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Safety and efficacy of biodegradable stents in octogenarian patients with esophageal achalasia

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ABSTRACT

Backgrounds and study aims Treatment of octogenarian patients with achalasia with conventional treatments is effective but with compromised safety. Biodegradable stents (BS) are promising. We aimed to evaluate their safety, efficacy and clinical outcomes at early, mid and long-term in this population.

Patients and methods Naïve or previously-treated achalasic octogenarian patients underwent to BS placement (BSP) between December, 2010 and November, 2011, and were followed-up for 9-years. A strict follow-up was performed.

Results Thirty-two patients were included, (17 men [53.1 %]; median age 82 years [78–92]). BSP was performed in all patients. At 9y, 18/32 (56.2 %) completed protocol. Mean BSP time was 37.5±12.1 min and 34.4 % presented thoracic pain. At 1 m, six BS were migrated (18.7 %), requiring a second BSP fixed with hemoclips. At 3 m, twenty-three (72.8 %) completed degradation process. At 6 m, eighteen (56.2 %) presented clinical dysphagia, of whom 5/32 (15.6 %) presented stenotic-tissue hyperplasia, responding to balloon dilation in all cases. Pre-BSP Eckardt, Timed barium esophagram and integrated relaxation pressure improved post-BSP 6 m values (9 vs 2, p = 0.001; < 50 % = 93.8 % vs > 80 % = 81.5 %, p = 0.003 and 18.8 ± 3.2 vs 11.1 ± 2.6 mmHg, p = 0.001, respectively), and there were no significant changes up to 9y post-BSP. Esophagitis grade A or B was presented between 4.7 % to 11.2 % and controlled with PPI. After 9 years we had clinical success rates of 94.4 %, 72 %, and 65.4 % for time point evaluation, per protocol and intention to treat analysis, respectively.

Conclusions BSP represents a feasible alternative option in octogenarian patients with achalasia who are high risk with other treatments, presenting acceptable early, mid-, and long-term outcomes.

Introduction

Esophageal achalasia is a primary esophageal motor disorder characterized by aperistalsis and failure in lower esophageal sphincter (LES) relaxation [1]. Treatment aim is to decrease LES pressure and integrated relaxation pressure (IRP), in order to improve symptoms and quality of life [2, 3]. Laparoscopic Heller Myotomy (LHM) and Peroral endoscopic myotomy (POEM) are considered the gold standard of treatment [4–6]; however, safety is compromised in some populations, such as in elderly patients (adverse events of 2 % to 11.5 % in LHM and 5 % to 7.8 % for POEM [7–9]), representing high-risk procedures for them. Alternative treatments include pneumatic dilation (PD) (73 %–88 % early and mid-term efficacy, but a median of 1.9 % perforation rate [4–10]) and botulinum toxin injection (BTI) (initial 87 % to 92 %, but 22 % to 31 % mid-term efficacy

[8, 11]). Fully or partially covered self-expandable metal stents (SEMS) have been used with variable clinical remission rates (88 % to 100 % at early-term and 49 % to 91 % at long-term [12, 13]), but with concerning adverse events (AEs) (thoracic pain 35 % to 44 %, reflux symptoms 28 % to 36 %, migration 8.5 % to 18 %, and bleeding 8 % to 12 % [14–16]).

Biodegradable stents have appeared as a promising alternative for different gastrointestinal diseases, including benign esophageal strictures (BES) [17, 18]. Their main advantage is the ability of exert a continuous radial force that last up to 6 weeks before degradation process begins, avoiding the need for endoscopic removal [19]. In peptic BES, promising results have been observed in 65 % to 87.5 %, 45 % to 60 % and 25 % at early, mid- and long-term evaluations, respectively [20], with AEs that include migration (8 %–20 %), thoracic pain (10 %–57 %) and tissue hyperplasia (5 %–60 %) [21, 22], representing a good alternative of treatment in achalasic patients, especially in high-risk groups such as octogenarians. Therefore, we aimed to investigate the safety and efficacy of BS in a group of octogenarian patients with achalasia.

Patients and methods

Study design and ethical considerations

This was a prospective study performed between December, 2010 and October, 2020 in a tertiary-care center in Mexico City, Mexico. We included all octogenarian patients with naïve or previously-treated achalasia at any stage who were at high risk for surgery (e. g. patients with severe cardiopulmonary conditions, significant coagulation disorders, etc.), but without contraindication to an upper endoscopy (UE) or those who didn't accept other treatment modalities such as POEM or PD. Patients who were unable to receive general anesthesia, those with pseudoachalasia, esophagogastric tumors, peptic strictures, or suspicion of gastrointestinal malignancy were excluded. All BS were placed between December, 2010 and November, 2011, and then completed protocol up to October, 2020.

This protocol was approved on sept 22, 2010, by the Local Ethics Committee (R-2010-3601-096; trial registration number: 2010-CMN112). Informed consent was obtained from all patients.

Patients

Diagnosis of achalasia was based on clinical, radiological, endoscopic and manometric characteristics [4]. All patients underwent UE, chest computed tomography, Chagas testing, high-resolution manometry (HRM) using Chicago's classification for achalasia subtypes [23, 24], and timed barium esophagram (TBE) (at 1, 2, and 5 minutes). Clinical evaluation was done using the Eckardt scale [25].

Biodegradable stent placement

First, the esophagus was cleaned before BSP. Esophageal classification was evaluated according to Rezende's classification [26]. All procedures were performed under deep-sedation anesthesia and fluoroscopy guidance. A 9.8-mm outer diameter with a 2.8-mm working channel endoscope was used (EG-450WR5 or EG590WR; Fujinon, Tokyo, Japan). After endoscopic revision and esophagogastric junction (EGJ) level documentation, 1 mL of non-ionic contrast agent at 50 % (Omnipaque, GE Healthcare, Ireland Limited, Cork, Ireland) was injected at submucosal level 1 cm above EGJ. Then, a metallic 200 cm long Savary-Gilliard wire-guide (Cook Medical, Bloomington, Indiana, United States) was introduced and placed on gastric antrum. Finally, a polydioxanone biodegradable stent of 25 mm × 60 mm (Ella-CS, Hradec Kralove, Czech Republic) was placed under fluoroscopic guidance throughout the guide and deployed, assuring that the middle part of the stent was placed over the submucosal marker. Final endoscopic review was performed and confirmation of adequate BSP documented (▶ **Fig. 1**).

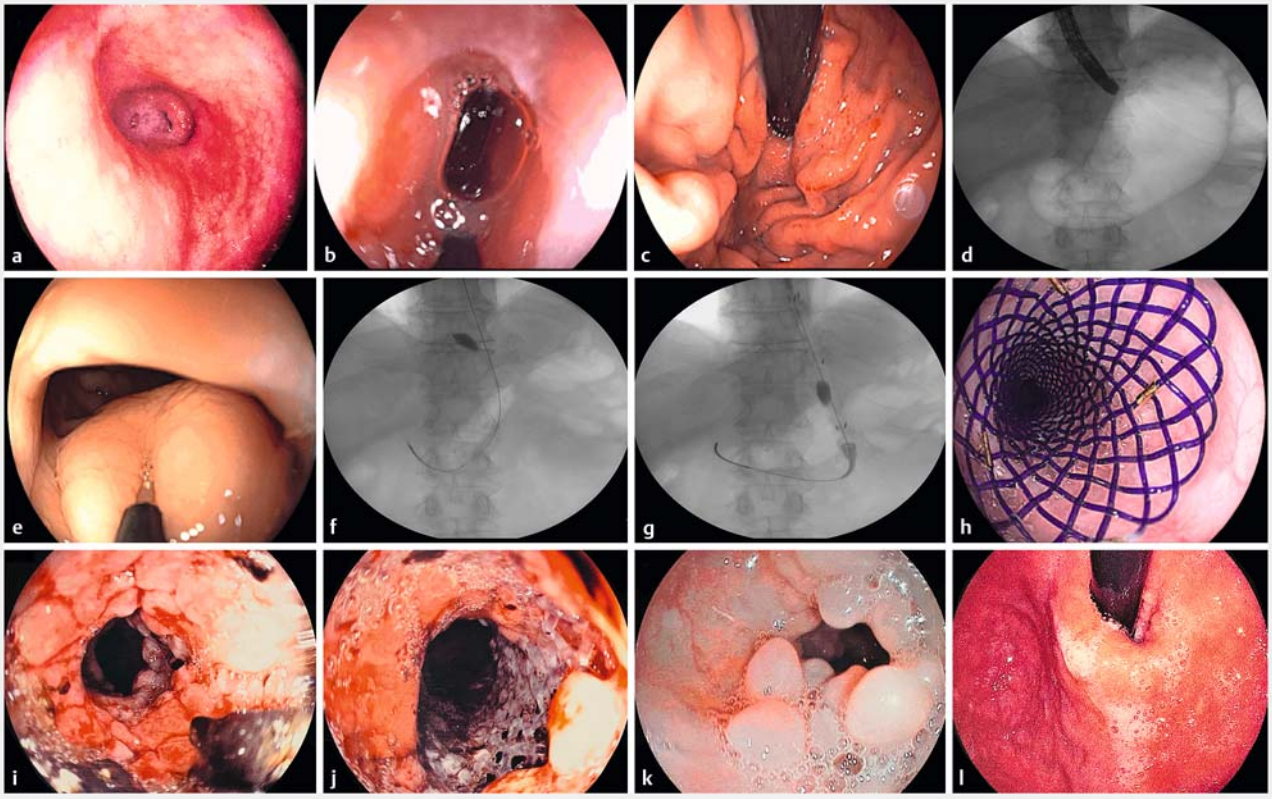
Follow-up

After the procedure, patients were hospitalized for detection of potential adverse events (AE), then liquid diet was initiated and continued for 2 days, and progressed to soft by 3 days and then normal diet. Proton pump inhibitors (PPI) were administered initially for 3 months to prevent reflux and avoid premature stent degradation, and then accordingly to results of reflux assessment. Patients underwent clinical (dysphagia evaluated according to Dakkak and Bennett score) [27], and radiological assessment at 1 and 2 months. Then, UE, TBE, HRM, Eckardt and esophageal 24-hour pH monitoring were performed at 3 and 6 months, and then annually for up to 9 years. If stenotic tissular hyperplasia (STH) was found on UE, patients underwent balloon dilation program up to 15 mm with CRE balloon (Boston Scientific, Natick, Massachusetts, USA). If migration of stent was presented, a second BS of the same characteristics was inserted and fixed with hemoclips to avoid migration (Boston Scientific, Natick, Massachusetts, United States).

Clinical success (CS) was defined when after 6 months of BSP, we observed an Eckard score < 3, TBE ≥ 80 % at 5 minutes, and integrated relaxation pressure (IRP) < 15 mmHg; failure when Eckardt ≥ 3, TBE < 50 % and IRP ≥ 15 mmHg; partial response (PR), when patients had an Eckardt ≥ 3 and IRP ≥ 15 mmHg or delayed TBE (between 50 % to 80 % or < 50 %). Finally, IRP or TBE failure criteria alone were not considered as patients with PR. When PR was found after two consecutive follow-ups, they were considered as failures and underwent PD, as rescue therapy with Rigiflex balloon (Microvasive, Watertown, Massachusetts). In cases with failure criteria, if a second follow-up showed failure criteria again or PR, they also underwent the PD program. If esophagitis on UE or 24-hour pH monitoring were documented, PPI was administered indefinitely. Adverse events were graded according to the American Society for Gastrointestinal Endoscopy Lexicon [28].

Statistical analyses

The sample size was calculated based on the formula for difference of proportions for paired measurements (clinical improvement before and after BSP). According to previous studies [12–16], there is a mean 80 % clinical improvement after procedure. Thus, in spite of no previous BSP studies in achalasic patients, we hypothesized an improvement of at least 80 %, assuming a 20 % dropout rate with a significance alpha level of 0.05 (Type I



▶ **Fig. 1** Biodegradable stent placement technique and changes at 3 and 7 years after. **a** Octogenarian patient with Type I achalasia, showing a grade III dilated esophagus. **b** EGJ without mucosal abnormalities. **c** Retroflexion view. **d** Radiological view of EGJ position. **e** Injection of 1 mL of non-ionic contrast agent at 50 % 1 cm above EGJ. **f** Fluoroscopic view of submucosal injection of contrast, and Savary guidewire placement. **g** Biodegradable stent placement with fluoroscopic guidance. **h** Endoscopic view of biodegradable stent in adequate position. **i** Partial degradation process after 3 months of BSP. **j** Non-stenotic tissular hyperplastic reaction at EGJ level. **k** Same patient, showing non-stenotic mucosal changes at 7 years after BSP. **l** Retroflexion view showing a slightly opened EGJ with hyperplasic mucosal changes of biodegradable stent.

error of 5 %) and a beta of 0.20 (Type II error of 20 %). Using an online statistically-validated program of sample size calculation (EpiInfo, United States), we calculated a sample of 20 patients.

The clinical characteristics of patients, procedures and outcomes are documented as mean with standard deviation (SD) or medians with interquartile ranges (IQR) for quantitative variables, according to their distribution. Qualitative data are expressed as frequencies and percentages. Evaluation of BSP outcomes were performed using Friedman, Wilcoxon, Student's t-test and ANOVA tests for quantitative data, and linear-by-linear association test for qualitative variables. CS was evaluated according to per protocol (PP) and intention to treat (ITT) analysis and time point evaluation (TPE). $P<0.05$ was considered statistically significant. SPSS 23.0 for Mac (IBM) was used for statistical analysis.

Results

Baseline characteristics

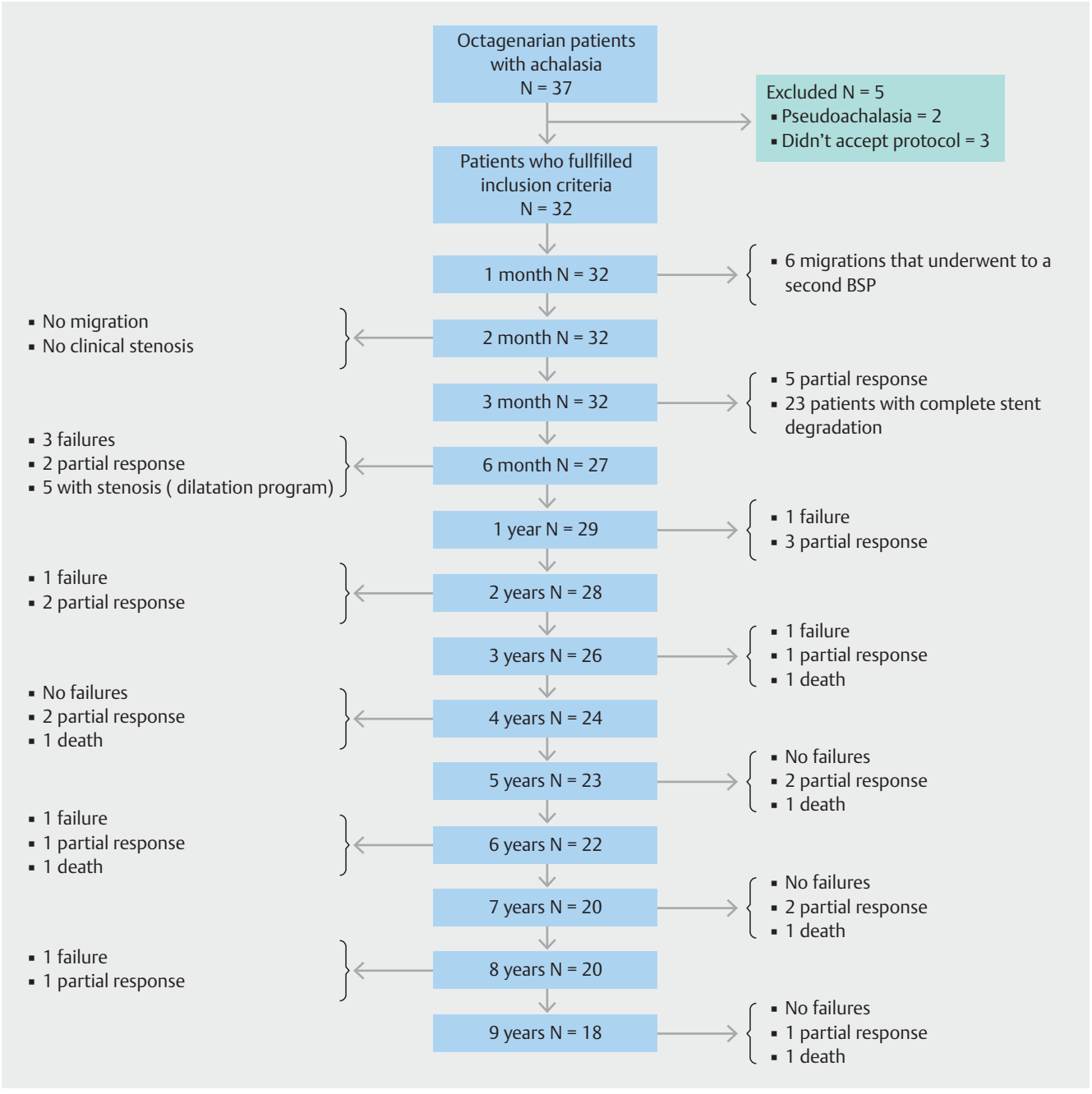
Of 37 octogenarian patients with achalasia, five were excluded. Thirty-two were included for BSP that was performed successfully in all cases between December, 2010 and November, 2011 (17 men [53.1 %]; median age 82 years [78–92]). After 9 years, 18 of 32 patients (56.2 %) completed 9-year follow-up (▶ **Fig. 2**).

The median body mass index (BMI) was 19.2 (14.2–24.1). The most common achalasia subtype was Type I in 62.5 %. Grade II, III and IV were found in 34.4 %, 25 %, and 15.6 %, respectively. Twenty-one (65.6 %), were previously treated (PD in 28.1 %). The median Eckardt pre-BSP was 9 (6–12), and 93.8 % of the patients had a pre-BSP TBE < 50 % (▶ **Table 1**).

Biodegradable stent placement (early outcomes)

The mean BSP time was 37.5 ± 12.1 minutes. Chest pain was present in 34.4 % (controlled with nonsteroidal anti-inflammatory drugs [NSAIDs]), followed by transprocedural self-limited mild bleeding (12.5 %). The median length of stay was 1 day (1–2), diet was progressed successfully.

At 1 month, we had six migrations, requiring a second stent placement, fixed with a median of three hemoclips (2–4). At 2 months all stents were in place. At 3 months, complete and partial degradation of the stent were present in 23 (72.8 %) and nine (27.2 %), respectively.



▶ **Fig. 2** Flowchart of the cohort of octogenarian patients with achalasia.

Endoscopic stenosis after BSP

No dysphagia was present before 3 months; however, at 3 months post-BSP, 12 of 32 (37.5 %) and three of 32 (9.3 %), presented dysphagia to some solid and semi-solid food, respectively. For UE, 50 % presented with an opened esophagogastric junction (OEGJ), and 50 % non-stenotic tissular hyperplasia (NSTH).

At 6 months, we had some degree of dysphagia in 18 of 32 (56.2 %), in 10 of whom (31.3 %) it was to solid food, not requiring endoscopic treatment. However, it was clinically significant in eight of 32 patients (25 %), in five of whom (15.6 %) it was to semi-solid food (NSTH = 2/STH = 3), and in three (9.3 %), to liquids (NSTH = 1/STH = 2). All STH (5/32 [15.6 %]), required CRE balloon dilation up to 15 mm, requiring one, two, and three to five sessions in one, two, and two patients, respectively (▶ **Table 2**).

Biodegradable stent placement (early, mid-, and long-term outcomes)

The median pre-BSP Eckardt score was 9 (6–12), and decreased to 4 (2–6) after 1 month (P = 0.001), and maintained up to 9 years (2 [1–3]; P = 0.14). Dakkak score didn't show changes between pre-BSP and post-BSP 1-month and 2-month values;

▶ **Table 1** Characteristics of patients and procedures.

	N = 32
Age, median (IQR), years	82 (78–92)
Gender, n (%), male	17 (53.1 %)
BMI, median (IQR), score	19.2 (14.2–24.1)
Time before achalasia diagnosis, median (IQR), months	210 (22–601)
Previous treatments, (%)	
▪ Treatment naïve	11 (34.4 %)
▪ Previously treated	21 (65.6 %)
▪ Post-LHM	7 (21.9 %)
▪ Botulinum toxin injection	5 (15.6 %)
▪ Pneumatic dilation	9 (28.1 %)
Achalasia subtype, n (%)	
▪ Type I	20 (62.5 %)
▪ Type II	11 (34.4 %)
▪ Type III	1 (3.1 %)
Type of esophagus, n (%)	
▪ Normal	2 (6.3 %)
▪ Grade I	6 (18.8 %)
▪ Grade II	11 (34.4 %)
▪ Grade III	8 (25 %)
▪ Grade IV	5 (15.6 %)
Eckardt pre-BSP, median (IQR), points	9 (6–12)
IRP pre BSP, mean (SD), mmHg	18.8 ± 3.2
TBE pre BSP, n (%)	
▪ < 50 %	30 (93.8 %)
▪ 50 %–80 %	2 (6.2 %)
▪ > 80 %	0 (0 %)
BSP duration, mean (SD), min	37.5 ± 12.1
Adverse events, n (%)	
▪ Chest pain	11 (34.4 %)
▪ Bleeding	4 (12.5 %)
▪ None	17 (53.1 %)

SD, standard deviation; IQR, interquartile range; BMI, body mass index; LHM, laparoscopic heller myotomy; IRP, integrated relaxation pressure; TBE, timed barium esophagram; BSP, biodegradable stent placement.

however, they improved at 3 months (pre-BSP = 4 [2–4] vs post-BSP 3 months = 1 0–2; P = 0.001), and values were maintained up to 9 years (post-BSP 3 months = 1 0–2 vs post-BSP 9 years = 2 0–2; P = 0.09).

The IRP pressure improved from pre-BSP = 18.8 ± 3.2 mmHg to post-BSP 3 months = 12 ± 2.6 mmHg (P = 0.001); and maintained up to 9 years. DeMeester score after BSP was stable from 3 months to 9 years (post-BSP 3 months = 11.8 ± 5.0 vs post-BSP 9 years = 10.8±2.1; P = 0.12).

Pre-BSP TBE was < 50 % in 93.8 % and improved to post-BSP TBE > 80 % in 71.9 %, 81.5 %, 93 %, and 80.8 % for 3 months, 6 months,1 years and 2 years, respectively (P = 0.003). After 3 years post-BSP TBE was maintained up to 9 years (P = 0.11), and up to 61.1 % of our patients presented a TBE > 80 % after 9 years of BSP (▶ **Fig. 3**).

Pre-BSP UE showed a closed esophagogastric junction (CEGJ) in all cases, which improved to post-BSP at 3 months (NSTH = 18/32 [56.3 %] and OEGJ = 14/32 [43.8 %]; P = 0.03). At post-BSP 6 months, five of 32 (15.6 %) changed from NSTH to STH (P = 0.01), and were temporarily separated from the cohort (n = 27), once the dilation program ended, they were included at 1-year follow-up. At post-BSP 1 year, 72.4 % presented OEGJ, 20.7 % NSTH, 10.3 % LGE, and 6.9 % CEGJ. Similar values were found at 9 years without statistically significant differences (▶ **Table 3**).

Regarding TPE assessment, all patients were failed before BSP and improved by post-BSP 6 months (CS = 22 [81.5 %], PR = 2 [7.4 %] and failure = 3 [11.1 %]; P = 0.001), and improved at post-BSP 1 year (CS = 25 [86.2 %], PR = 3 [10.3 %] and failure = 1 [3.5 %]; P = 0.003). No changes were found up to post-BSP 9 years (CS = 17 [94.4 %], PR = 1 [5.6 %] and failure = 0 [0 %]; P = 0.19). In the PP analysis, we had a final post-BSP 9 years: CS = 17 of 26 (65.4 %); PR = one of 26 (3.9 %) and failure = eight of 26 (30.7 %), and in the ITT, we had CS = 23 of 32 (72 %); PR = one of 32 (3 %) and failure = eight of 32 (25 %) (▶ **Fig. 4**). We had six deaths (18.8 %) (not related to BSP and all were successful before they died). Finally, we performed a bivariate analysis of success and failure patients at 9 years after BSP, including clinically-relevant variables; however, we observed no differences between groups.

Discussion

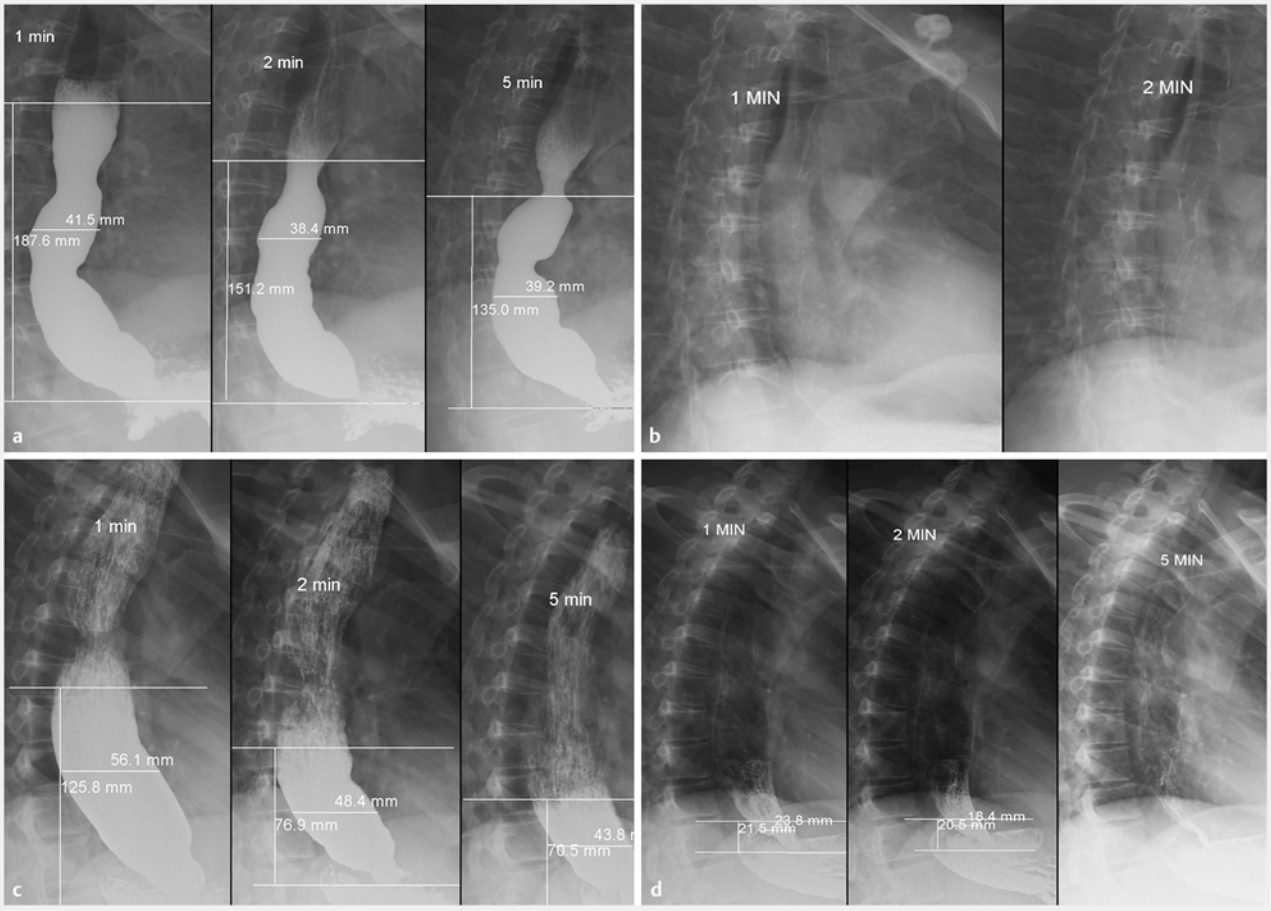
In this paper, we evaluated the feasibility, safety and efficacy of BSP in a group of octogenarian patients with achalasia, at early, mid and long-term.

POEM and LHM represent the cornerstone of treatment in young patients. POEM has a clinical success in octogenarians of > 90 %, but AE ranging from 5–7.8 %, most of them mild, but up to 10.7 % could be severe [7, 29–31]. LHM has been associated with perioperative complications (bleeding [5–18 %], perforation [2 %–5 %], postsurgical infection [3 %–6 %]) [8, 9, 32, 33]. PD has a median perforation rate of 1.9 % [4, 8], and BTI has a temporary effect (mid-term efficacy 22 %–31 %) [11]; moreover, if a more definite treatment is offered, submucosal fibrosis and mucosal injury rate are increased (4 %–12 %) [2, 4, 8]. Other options include fully or partially covered SEMS, with variable results (49 %–91 % long-term efficacy and 8 %–45 % AE) [14–16].

Therefore, we considered the use of BSP, based on two reasons: first, because of its safety and efficacy observed in other gastrointestinal diseases, such as BES and small bowel strictures [17]. Second, BSP is performed in a conventional fluoroscopy

▶ **Table 2** Endoscopic stenosis after biodegradable stent placement.

	3 months N = 32	Endoscopic evaluation at 3 months n = 32			6 months N = 32	Endoscopic evaluation at 6 months n = 32			Dilation endoscopic sessions n = 5		
Clinical dysphagia		NSTH	STH	OEGJ		NSTH	STH	OEGJ	1	2	3–5
None (0)	17 (53.2 %)	4 (23.5 %)	0 (0 %)	13 (76.5 %)	14 (43.8 %)	4 (28.6 %)	0 (0 %)	10 (71.4 %)	0 (0 %)	0 (0 %)	0 (0 %)
To some solid food (1)	12 (37.5 %)	9 (75 %)	0 (0 %)	3 (25 %)	10 (31.3 %)	6 (60 %)	0 (0 %)	4 (40 %)	0 (0 %)	0 (0 %)	0 (0 %)
To semisolid food (2)	3 (9.3 %)	3 (100 %)	0 (0 %)	0 (0 %)	5 (15.6 %)	2 (40 %)	3 (60 %)	0 (0 %)	1 (33 %)	2 (66 %)	0 (0 %)
To liquids (3)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	3 (9.3 %)	1 (33 %)	2 (66 %)	0 (0 %)	0 (0 %)	0 (0 %)	2 (100 %)
Complete dysphagia (4)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)



▶ **Fig. 3** Timed barium esophagram emptying before and after BSP. a Emptying < 50 % at 5 minutes before BSP was observed in a patient with sigmoid-type achalasia. b Emptying > 80 % inclusive at 2 minutes was observed at 1 year after BSP. c Octogenarian patient with grade II achalasia showing emptying < 50 % at 5 minutes. d More than 80 % of emptying at 5 minutes was observed after 7 years after BSP.

and endoscopy suite, only deep sedation is needed, there is easy placement, and no removal is needed [18, 20–22], representing a promising alternative in octogenarian patients with a high-risk nature (comorbidity, esophageal mucosal fragility, and anatomic esophageal changes due to aging) [1, 8, 10, 17]. Diameter use was based on previous studies with SEMS. Cheng et al [12] compared the efficacy of a temporary use of 3 different diameter SEMS (20, 25, and 25 mm), in a prospective comparative study with a long-term follow-up (10 years); they concluded that 30 mm was superior and suggested that wider stents could have better outcomes. Therefore, we used the widest BS available (25 mm).

Our octogenarian group had demographic characteristics similar to other authors that have studied and treated octogen-

▶ **Table 3** BSP outcomes at early, mid- and long-term evaluations.

Pre-BSP (n = 32)		Post-BSP													
		1 month (n = 32)	2 months (n = 32)	3 months (n = 32)	6 months (n = 27)	1 year (n = 29)	2 years (n = 28)	3 years (n = 26)	4 years (n = 24)	5 years (n = 23)	6 years (n = 22)	7 years (n = 20)	8 years (n = 20)	9 years (n = 18)	P
Eckardt, median (IQR) points	9 (6–12)	4 (2–6)	3 (1–5)	3 (1–7)	2 (2–6)	2 (1–6)	2 (1–5)	2 (1–5)	2 (1–5)	2 (1–5)	2 (1–7)	2 (1–3)	2 (1–5)	2 (1–3)	Pre-BSP vs 1 month – 9 years = 0.001[1] Post-BSP 1 month vs 2 month – 9 years = 0.14[2]
Dysphagia	3 (1–3)	2 (0–2)	2 (0–2)	2 (1–3)	1 (0–3)	1 (0–2)	1 (0–2)	1 (0–1)	1 (0–2)	1 (0–2)	1 (0–3)	1 (0–2)	1 (0–2)	1 (0–2)	
Regurgitation	2 (0–3)	1 (1–2)	1 (0–2)	1(0–2)	1 (0–2)	1 (0–2)	1 (0–1)	1 (0–2)	1 (0–1)	1 (0–1)	1 (0–2)	1 (0–1)	1 (0–2)	1 (0–1)	
Chest Pain	1 (0–3)	1 (0–2)	0 (0–1)	0(0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–2)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0)	0 (0–1)	0 (0)	
Weight Loss	3 (2–3)	0 (0)	0 (0)	0 (0–1)	0 (0)	0 (0–1)	0 (0–1)	0 (0)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0)	0 (0)	0 (0)	
IRP pressure, mean (SD), mmHg	18.8 ± 3.2	–	–	12.0 ± 2.6	11.1 ± 2.6	10.2 ± 1.9	11.0 ± 1.5	11.8 ± 1.7	11.9 ± 1.1	11.5 ± 1.4	12.1 ± 1.5	12.1 ± 1.5	13.4 ± 1.2	13.6 ± 0.7	Pre-BSP vs 1 month – 9 years = 0.001[3] Post-BSP 3 months vs 6 months – 9 years = 0.20[4]
TBE, n (%)															
< 50 %	30 (93.8)	–	–	0 (0)	3 (11.1)	1 (3.5)	1 (3.6)	1 (3.8)	0 (0)	0 (0)	1 (4.5)	0 (0)	1 (5)	0 (0)	Pre-BSP vs 3 months – 9 years = 0.003[5] Post-BSP 3 months vs 6 months, 1 year and 2 years = 0.45[5] Post-BSP 3 months vs 3 years – 9 years = 0.02[5] Post-BSP 2 years vs 3 years – 9 years = 0.01[5] Post-BSP 3 years vs 4 years – 9 years = 0.11[5]
50–80 %	2 (6.2)	–	–	9 (28.1)	2 (7.4)	1 (3.5)	1 (3.6)	4 (15.4)	5 (20.8)	6 (26.1)	4 (18.1)	6 (30)	8 (40)	7 (38.9)	
> 80 %	0 (0)	–	–	23 (71.9)	22 (81.5)	27 (93)	26 (89.2)	21 (80.8)	19 (79.2)	17 (73.9)	17 (77.4)	14 (70)	11 (55)	11 (61.1)	
DeMeester, mean (SD)	–	–	–	11.8 ± 5.0	12.8 ± 4.2	12.2 ± 3.7	8.7 ± 2.9	9.6 ± 3.7	8.1 ± 2.8	9.1 ± 2.5	8.8 ± 2.1	7.9 ± 2.2	9.3 ± 2.6	10.8 ± 2.1	Post-BSP 3 months vs others = 0.12[4]
Clinical outcomes by time point evaluation (TPE), n (%)															Pre-BSP vs 6 months – 9 years = 0.001[5] Post-BSP 6 months vs 1 year – 9 years = 0.003[5] Post-BSP 1 year vs 2 years – 9 years = 0.19[5]
Failure	32 (100)	–	–	–	3 (11.1)	1 (3.5)	1 (3.6)	1 (3.8)	0 (0)	0 (0)	1 (4.5)	0 (0)	1 (5)	0 (0)	
PR	–	–	–	–	2 (7.4)	3 (10.3)	2 (7.2)	1 (3.8)	2 (8.3)	2 (13.1)	1 (4.5)	2 (10)	1 (5)	1 (5.6)	
Success	–	–	–	–	22 (81.5)	25 (86.2)	25 (89.2)	24 (92.4)	22 (91.7)	21 (86.9)	20 (91)	18 (90)	18 (90)	17 (94.4)	

▶ **Table 3** (Continuation)

Pre-BSP (n = 32)		**Post-BSP**													
		1 month (n = 32)	**2 months (n = 32)**	**3 months (n = 32)**	**6 months (n = 27)**	**1 year (n = 29)**	**2 years (n = 28)**	**3 years (n = 26)**	**4 years (n = 24)**	**5 years (n = 23)**	**6 years (n = 22)**	**7 years (n = 20)**	**8 years (n = 20)**	**9 years (n = 18)**	**P**
Upper endoscopy, n (%)					n = 32										Pre-BSP vs 3 months – 9 years = 0.03[5] Post-BSP 3 m vs 6 m = 0.01[5] Post-BSP 6 m vs 1 y – 9y = 0.02[5] Post-BSP 1y vs 2y – 9y = 0.88[5]
NSTH	–	–	–	18 (56.3)	11 (34.4)	6 (20.7)	3 (10.7)	3 (11.6)	1 (4.2)	3 (13.1)	3 (13.6)	3 (15)	1 (5)	2 (11.2)	
STH	–	–	–	0 (0)	5 (15.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
OEGJ	–	–	–	14 (43.8)	13 (40.6)	21 (72.4)	22 (78.6)	21 (80.8)	22 (91.6)	19 (82.6)	17 (77.3)	16 (80)	17 (85)	15 (83.2)	
LGE	–	–	–	0 (0)	0 (0)	3 (10.3)	2 (7.1)	2 (7.6)	1 (4.2)	1 (4.3)	0 (0)	1 (5)	1 (5)	2 (11.2)	
CEGJ	32 (100)	–	–	0 (0)	3 (9.4)	2 (6.9)	3 (10.7)	2 (7.6)	1 (4.2)	1 (4.3)	2 (9.1)	1 (5)	2 (10)	1 (5.6)	
Dysphagia score, median (IQR)	4 (2–4)	3 (1–3)	3 (1–3)	1 (0–2)	0 (0–3)	0 (0–2)	1 (1–2)	1 (0–2)	1 (0–3)	1 (0–2)	2 (1–2)	1 (0–2)	1 (0–1)	2 (0–2)	Pre-BSP vs 1 m and 2 m = 0.22[1] Pre-BSP vs 3 m – 9y = 0.001[2] Post-BSP 1 m and 2 m vs 3 m – 9y = 0.09[2] Post-BSP 3 m vs 6 m – 9y = 0.33[2]

IQR, interquartile range; SD, standard deviation; TBE, timed barium esophagram; BSP, biodegradable stent placement; NSTH, non-stenotic tissular hyperplasia; STH, stenotic tissular hyperplasia; OEGJ, opened esophagogastric junction; CEGJ, closed esophagogastric junction; LGE, low grade esophagitis; TPE, time point evaluation.

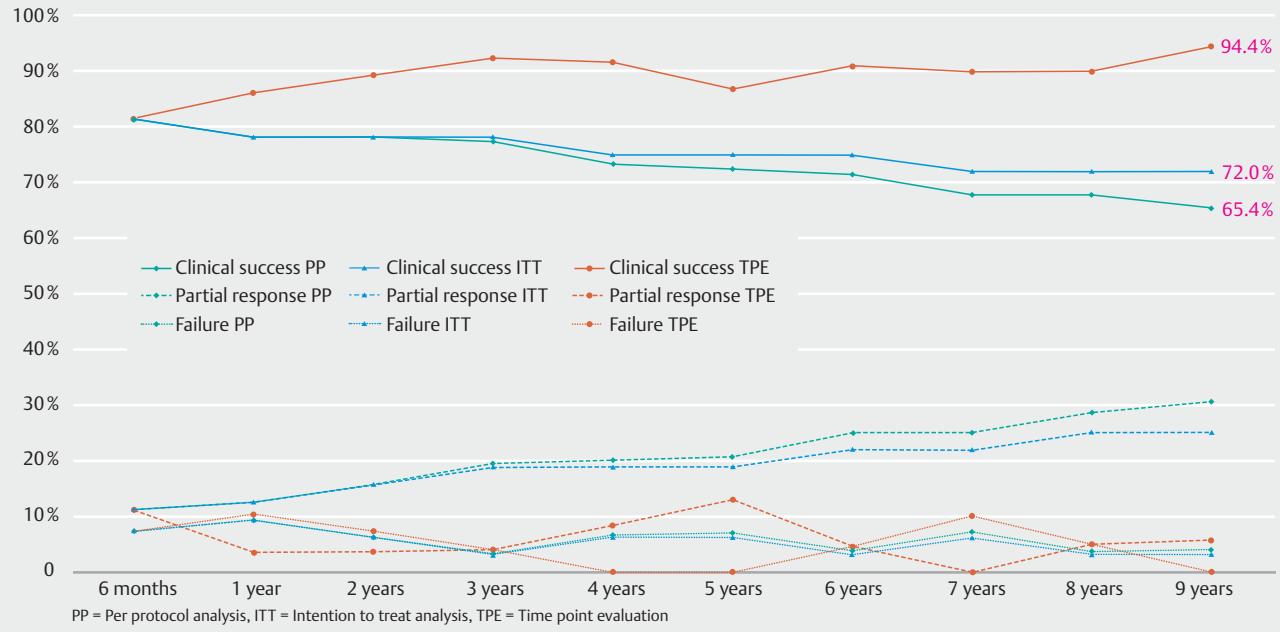
[1] Wilcoxon test.

[2] Friedman test.

[3] Student's *t*-test

[4] ANOVA test.

[5] Linear by linear association test.



▶ **Fig. 4** BSP outcomes according to follow-up and analysis subtype.

arian patients with achalasia [29–31], with some slight normal differences between populations, but without affecting the results of our study.

Biodegradable stent placement had a technical success of 100%, with a mean placement duration of 37.5 ± 12.1 minutes, which is similar to reports using BS in other gastrointestinal diseases (42.1 ± 14 minutes) [18, 19, 22]. After BSP, our most frequent AE was thoracic pain in 34.4% (controlled with NSAIDs), similar to other authors (10%–57%) [21, 22], Our migration rate was (18.7%) during the first month after BSP, which is similar to other reports (8%–20%) [18, 20, 21], and we confirmed that the use of hemoclips in order to avoid this AE could be feasible (100% of efficacy in our cohort, but between 82% and 95% in other reports) [17, 18, 20, 21].

Complete degradation was presented as expected in 72.8% at 3 months, which is similar to the reported mechanism of action of these stents (patency of 6–8 weeks) [17]; at this point, five presented PR, of whom three finally presented failure in the next evaluation at 6 months (underwent PD). We think that this time before BS is completely degraded is enough to exert a "continuous dilation" at the EGJ, allowing the clinical effect of these stents in achalasia.

After BSP, we found a direct relationship between clinical dysphagia and endoscopic evaluations at 3- and 6-month assessments. Higher dysphagia scores showed worst endoscopic features. We think that the 6-month evaluation is the best early TPE in clinical practice, because at this point all stents (including those from second placement) are completely degraded, and clinical effect is available. We observed that patients with scores 2 or 3 at this point have a 60% probability of performing tissular hyperplasia that will require endoscopy dilation (5 cases in our cohort). Fortunately, response in all cases has an endpoint of 15 mm in less than 5 sessions. This is similar to other reports that show between 30% and 100% tissular hyperplasia that requires endoscopic balloon dilation in 40% to 70% of cases [7, 8, 17, 20, 21].

Clinical success was assessed by TPE, ITT, and PP analysis, based on objective parameters. We confirmed encouraging percentages of 81.5% at early; 86.9%,76.9%, and 73.4% at mid-term; and 94.4%, 72%, and 64.2% at long-term evaluation. When success was evaluated at each follow-up, without considering failures or deaths, we had the best percentages (94.4% at 9 years). However, in the PP and ITT analysis the success decreased to 72% and 65.4%, respectively, which represents a more realistic clinical evaluation of all the cohort; therefore, we could conclude that BS has long-term clinical efficacy of 65% to 70%. These results seem to be less effective when compared to other authors. However, SEMS has variable results. Zhao et al [13] reported the surprising clinical success of 100% at 5 years and 83.3% at 10 years. This compared to Zeng et al [34], which used FCSEMS and found cumulative clinical remission rates at 6, 12, 18, 24, 30, and 36 months after stent removal of 90.9%, 81.8%, 76.4%, 69.1%, 65.5%, and 49.1%, respectively. This could be explained by the lack of complete evaluation methods used. In our case, we tried to include clinical, endoscopic, manometric, radiologic and 24-hour pH test, coupled with a very strict follow-up, giving us reliable data. POEM is a safe and effective technique with clinical success of 85% to 100% at early and mid-term evaluations, but is risky in octogenarians. Abe et al [30] retrospectively compared the feasibility of POEM in a group of octogenarian vs non-octogenarian patients. Octogenarians had a 100% clinical success at 1 year, but higher incidence of perioperative AE (28.6% vs 10.2%; P< 0.0001), of whom 25% were major (these included: prolonged

ICU stay, bleeding/hepatoma requiring blood transfusion, surgery, leak, cardiac arrhythmia and respiratory issues). In our cohort, we had two minor AE: Chest pain in 34 % and intraprocedural bleeding in 12.5 %. Sanaka et al [29], compared geriatric (>65 years) vs non-geriatrics (<65 years) retrospectively, and they found no differences in success at 2 months (94.9 % vs 94.7 %; P = NS), and similar AE (10.1 % vs 3.8 %; P = 0.42), confirming good safety and efficacy. Chen et al [31], in an international multicenter retrospective study, evaluated 76 octogenarian patients and found at mid-term (265 days), a 93.4 % of clinical success, but up to 14.5 % AE, of whom 7.1 % were severe, confirming, that in spite of POEM being safe and effective in younger patients, serious AE could be presented in octogenarian population, being higher in LHM (AE = 3 %–19 %) for these patients [8–10].

Low-grade esophagitis was defined as grade A or B according to LA classification system [35] and it was presented in 4.7 % to 11.2 % of our patients during follow-up. We didn't have more severe cases of reflux disease (grade C, D or Barrett's esophagus). Being these numbers being similar to those found in LHM or even POEM [5, 7, 8], and all were controlled with PPI medication. DeMeester score was <14.8 during follow-up, and we didn't observe any reflux disease complication at long-term, as observed in long-term reports of achalasia when LHM was performed [5, 32].

Our study has some limitations: first, we didn't have a comparison group (with POEM, PD, BTI or MLH), which could have supported our results. Second, we can't extrapolate these results to younger patients, because they were not the objective of our study; however, exploring the effects of BS in those patients as a comparison group could have given us a broader picture of the early, mid and long-term effects of these stents in achalasia at different ages. Third, these results only apply with a 25-mm stent; we didn't explore other diameters, limiting its widespread use; and fourth, this was a single-center study, while a multicenter study could support our data. However, our strengths include: early, mid and long-term evaluations; prospective nature, objective and reproducible evaluations; strict protocol at follow-up, sample size considering the group of patients. Finally, this is the first study that evaluates the role of these stents as an option for achalasia treatment in this population.

Conclusions

In conclusion, BSP represents a feasible alternative of treatment for octogenarian patients with esophageal achalasia, with acceptable early, mid and long-term results, especially for those who are high-risk for other treatment options. However, comparative and multicenter studies are needed to clarify and confirm the role of these stents in octogenarian patients with achalasia.

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Competing interests

The authors declare that they have no conflict of interest.

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