



Multicenter survey on the use of device-assisted enteroscopy in Portugal

Rolando Pinho^{1,2}, Miguel Mascarenhas-Saraiva¹, Susana Mão-de-Ferro³, Sara Ferreira³, Nuno Almeida^{4,5}, Pedro Figueiredo^{4,5}, Adélia Rodrigues², Hélder Cardoso⁶, Margarida Marques⁶, Bruno Rosa⁷, José Cotter^{7,8,9}, Germano Vilas-Boas¹⁰, Carla Cardoso¹⁰, Marta Salgado¹¹ and Ricardo Marcos-Pinto¹¹

Abstract

Background: Device-assisted enteroscopies (DAEs) are recent endoscopic techniques that enable direct endoscopic small-bowel evaluation.

Objective: The objective of this article is to evaluate the implementation of DAEs in Portugal and assess the main indications, diagnoses, diagnostic yield, therapeutic yield and complication rate.

Methods: We conducted a multicenter retrospective series using a national Web-based survey on behalf of the Portuguese Small-Bowel Study Group. Participants were asked to fill out two online databases regarding procedural data, indications, diagnoses, endoscopic therapy and complications using prospectively collected institutional data records.

Results: A total of eight centers were enrolled in the survey, corresponding to 1411 DAEs. The most frequent indications were obscure gastrointestinal bleeding (OGIB), inflammatory bowel disease and small-bowel tumors. The pooled diagnostic yield was 63%. A relation between the diagnostic yield and the indications was clear, with a diagnostic yield for OGIB of 69% ($p=0.02$) with a 52% therapeutic yield. Complications occurred in 1.2%, with a major complication rate of 0.57%. Perforations occurred in four patients (0.28%).

Conclusion: DAEs are safe and effective procedures, with complication rates of 1.2%, the most serious of which is perforation. Most procedures are performed in the setting of OGIB. Diagnostic and therapeutic yields are dependent on the indication, hence appropriate patient selection is crucial.

Keywords

Enteroscopy, double-balloon enteroscopy, single-balloon enteroscopy, spiral enteroscopy, small-bowel, survey, diagnosis, therapy, complications

Received: 25 May 2015; accepted: 15 August 2015

Introduction

In recent years, two major innovations revolutionized small-bowel endoscopic exploration: capsule endoscopy (CE) and deep enteroscopy. CE was developed in 2001¹ and rapidly evolved as the ideal technique for the endoscopic evaluation of small-bowel pathology, as it is a safe, easy and noninvasive technique that enables complete small-bowel visualization. However, it has some major limitations, mostly lack of movement control and therapeutic capabilities. Deep enteroscopy, on the other hand, allows direct endoscopic visualization and control, as well as most diagnostic and therapeutic endoscopic techniques. The concept of deep

¹ManopH, Instituto CUF, Portugal

²Serviço de Gastreenterologia, Centro Hospitalar de Gaia/Espinho, Portugal

³Serviço de Gastreenterologia, Instituto Português de Oncologia de Lisboa Francisco Gentil, EPE, Portugal

⁴Faculdade de Medicina da Universidade de Coimbra, Portugal

⁵Serviço de Gastreenterologia, Centro Hospitalar e Universitário de Coimbra, Portugal

⁶Serviço de Gastreenterologia, Centro Hospitalar de São João, Portugal

⁷Serviço de Gastreenterologia, Centro Hospitalar do Alto Ave, Portugal

⁸Instituto de Ciências da Vida e Saúde (ICVS), Escola de Ciências da Saúde, Universidade do Minho, Portugal

⁹ICVS/3B's, Laboratório Associado, Braga/Guimarães, Portugal

¹⁰Serviço de Gastreenterologia, Hospital Pedro Hispano, Portugal

¹¹Serviço de Gastreenterologia, Centro Hospitalar do Porto, Portugal

Corresponding author:

Rolando Taveira Pinho, Serviço de Gastreenterologia—Centro Hospitalar de Vila Nova de Gaia, Rua Conceição Fernandes, 4434-502—Vila Nova de Gaia, Portugal.

Email: rolandopinho@gmail.com

enteroscopy was introduced with the development of double-balloon enteroscopy (DBE) in 2003 by Yamamoto et al.² Soon, single-balloon enteroscopy³ (SBE) and spiral enteroscopy⁴ (SE) were also introduced. These techniques are grouped under the designation of device-assisted enteroscopy (DAE).

The experience with DAE mostly relies on single-center series from experienced referral centers, and on multicenter studies also usually from referral centers focusing on specific pathologies or technical comparisons. There is limited evidence on the national use of DAEs in the community, particularly in Portugal.

Hence, the authors aimed to evaluate the Portuguese experience with DAEs, focusing on two different aspects: technical ones, related to the equipment, logistics and training capabilities; and clinical ones such as indications, diagnoses, therapeutic procedures, diagnostic and therapeutic yield and complications.

Methods

We conducted a multicenter retrospective descriptive study of medical centers performing DAEs in Portugal. A national survey of centers performing DAEs was performed, on behalf of the Portuguese Small-Bowel Study Group (GEPID—“Grupo de Estudos Português do Intestino Delgado”), a section of the Portuguese Society of Gastroenterology (SPG—“Sociedade Portuguesa de Gastrenterologia”). A formal invitation letter to participate in the study was sent from the SPG to all Portuguese gastroenterology departments. This invitation letter explained the nature of the multicenter survey and the purpose of data collection. The invitation letter also contained links to two online questionnaires for data collection.

Questionnaires

Centers enrolled in the survey were asked to fill out two online questionnaires. The links sent in the invitation letter gave access to online forms for which only data entry was possible. The deadline for data entry was set to May 7, 2014. Participants were not able to see the questionnaires from other centers. Patients were inserted anonymously by the participants entering data. Access to the database was granted only to investigators directly involved in data analysis.

The first questionnaire (Form #1) aimed to characterize individual centers performing DAEs and the second questionnaire (Form #2) aimed to collect data from individual patients undergoing DAEs in each center (Table 1).

DAE procedures

Participants were invited to include all procedures performed until the deadline for data inclusion. All DAE procedures were performed according to each institution's individual protocol, reflecting standard community practice. Each patient gave informed consent for DAE, complementary diagnostic and therapeutic procedures and sedation. The survey was approved by the ethics committees and both the SPG and GEPID boards.

Statistical analysis

Data from the online forms were exported as an “.xls”-file spreadsheet and imported to SPSS v19.0 for data analysis. Data were reviewed for homogeneity, and inconsistencies and some answers were grouped into different categories when appropriate.

Descriptive statistics were used to summarize data: Fisher's exact test to compare discrete variables (diagnostic yield, complications); Spearman's correlation coefficient to correlate the satisfaction score with the total number of procedures; and the Mann-Whitney test was used to compare the satisfaction score with the type of enteroscope.

Results

Individual centers and DAE techniques

Eight centers, from 11 centers performing DAE in Portugal, agreed to participate in the survey and answered the online forms (Table 2). All centers are located in the Northern region of Portugal, except for one center in the Central and one center in the Southern regions. Five centers used exclusively SBE, two centers exclusively DBE and one center both DBE and SE. One center performing DBE used the diagnostic enteroscope (EN-450P5/20) and the remaining the therapeutic enteroscope (EN-450T5). One of these centers recently upgraded their DBE to the new EN-580T. Only one of the responding centers (ManopH-ICUF) is located in an outpatient facility and the remaining are hospital-based centers.

Two of these centers started DAEs in 2005, one in 2007, 2008, 2009, 2010 and two in 2013. The first three centers implementing DAEs adopted DBE and all the remaining centers from 2008 onward selected SBE.

A total of 23 endoscopists have performed DAEs in these eight centers. Currently, 20 of them routinely perform DAEs, ranging from two to three in each center.

Use of DAE

Only three of the eight centers declared using DAE in the emergency setting for active OGIB.

Table 1. Questionnaires sent to gastroenterology departments performing device-assisted enteroscopy in Portugal

Form #1

- Names of individual physicians performing DAE in your center
- Type of DAE used (DBE, SBE or SE).
- The date when DAE was started in your center
- Number of procedures preceded by CE
- Number of urgent procedures for active small-bowel bleeding
- Number of therapeutic procedures
- Number of procedures where the purpose of the examination was considered fulfilled
- Degree of satisfaction with the technique
- Use of DAE for procedures other than small-bowel enteroscopy
- Availability of fluoroscopy in the examination room
- Availability of an anesthesiology team during the procedure
- Type of sedation used: mild sedation, deep sedation, general anesthesia
- Training capacity for residents or specialists from other centers without experience in DAE

Form #2:

- Anonymous patient identification
- Age
- Sex
- Indication for DAE
- Type of DAE used (DBE, SBE or SE).
- Route of insertion
- Depth of insertion
- Reason to interrupt the progression
- Duration of the procedure
- Type of sedation
- Diagnosis
- Additional diagnostic or therapeutic procedures performed during DAE
- Complications
- Identification of the physician filling the questionnaire

DAE: device-assisted enteroscopy; DBE: double-balloon enteroscopy; SBE: single-balloon enteroscopy; SE: spiral enteroscopy; CE: capsule endoscopy.

Table 2. Summary of the characteristics of individual centers

Center	Region	Type of DAE	Start of DAE	Number of procedures	Number of procedures/month	Number of endoscopists performing DAE	Availability of fluoroscopy	Satisfaction score	Training of fellows	Training of specialists
ManopH-ICUF	North	DBE, SE	2005	528	4.7	2	No	7	4	2
CHUC	Center	DBE	2005	215	1.9	3	No	6	5	1
IPOLFG	South	DBE	2007	316	4.0	2	No	6	5	2
CHAA	North	SBE	2008	25	0.4	3	No	7	4	-
CHGE	North	SBE	2009	155	2.9	2	No	8	6	4
CHSJ	North	SBE	2010	135	2.9	3	Yes	7	3	-
HPH	North	SBE	2013	21	1.4	2	No	3	-	-
CHP	North	SBE	2013	13	1.3	2	Yes	5	-	-

ManopH-ICUF: ManopH, Instituto CUF, Porto; CHUC: Centro Hospitalar da Universidade de Coimbra; IPOLFG: Instituto Português de Oncologia de Lisboa, Francisco Gentil; CHAA: Centro Hospitalar do Alto Ave; CHGE: Centro Hospitalar de Vila Nova de Gaia/Espinho; CHSJ: Centro Hospitalar de São João; HPH: Hospital Pedro Hispano; CHP: Centro Hospitalar do Porto; DAE: device-assisted enteroscopy; DBE: double-balloon enteroscopy; SBE: single-balloon enteroscopy; SE: spiral enteroscopy.

Half ($n = 4$) of the centers reported using the enteroscopy for other purposes than small-bowel enteroscopy (ManopH-ICUF, CHGE, CHUC and HPH), mainly to perform difficult colonoscopies and push enteroscopies.

Only two centers (CHGE and HPH) reported its use to perform endoscopic retrograde colangiopancreatography (ERCP) in patients with surgically altered anatomy.

Satisfaction with DAE was evaluated on a subjective analog scale ranging from 0 (no satisfaction) to 10 (complete satisfaction). The median satisfaction score was 6.5 ranging from 3 to 8 and was not correlated with the total number of procedures ($p=0.3$) or the type of enteroscope used ($p=0.9$).

Only two centers (CHSJ and CHP) have fluoroscopy available in the examination room used to perform DAEs, although all centers (except ManopH-ICUF) have fluoroscopy available in other locations on request.

All participating centers declared having an anesthesiologist during the procedure. In all centers, most cases were performed under deep sedation with propofol without orotracheal intubation. In three centers, 24 (1.7%) patients were examined under general anesthesia and in one center, 55 (3.9%) patients were examined under mild midazolam sedation.

Regarding the capacity to train gastroenterology fellows and specialists from other centers without experience in DAE, six centers reported training capacity. The two centers whose activity started only in 2013 declared no training capacity at their current stage. A total of 27 gastroenterology fellows have already been trained in DAE in the six centers with training capacity. A total of five centers have already trained nine gastroenterology specialists from other centers (CHGE: four, ManopH-ICUF: two, IPOLFG: two and CHUC: one).

Case series

A total of 1411 cases were recorded in the online Form #2, from the eight participating centers. From these, 1054 were DBE, 351 SBE and six SE.

The mean age was 57.6 years (SD 18.3), ranging from 9 to 98 years old. Males accounted for 53.3% of patients. Of the 1411 procedures, 16 (1.1%) were pediatric patients (<18 years old) and 567 (40.2%) were elderly patients (≥ 65 years old).

The indications for DAE are summarized in Table 3. As expected, the main indications were OGIB, suspected/confirmed small-bowel inflammatory bowel disease and suspected small-bowel tumors.

The route of insertion according to the different types of DAE and indications is detailed in Table 3. Predictably, the oral route of insertion was more frequently used with all DAE techniques.

Total enteroscopy was rarely attempted as the goal of most procedures was dictated by the findings of a previous examination, mostly CE ($n=1033$, 73.2%). The rate of total enteroscopy could not be determined as the database was not designed to evaluate the limit of insertion in the uncommon procedures in which it

was attempted. However, total enteroscopy was reported in 22 procedures (DBE: 19, SBE: two, SE: one).

The main diagnoses established in each enteroscopy according to the type of DAE and the route of insertion are detailed in Table 4. No significant findings were established in 37.1% of patients. As expected from other case series, angiectasias, Crohn's disease and tumors/polyps were the most frequent diagnoses, accounting for 43.8% of all diagnoses.

The diagnostic and therapeutic procedures performed during DAEs according to the type of DAE used are detailed in Table 5. In 595 (42.2%) patients no additional endoscopic procedures other than occasional tattooing were performed and in 380 (26.9%) of patients only biopsies were taken. Therapeutic procedures were performed in 436 (30.9%) patients. As detailed in Table 4, argon-plasma coagulation and polypectomy represented the most frequently used therapeutic techniques.

The diagnostic and therapeutic yield according to the indication is detailed in Table 6. A pooled diagnostic yield for all indications of 63% was found. Compared to this pooled diagnostic yield, the diagnostic yield was higher for anemia/OGIB (69%, $p=0.02$), Peutz-Jeghers Syndrome (PJS) (95%, $p<0.0001$) and familial adenomatous polyposis (FAP)/*MUTYH*-associated polyposis (MAP) (100%, $p=0.009$) and lower for suspected tumors (52%, $p=0.001$), abnormal radiologic studies (42%, $p=0.04$) and miscellaneous less-frequent indications (40%, $p<0.0001$).

Major complications are reported in Table 7. Anesthetic complications requiring interruption of the procedures were reported in nine (0.6%) patients, all under deep propofol sedation, six of them age 65 or older ($p>0.05$) and seven of them performing oral DAEs ($p>0.05$). Perforation was reported in 0.28%, including one diagnostic procedure in a patient with radiation enteritis and three therapeutic procedures: a balloon-dilation, argon-plasma coagulation of an angiectasia and a direct percutaneous endoscopic jejunostomy (DPEJ).⁵ In a patient with PJS undergoing polypectomy of a large polyp, snare entrapment occurred during polypectomy requiring surgical intervention.

Discussion

This is the first audit ever performed to evaluate the practice of DAE in Portugal. Although the study was extended to all Portuguese centers, a small fraction declined to participate. However, all centers with the most experience and greater casuistic were enrolled, allowing the results to be representative of the national experience.

Table 3. Indications for DAE, according to the type of DAE and route of insertion

Indications	DBE	SBE	SE	Total
Global				
Anemia/OGIB	436	120	4	560
Suspected tumor	189	48	1	238
Suspected IBD	121	55	–	176
Confirmed IBD	88	26	1	115
Polyp(s)	9	27	–	36
PJS	69	4	–	73
FAP/MAP	10	1	–	11
Stenosis	19	12	–	31
Abnormal radiologic studies	14	12	–	26
Malabsorption syndromes	18	12	–	30
Other	81	34	–	115
Total	1054	351	6	1411
Oral route of insertion				
Anemia/OGIB	361 (4 ^a)	90 (4 ^a)	4	455
Suspected tumor	139 (1 ^a)	36 (2 ^a)	1	176
Suspected IBD	73 (2 ^a)	25 (3 ^a)	0	98
Confirmed IBD	45	7	1	53
Polyp(s)	9 (1 ^a)	24	0	33
PJS	65	3	0	68
FAP/MAP	9	1	0	10
Stenosis	13	7	0	20
Abnormal radiologic studies	11	11	0	22
Malabsorption syndromes	16	7	0	23
Other	58 (1 ^a)	28	0	86
Total	799	239	6	1044
Anal route of insertion				
Anemia/OGIB	75	30	–	105
Suspected tumor	50	12	–	62
Suspected IBD	48	30	–	78
Confirmed IBD	43	19	–	62
Polyp(s)	–	3	–	3
PJS	4	1	–	5
FAP/MAP	1	–	–	1
Stenosis	6	5	–	11
Abnormal radiologic studies	3	1	–	4
Malabsorption syndromes	2	5	–	7
Other	23	6	–	29
Total	255	112	–	367

^aNumber of patients in whom oral and anal DAE was performed the same day. These procedures are recorded as a single procedure, and detailed in the oral route of insertion section. DAE: device-assisted enteroscopy; SBE: single-balloon enteroscopy; SE: spiral enteroscopy; OGIB: obscure gastrointestinal bleeding; IBD: inflammatory bowel disease; PJS: Peutz-Jeghers syndrome; FAP: familial adenomatous polyposis; MAP: *MUTYH*-associated polyposis.

DAE was introduced early in Portugal, shortly after the description of the procedure. In 2005, two centers were already performing the technique and, a few years later, DAE was introduced in a larger number of centers. The later widespread dissemination consisted

mostly of SBE, as in Portugal a greater proportion of endoscopy centers use Olympus equipment, hence limiting acquisition costs to the enteroscope itself. According to the organization of the Portuguese national health system, most enteroscopy centers are

Table 4. Main diagnostic finding established in all enteroscopies according to the route of insertion and type of enteroscope used

Diagnosis	DBE	SBE	SE	Total
Oral route of insertion				
Normal	284 (5 ^a)	78 (1 ^a)	1	363
Vascular lesion(s)	216	63	4	283
• Angiectasia(s)	206	57 (2 ^a)	4	267
• Dieulafoy	2	3	-	5
• Active bleeding	6 (1 ^a)	-	-	6
• Portal hypertensive enteropathy	2	3 (1 ^a)	-	5
Inflammatory lesion(s)	95	25	1	121
• Crohn's disease	35	13 (1 ^a)	1	49
• Non-specific enteritis	34 (2 ^a)	12	-	46
• Celiac disease	14	-	-	14
• NSAIDs enteropathy	9	-	-	9
• Radiation enteritis	3	-	-	3
Polyps/polyposis	92	26	-	118
• PJS	64	2	-	66
• FAP/MAP	9	1	-	10
• Polyp(s)	19 (1 ^a)	23 (1 ^a)	-	42
Tumor	62	9 (1 ^a)	-	71
Stenosis	12	11 (1 ^a)	-	23
Extra-small-bowel findings	10	-	-	10
Other findings	28	27 (1 ^a)	-	55
Total	799	239	6	1044
Anal route of insertion				
Normal	122	39	-	161
Inflammatory lesion(s)	63	43	-	106
• Crohn's disease	34	35	-	69
• Non-specific enteritis	25	6	-	31
• Radiation enteritis	2	2	-	4
• NSAIDs enteropathy	1	-	-	1
• Celiac disease	1	-	-	1
Vascular lesion(s)	17	4	-	21
• Angiectasia(s)	16	4	-	20
• Active bleeding	1	-	-	1
Stenosis	9	6	-	15
Extra-small bowel findings	11	2	-	13
Polyps/polyposis	10	3	-	13
• PJS	2	1	-	3
• FAP/MAP	1	-	-	1
• Polyp(s)	7	2	-	9
Tumor	9	2	-	11
Other findings	14	13	-	27
Total	255	112	-	367
All patients				
Normal	406	117	1	524
Vascular lesion(s)	233	67	4	304

(continued)

Table 4. Continued

Diagnosis	DBE	SBE	SE	Total
● Angiectasia(s)	222	61	4	287
● Active bleeding	7	-	-	7
● Dieulafoy	2	3	-	5
● Portal hypertensive enteropathy	2	3	-	5
Inflammatory lesion(s)	158	68	1	227
● Crohn's disease	69	48	1	118
● Non-specific enteritis	59	18	-	77
● Celiac disease	15	-	-	15
● NSAIDs enteropathy	10	-	-	10
● Radiation enteritis	5	2	-	7
Polyp(s)/polyposis	102	29	-	131
● PJS	66	3	-	69
● FAP/MAP	10	1	-	11
● Polyp(s)	26	25	-	51
Tumor	71	11	-	82
Stenosis	21	17	-	38
Extra-small bowel findings	21	2	-	23
Other findings	42	40	-	82
Total	1054	351	6	1411

^aNumber of patients in which oral and anal DAE was performed the same day. These procedures are recorded as a single procedure, and detailed in the oral route of insertion section. DAE: device-assisted enteroscopy; SBE: single-balloon enteroscopy; SE: spiral enteroscopy; NSAIDs: nonsteroidal anti-inflammatory drugs; PJS: Peutz-Jeghers syndrome; FAP: familial adenomatous polyposis; MAP: *MUTYH*-associated polyposis.

Table 5. Diagnostic and therapeutic procedures performed during DAE. Only one technique is reported per procedure. In some cases, more than one technique has been used - for instance, in procedures where polypectomy has been performed, injection and tattooing could also have been used

Procedures	DBE	SBE	SE	Total
None/tattooing	461	130	4	595
Only biopsies	271	109	-	380
Hemostatic/ablative therapies	235	64	1	300
● Argon plasma coagulation	210	57	1	268
● Only adrenaline injection	20	2	-	22
● Hemostatic clips	5	5	-	10
Polypectomy	72	24	-	96
Balloon dilation	6	10	1	17
Foreign body removal	9	5	-	14
DPEJ	-	8	-	8
Stenting	-	1	-	1
Total	1054	351	6	1411

DAE: device-assisted enteroscopy; SBE: single-balloon enteroscopy; SE: spiral enteroscopy; DPEJ: direct percutaneous endoscopic jejunostomy.

public inpatient facilities. In each center, two or three endoscopists are dedicated to performing DAEs. The rate of complete enteroscopy, diagnostic and therapeutic yields and the complication rate of DBE and

SBE were compared in two recent meta-analyses.^{6,7} They were found to be comparable regarding all aspects except the rate of complete enteroscopy, which was found to be slightly higher with DBE. This is, however,

Table 6. Diagnostic and therapeutic yield according to the indication

Indication	Diagnostic yield (DY), n/%	p (compared with pooled DY)	Therapeutic yield n/%	Patients, n
Anemia/OGIB	384/69%	0.02	289/52%	560
Suspected tumor	123/52%	0.001	-	238
Suspected IBD	101/57%	0.2	-	176
Confirmed IBD	82/71%	0.09	-	115
Polyp(s)	22/61%	0.9	11/31%	36
PJS	69/95%	<0.0001	51/70%	73
FAP/MAP	11/100%	0.009	6/55%	11
Stenosis	19/61%	0.8	-	31
Abnormal radiologic studies	11/42%	0.04	-	26
Malabsorption syndromes	19/63%	1.0	-	30
Other	46/40%	<0.0001	-	115
All indications	887/63%		-	1411

OGIB: obscure gastrointestinal bleeding; IBD: inflammatory bowel disease; PJS: Peutz-Jeghers syndrome; FAP: familial adenomatous polyposis; MAP: *MUTYH*-associated polyposis.

Table 7. Complications of device-assisted enteroscopy

Complications	DBE (n/%)	SBE (n/%)	SE (n/%)	Total (n/%)
Anesthetic complications ^a	9/0.85%	-	-/-	9/0.64%
Perforation	3/0.28%	1/0.28%	-/-	4/0.28%
Pancreatitis	2/0.19%	-/-	-/-	2/0.14%
Post-polypectomy syndrome	-/-	1/0.28%	-/-	1/0.07%
Snare entrapment	1/0.09%	-/-	-/-	1/0.07%
Total	14/1.33 %	2/0.57%	-/-	17/1.20%

^a6-Oxygen desaturation, 2-persistent bradycardia; 1-vomiting. DBE: double-balloon enteroscopy; SBE: single-balloon enteroscopy; SE: spiral enteroscopy.

of arguable clinical significance as the goal of each examination can usually be reached using both techniques, as expected by their similar diagnostic and therapeutic yields.

The use of DAE in the emergency setting is still uncommon. This may result from organizational difficulties, as the two or three endoscopists experienced in DAEs in each center may not be assigned to emergency procedures at that time; and logistical obstacles, since the procedure is time and resource consuming requiring a long allotment of time and significant staff including an anesthesiologist, for the entire duration of the procedure. Furthermore, in some centers CE is not routinely performed in the emergency setting to guide the use of DAE. This has important clinical implications since the use of CE and DAE⁸ early in the presentation of overt OGIB improves both the diagnostic and therapeutic yields.

Only half the centers involved reported the use of DAE for purposes other than small-bowel evaluation and only 25% reported its use for ERCP (DAE-ERCP)

in patients with surgically modified anatomy. This may be explained in part by the different areas of expertise of endoscopists performing DAE, as most of them may not be proficient in other techniques such as ERCP. DAE-ERCP enables access to the biliary system and most conventional biliary therapeutics in the great majority of this subset of patients.⁹⁻¹¹ Nevertheless, it is very demanding, time consuming, and limited by the availability of specific accessories,¹² which also adds technical and logistic difficulties to its widespread implementation.

Only two centers rated the subjective satisfaction with DAE with a score equal to or below 5 (0-10). In these two centers the technique was introduced in the year previous to the survey, hence these centers had performed a limited number of procedures (13 and 21). The remaining centers rated the satisfaction between 6 and 8, probably reflecting greater experience, although a correlation between the satisfaction score and the total number of procedures was not found.

Significant findings were found in 63% of patients, a diagnostic yield similar to a recent systematic review¹³ of 12,823 DBEs in which a pooled diagnostic yield of 68.1% was found. In this review, the most frequent findings were inflammatory lesions (either Crohn's disease or non-specific inflammatory lesions), vascular lesions and tumoral lesions (either benign or malignant). In our series these were also the most frequent findings, accounting for 84% (745/887) of all positive findings and 52.8% of all diagnoses (745/1411). This high rate of positive findings is derived from the fact that DAE is considered a secondary procedure after an initial positive diagnostic test, as recommended by current European guidelines.¹⁴

Small-bowel polyposis syndromes accounted for 6% (84/1411) of the examinations. Most (86.9%; 73/84) consisted of PJS referred for endoscopic polypectomy of polyps larger than 10 mm detected in surveillance CE. Snare entrapment in a large polyp was reported in one procedure (1.4%), requiring surgical intervention to remove the snare and resect the polyp. No perforations were recorded after polypectomy in contrast to high rates of post-polypectomy perforations previously reported in PJS.^{15,16} A multicenter series of 46 procedures comprising a survey wherein polypectomy was performed was recently published,¹⁷ in which 214 polyps with a median size of 30 mm were removed. In six of these 46 procedures, surgical intervention was required (jejunal neoplasia: one case, polyps locally concentrated in large numbers: two cases, bulky polyps: two cases with a size up to 60 mm and invaginated polyp: one case). All remaining polyps were managed endoscopically.

DAE is frequently used for therapy of small-bowel lesions detected in other procedures.^{14,18–20} This is reflected in a high percentage of therapeutic procedures (30.9%). As expected from the main indications and other series,^{13,15,18,21} hemostatic therapies, namely argon-plasma coagulation, were the most frequently employed endoscopic therapies. Polypectomy, frequently in the setting of PJS, was also commonly performed.

The diagnostic yield was high in all indications, reflecting an appropriate patient selection, since in most cases DAE followed a positive CE as in other series.¹⁸ In patients with OGIB, the most frequent indication for CE and DAE,^{13,16,22,23} the diagnostic yield was 69%, similar to other series,^{15,21} and the therapeutic yield was also high at 52%. In patients with polyposis syndromes, the diagnostic yield was near 100% (95% and 100% for PJS and FAP/MAP) and the therapeutic yield was also high (70% for PJS and 55% for FAP/MAP). Although not directly evaluated in the present study, since in Portugal the surveillance of these patients is typically performed with CE these

data also point to a good accuracy of CE for screening these patients. Although several reports show that CE^{24,25} and cross-sectional radiological modalities²⁶ may miss significant mass lesions, both have a role for small-bowel screening.^{25,27}

The diagnostic yield for suspected small-bowel tumors (52%) was below the pooled diagnostic yield ($p=0.001$). Although DAE is regarded as the gold standard for the diagnosis of small-bowel tumors,²⁸ this lower diagnostic yield reflects a significant portion of false-positive tumors in CE, probably resulting from bulges due to compressions from adjacent organs or bowel loops.²⁹

Most examinations were performed under anesthesiologist-administered propofol sedation, a common practice in deep sedation for endoscopic procedures in Portugal.³⁰ Anesthetic complications occurred in 0.6% of DAEs and consisted mainly of oxygen-desaturation and less frequently bradycardia and vomiting. All cases were reversed after the interruption of the procedure. Minor oxygen desaturation not requiring the interruption of the procedure was not regarded as a complication. In a recent study, Lara et al.³¹ reported anesthetic adverse events in 15 of 432 procedures (3.5%) performed under deep sedation, mostly oxygen desaturation. Based on this high rate of anesthetic adverse events, the authors currently perform endotracheal intubation for antegrade DAEs. However, this sedation-related complication rate is superior to previous reports.^{15,32} A recent large multicenter study from Germany, a country where non-anesthesiologist propofol-sedation is common practice, reported 11 (0.5%) sedation-related adverse events in 2245 procedures.¹⁵ No more sedation-related adverse events were found in elderly patients, as previously reported.³³

Complications were reported in 1.2% (17/1411), similar to the multicenter German study¹⁵ in which a complication rate of 1.2% (27/2245) was also found. Major complications were reported in 0.57% (eight of 1411), similar to a recent systematic review where major complications were reported in 0.72% of examinations.¹³ Only two cases of acute pancreatitis were recorded. However, this complication is probably underreported, as it occurs frequently several hours after the procedure and most centers perform DAEs for patients from other institutions. Perforation occurred in four patients (0.28%), most of them after therapeutic procedures, as previously reported.^{15,16}

The authors acknowledge some limitations. Although all centers enrolled in the survey maintained prospective data records of all procedures, the databases were not designed for this survey. Consequently some minor variations in data collection, registration and follow-up may have occurred. One participant at each institution compiled the database. Although it was

a simple database and the required fields were easy to follow, some inconsistencies in the records may have occurred. However, the database was checked for possible inconsistencies by two authors (RP, MMS). Most centers perform procedures for other institutions and the institution with the highest volume is an outpatient center performing procedures exclusively for other institutions. Hence patient follow-up and recording of delayed complications such as acute pancreatitis may be compromised.

Conclusions

This is the first published survey on the use of DAEs in Portugal. It shows that DAE is widely available in Portugal, mostly in Northern centers, with good performance and training capabilities. Earlier centers adopted DBEs whereas the centers that recently introduced DAE elected SBE. The diagnostic and therapeutic yields are high as most procedures were performed to manage abnormalities detected in other examinations, mostly CE. The complication rate is low, mostly anesthetic complications promptly reversed after the interruption of the procedure. Perforations are rare (0.28%) and occur mainly in therapeutic procedures.

Acknowledgments

Mário Dinis-Ribeiro: ManopH, Instituto CUF; Serviço de Gastreenterologia, Instituto Português de Oncologia do Porto

Fernando Castro-Poças: ManopH, Instituto CUF; Serviço de Gastreenterologia, Centro Hospitalar do Porto

Sandra Lopes: Serviço de Gastreenterologia, Centro Hospitalar e Universitário de Coimbra

Carlos Sofia: Serviço de Gastreenterologia, Centro Hospitalar e Universitário de Coimbra

Ana Rita-Lopes: Serviço de Gastreenterologia, Centro Hospitalar e Universitário de Coimbra

Diogo Branquinho: Serviço de Gastreenterologia, Centro Hospitalar e Universitário de Coimbra

Iolanda Ribeiro: Serviço de Gastreenterologia, Centro Hospitalar de Gaia/Espinho

Ana Ponte: Serviço de Gastreenterologia, Centro Hospitalar de Gaia/Espinho

Joana Silva: Serviço de Gastreenterologia, Centro Hospitalar de Gaia/Espinho

Armando Ribeiro: Serviço de Gastreenterologia, Centro Hospitalar de São João

Filipe Vilas-Boas: Serviço de Gastreenterologia, Centro Hospitalar de São João

João Antunes: Serviço de Gastreenterologia, Centro Hospitalar de São João

Maria João Moreira: Serviço de Gastreenterologia, Centro Hospitalar do Alto Ave

José Soares: Serviço de Gastreenterologia, Hospital Pedro Hispano

Ángela Rodrigues: Serviço de Gastreenterologia, Centro Hospitalar do Porto

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of interest

None declared.

References

- Appleyard M, Glukhovskiy A and Swain P. Wireless-capsule diagnostic endoscopy for recurrent small-bowel bleeding. *N Engl J Med* 2001; 344: 232–233.
- Yamamoto H, Yano T, Kita H, et al. New system of double-balloon enteroscopy for diagnosis and treatment of small intestinal disorders. *Gastroenterology* 2003; 125: 1556; author reply 1557.
- Tsujikawa T, Saitoh Y, Andoh A, et al. Novel single-balloon enteroscopy for diagnosis and treatment of the small intestine: Preliminary experiences. *Endoscopy* 2008; 40: 11–15.
- Akerman PA, Agrawal D, Cantero D, et al. Spiral enteroscopy with the new DSB overtube: A novel technique for deep peroral small-bowel intubation. *Endoscopy* 2008; 40: 974–978.
- Pinho RT, Rodrigues MA and Proença ML. Overtubes and fluoroscopy for direct percutaneous endoscopic jejunostomy: Useful, although not always needful and sometimes harmful. *Dig Endosc* 2015; 27: 399–400.
- Wadhwa V, Sethi S, Tewani S, et al. A meta-analysis on efficacy and safety: Single-balloon vs. double-balloon enteroscopy. *Gastroenterol Rep (Oxf)* 2015; 3: 148–155.
- Lipka S, Rabbanifard R, Kumar A, et al. Single versus double balloon enteroscopy for small bowel diagnostics: A systematic review and meta-analysis. *J Clin Gastroenterol* 2015; 49: 177–184.
- Pinto-Pais T, Pinho R, Rodrigues A, et al. Emergency single-balloon enteroscopy in overt obscure gastrointestinal bleeding: Efficacy and safety. *United European Gastroenterol J* 2014; 2: 490–496.
- Skinner M, Popa D, Neumann H, et al. ERCP with the overtube-assisted enteroscopy technique: A systematic review. *Endoscopy* 2014; 46: 560–572.
- Pais TP, Pinho R, Proença L, et al. Single-balloon enteroscopy assisted endoscopic retrograde cholangiopancreatography with the rendezvous technique. *GE Portuguese Journal of Gastroenterology* 2015; 22: 39–41.
- Pinto-Pais T, Pinho R, Proença L, et al. Iatrogenic biliary injury in a patient with Roux-en-Y hepaticojejunostomy: Stenting repair with single-balloon enteroscopy-assisted ERCP. *Endoscopy* 2014; 46(Suppl 1 UCTN): E506–E507.
- Pinho R, Proença L, Alberto L, et al. Biliary self-expandable metallic stent using single balloon

- enteroscopy assisted ERCP—overcoming limitations of current accessories. *Rev Esp Enferm Dig* 2013; 105: 561–564.
13. Xin L, Liao Z, Jiang YP, et al. Indications, detectability, positive findings, total enteroscopy, and complications of diagnostic double-balloon endoscopy: A systematic review of data over the first decade of use. *Gastrointest Endosc* 2011; 74: 563–570.
 14. Pennazio M, Spada C, Eliakim R, et al. Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy* 2015; 47: 352–386.
 15. Möschler O, May A, Müller MK, et al. Complications in and performance of double-balloon enteroscopy (DBE): Results from a large prospective DBE database in Germany. *Endoscopy* 2011; 43: 484–489.
 16. Möschler O, May AD, Müller MK, et al. Complications in double-balloon-enteroscopy: Results of the German DBE register [article in German]. *Z Gastroenterol* 2008; 46: 266–270.
 17. 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 multi-center study. *Rev Esp Enferm Dig* 2013; 105: 594–599.
 18. Sethi S, Cohen J, Thaker AM, et al. Prior capsule endoscopy improves the diagnostic and therapeutic yield of single-balloon enteroscopy. *Dig Dis Sci* 2014; 59: 2497–2502.
 19. Pinho R. The vanishing frontiers of therapeutic enteroscopy. *GE Portuguese Journal of Gastroenterology* 2015; 22: 137–142.
 20. Fernandes C, Pinho R, Rodrigues A, et al. Argon plasma coagulation of a bleeding angioectasia in a jejunal diverticulum by single-balloon enteroscopy. *Endoscopy* 2015; 47(Suppl 1 UCTN): E62.
 21. May A, Nachbar L and Ell C. Double-balloon enteroscopy (push-and-pull enteroscopy) of the small bowel: Feasibility and diagnostic and therapeutic yield in patients with suspected small bowel disease. *Gastrointest Endosc* 2005; 62: 62–70.
 22. Frantz DJ, Dellon ES, Grimm IS, et al. Single-balloon enteroscopy: Results from an initial experience at a U.S. tertiary-care center. *Gastrointest Endosc* 2010; 72: 422–426.
 23. Ribeiro I, Pinho R, Rodrigues A, et al. Obscure gastrointestinal bleeding: Which factors are associated with positive capsule endoscopy findings? *Rev Esp Enferm Dig* 2015; 107: 334–339.
 24. Soares J, Lopes L, Vilas Boas G, et al. Wireless capsule endoscopy for evaluation of phenotypic expression of small-bowel polyps in patients with Peutz-Jeghers syndrome and in symptomatic first-degree relatives. *Endoscopy* 2004; 36: 1060–1066.
 25. Ribeiro I, Pinho R, Rodrigues A, et al. The importance of alternative diagnostic modalities in the diagnosis of small bowel tumors after a negative capsule endoscopy. *GE Portuguese Journal of Gastroenterology* 2015; 22: 112–116.
 26. Louro-da-Ponte AI, Taveira-Pinho R, Rodrigues MA, et al. Advances and pitfalls in the management of small bowel polyps in Peutz-Jeghers syndrome. *Rev Esp Enferm Dig* 2015; 107: 390–391.
 27. van Lier MG, Wagner A, Mathus-Vliegen EM, et al. High cancer risk in Peutz-Jeghers syndrome: A systematic review and surveillance recommendations. *Am J Gastroenterol* 2010; 105: 1258–1264 (author reply 1265).
 28. Almeida N, Figueiredo P, Lopes S, et al. Double-balloon enteroscopy and small bowel tumors: A South-European single-center experience. *Dig Dis Sci* 2009; 54: 1520–1524.
 29. Girelli CM, Porta P, Colombo E, et al. Development of a novel index to discriminate bulge from mass on small-bowel capsule endoscopy. *Gastrointest Endosc* 2011; 74: 1067–1074; quiz 1115.e1-e5.
 30. Ferreira AO, Torres J, Dinis-Ribeiro M, et al. Endoscopic sedation and monitoring practices in Portugal: A nationwide web-based survey. *Eur J Gastroenterol Hepatol* 2015; 27: 265–270.
 31. Lara LF, Ukleja A, Pimentel R, et al. Effect of a quality program with adverse events identification on airway management during overtube-assisted enteroscopy. *Endoscopy* 2014; 46: 927–932.
 32. Sethi S, Thaker AM, Cohen J, et al. Monitored anesthesia care without endotracheal intubation is safe and efficacious for single-balloon enteroscopy. *Dig Dis Sci* 2014; 59: 2184–2190.
 33. Cangemi DJ, Stark ME, Cangemi JR, et al. Double-balloon enteroscopy and outcomes in patients older than 80. *Age Ageing* 2015; 44: 529–532.