertion depth is important. A deeper approach to the small bowel increases the probability of finding (additional) lesions to treat, and complete enteroscopy can be considered as the "deepest form" of enteroscopy. Many small-bowel diseases are not limited to 1 lesion but occur at multiple sites (ie, arteriovenous malformations, polyps in polyposis syndromes, strictures in Crohn's disease). In these patients, a complete enteroscopy may also have an important influence on the clinical outcome. Furthermore, a complete enteroscopy with negative findings can play a substantial role in the further management of patients because it avoids further speculation that relevant findings may have been missed by incomplete examination.[20]

DAE is generally considered a safe procedure with a low rate of AEs reported in the literature, namely about .8% for diagnostic procedures and up to 10% for interventions, resulting in an overall AE rate of 3% to 4% according to the current European Society of Gastrointestinal Endoscopy guideline.[27] No major AEs occurred during PSE in the current trial. The rate of minor AEs of 16.7% (5/30) appears to be high. However, 4 of these 5 events were clinically asymptomatic mucosal tears or submucosal hematomas that were documented under the conditions of a prospective feasibility trial and would not be of any clinical relevance in daily routine. This type of lesion seems to be typical for the spiral technique and caused no major AEs in a large prospective U.S. multicenter trial using manual spiral enteroscopy.[28] Furthermore, in 86.7% of all PSE procedures, some form of interventional procedure was performed, resulting in a higher a priori risk for AEs. A bouginage of the upper esophageal sphincter as per protocol caused no AEs in our trial. However, because there are no clinical data indicating the need for a bouginage in every case of antegrade MSE, the decision for or against bouginage may be left to the endoscopist's discretion in future trials.

The current trial has clear limitations. First, our case number was too small to reliably report efficacy and AE rates for a large-scale application. Second, the study was conducted at 2 highly experienced endoscopic referral centers with extensive experience in deep enteroscopy, including PSE and interventional endoscopy. Third, patients after major abdominal surgery and with altered GI anatomy were not part of the trial. Finally, there was no head-to-head comparison with current deep enteroscopy techniques.

Our trial must be seen as a prospective feasibility evaluation of the novel PSE technique from a retrograde approach and, in particular, with the aim for total enteroscopy. The results clearly justify further evaluation of PSE in a large prospective multicenter study preferably with inclusion of a control group.

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