Endoscopic ultrasound-guided gastroenterostomy versus duodenal stenting for malignant gastric outlet obstruction: an international, multicenter, propensity score-matched comparison

Authors
Roy L. J. van Wanrooij1, Giuseppe Vanella2, Michiel Bronswijk3,4, Peter de Gooyer5, Wim Laleman3, Hannah van Malenstein3, Francesco Vito Mandarino2, Giuseppe Dell’Anna2, Paul Fockens1,5, Paolo G. Arcidiacono2, Schalk W. van der Merwe3, Rogier P. Voermans5

Institutions
1 Department of Gastroenterology and Hepatology, Amsterdam UMC, Vrije Universiteit, Amsterdam Gastroenterology Endocrinology and Metabolism, Amsterdam, The Netherlands
2 Pancreatobiliary Endoscopy and Endosonography Division, Pancreas Translational and Clinical Research Centre, IRCCS San Raffaele Scientific Institute and University, Milan, Italy
3 Department of Gastroenterology and Hepatology, University Hospitals Gasthuisberg, University of Leuven, Leuven, Belgium
4 Department of Gastroenterology and Hepatology, Imelda General Hospital, Bonheiden, Belgium
5 Department of Gastroenterology and Hepatology, Amsterdam UMC, University of Amsterdam, Amsterdam Gastroenterology Endocrinology and Metabolism, Amsterdam, The Netherlands

ABSTRACT

Background Endoscopic duodenal stenting is the current standard treatment for malignant gastric outlet obstruction (GOO) in patients with limited life expectancy. However, duodenal stenting is prone to stent dysfunction. Endoscopic ultrasound-guided gastroenterostomy (EUS-GE) is a novel technique with potentially superior stent patency. We compared clinical success, safety, and stent dysfunction of EUS-GE and duodenal stenting in patients with malignant GOO using propensity score matching.

Methods This international, multicenter, retrospective study analyzed consecutive patients undergoing EUS-GE or duodenal stenting for GOO between 2015 and 2021 in three European centers. Primary outcomes were clinical success (GOO scoring system [GOOSS] ≥ 2) and stent dysfunction (GOOSS ≤ 1 after initial clinical success). A propensity score matching (1:1) analysis was performed using age, sex, underlying disease, disease stage, ascites, and peritoneal carcinomatosis as variables.

Results 214 patients underwent EUS-GE (n = 107) or duodenal stenting (n= 107). After propensity score matching, 176 patients were matched and compared. Technical success rates for EUS-GE and duodenal stenting were 94% (95%CI 89%–99%) vs. 98% (95%CI 95%–100%), respectively (P=0.44). Clinical success rates were 91% (95% CI 85%–97%) vs. 75% (95%CI 66%–84%; P=0.008). Stent dysfunction occurred in 1% (95%CI 0%–4%) vs. 26% (95%CI 15%–37%) of patients (P<0.001). Adverse event rate was 10% (95%CI 4%–17%) vs. 21% (95% CI 12%–29%; P=0.09).

Conclusion EUS-GE had higher clinical success and lower stent dysfunction, with similar safety, compared with duodenal stenting, suggesting that EUS-GE may be preferred over duodenal stenting in patients with malignant GOO.

Original article
Table 1 s, Fig.1 s
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Introduction
Gastric outlet obstruction (GOO) is a common complication of malignant tumors arising from the pancreas and gastric antrum. Less commonly, GOO may also arise due to malignant infiltration or external compression from tumors arising from bile ducts, gallbladder, duodenum, ampulla, retroperitoneum, or metastases. This may lead to recurrent vomiting, dehydration, malnourishment, and inability to tolerate chemotherapy, which severely impair quality of life [1]. Only a minority of patients with malignant GOO present with a resectable tumor; most often GOO is indicative of locally advanced disease and requires palliative treatment [2]. Traditionally, treatment options for GOO consisted of surgical (open/laparoscopic) gastroenterostomy or endoscopic duodenal stenting. Three underpowered randomized controlled trials comparing surgical management with endoscopic duodenal stenting yielded inconsistent results [3–5]. This has led various societies including the American Gastroenterology Association and American Society for Gastrointestinal Endoscopy (ASGE) to advise laparoscopic gastroenterostomy in clinically fit patients with an expected survival of more than 2–6 months because of long-term patency of the surgical anastomosis, whereas duodenal stenting is reserved for patients with an expected survival of less than 2–6 months [6, 7]. Duodenal stenting leads to rapid relief of symptoms and shows low morbidity compared with surgical gastroenterostomy but has been associated with a high rate of stent dysfunction due to tumor ingrowth, which requires reintervention [8]. However, in daily clinical practice, survival can be notoriously difficult to predict and surgeons are often reluctant to subject patients with malignant GOO to surgical interventions. This, together with patient preference, likely contributes to duodenal stenting still being used in the majority of patients with malignant GOO.

Endoscopic ultrasound-guided gastroenterostomy (EUS-GE) is a relatively new, minimally invasive technique that provides rapid relief of symptoms associated with low morbidity and long-term patency of the anastomosis. Recently, multiple retrospective series comparing EUS-GE with surgical gastroenterostomy have indeed shown similarly high technical and clinical success rates, with significantly faster relief of symptoms, shorter hospital stay, and lower morbidity with EUS-GE [9–12]. Data comparing EUS-GE and duodenal stenting are limited, with most studies not controlling for confounders, making interpretation of outcomes data difficult [13, 14]. More data on this matter are needed to define the most optimal treatment strategy in these frail patients. The aim of the current study was to compare efficacy, safety, and stent dysfunction rate of EUS-GE vs. duodenal stenting in patients with malignant GOO with propensity score matching to correct for confounders.

Methods
Patients and study design
A multicenter retrospective analysis was performed of all consecutive procedures involving either EUS-GE or duodenal stenting for GOO between January 2015 and May 2021 at the Amsterdam University Medical Center (Amsterdam UMC) in the Netherlands, IRCSS San Raffaele Scientific Institute in Italy, and University Hospitals Leuven in Belgium. Patients were identified by searching local endoscopic electronic databases. The EUS-GE group included patients from our previous multicenter analysis in which EUS-GE was compared with laparoscopic gastroenterostomy [9]. The study protocol was approved by the Institutional Review Board of Amsterdam UMC as well as in each participating center.

Inclusion criteria were: 1) symptomatic malignant GOO; 2) endoscopic and/or radiological confirmation of an obstruction at the gastric antrum or duodenum; and 3) primary intended intervention of either EUS-GE or duodenal stenting. Exclusion criteria were: 1) previous duodenal stenting, EUS-GE, or surgical gastroenterostomy; and 2) follow-up data for less than 30 days post-procedure.

Data collection
Data collection was conducted by manually extracting data from the electronic patient charts. Data storage, statistical analysis, and the matching procedure were performed using IBM SPSS statistics for windows version 26.0 (IBM, Armonk, NY, USA).

Study definitions and end points
The two primary end points were clinical success and stent dysfunction. Both primary end points were based on the gastric outlet obstruction scoring system (GOOSS). The GOOSS is an ordinal scoring system ranging from 0 to 3, which is based on the highest intake tolerability without vomiting (0 = no intake; 1 = liquid only; 2 = soft solids; 3 = full diet) [15].

Clinical success was defined as a GOOSS score of at least 2 after the initial intervention (EUS-GE or duodenal stenting). Stent dysfunction was defined as recurrence of obstructive symptoms (GOOSS ≤ 1) after initial clinical success.

Secondary end points included technical success, length of hospitalization after initial EUS-GE or duodenal stenting, adverse events (AEs), and overall survival. Technical success was defined as successful placement of a duodenal stent crossing the obstruction site or successful creation of a gastroenteric anastomosis by means of a luminal-apposing metal stent (LAMS). Intervention-related AEs such as perforation, stent migration, clinically relevant bleeding requiring intervention and/or blood transfusion, cholangitis, sepsis, pneumonia, post-procedural fever, and post-procedural pain that occurred within 30 days following the procedure were scored through the ASGE lexicon as mild, moderate, severe, or fatal [16].

Study procedures
EUS-GE
All procedures were performed under deep propofol sedation or general anesthesia. Prophylactic broad-spectrum antibiotic therapy was routinely administered. EUS-GE procedures were performed using the wireless EUS-gastroenterostomy simplified technique (WEST), as described previously [17]. In short, a 7-Fr nasoiliary drain or enteral feeding tube was advanced be-
yond the stenosis into the proximal jejunum (▶ Fig. 1a). The nasobiliary drain inside the jejunal loop was identified by EUS. Infusion of saline solution (with or without blue dye) through the drain or feeding tube resulted in dilation of the jejunal bowel loop (▶ Fig. 1b). The electrocautery-enhanced lumen-apposing metal stent (LAMS) was positioned in line with the small bowel loop. Using pure-cutting current the stent was brought into the jejunal lumen. EUS image: the distal flange was released under EUS guidance. The device was then retracted onto the gastric wall. The proximal flange was deployed inside the working channel of the endoscope, and slowly pushed out of the endoscope while at the same time gently pulling back the endoscope from the gastric wall. f Endoscopic image: saline infused through the nasobiliary catheter was, in this case, dyed with methylene blue and appeared in the gastric lumen after successful LAMS placement.

Endoscopic duodenal stenting

Endoscopic duodenal stenting was performed under propofol sedation or general anesthesia. A therapeutic gastroscopy or pediatric colonoscopy was advanced to the site of gastric or duodenal obstruction (▶ Fig. 2a). A double-lumen catheter and guidewire were then advanced through the stricture (▶ Fig. 2b). Contrast injection under fluoroscopy was used to determine the length of the stricture, relation to the papilla, and preferable size of the stent (▶ Fig. 2c). An uncovered self-expandable metal stent (SEMS) was then advanced over the wire and deployed under endoscopic and fluoroscopic guidance (▶ Fig. 2d). Wallflex duodenal stents (Boston Scientific) and Cook Evolution duodenal stents (Cook Medical, Bloomington, Indiana, USA) 6, 9, and 12 cm in length were used. The diameter of the stent was 22 mm in all cases. Adequate positioning of the stent was confirmed by means of fluoroscopy and endoscopy (▶ Fig. 2e,f).

Statistical analysis.

Categorical and binary variables were reported as frequencies (%) and were compared through either Fisher’s exact test or Pearson’s chi-squared test. Continuous variables were reported as means or median with SD or interquartile range (IQR) and
were analyzed through unpaired t tests or Mann–Whitney U test. The reported analyses were performed in the intention-to-treat population (intended procedure EUS-GE or duodenal stenting regardless of technical success), unless explicitly mentioned as per protocol (only patients with technical success). Outcomes were reported as odds ratios (OR) with a 95%CI. P values were considered statistically significant if <0.05.

To minimize selection bias of the observed data, a propensity score matching analysis was conducted. Propensity score was based on age, sex, GOO etiology, and disease stage, presence of ascites, and peritoneal carcinomatosis. Variables were selected based on demographic discrepancies of the main cohort and expected factors of influence based on recent studies [13, 18–20]. A stringent maximum propensity score difference of 0.05 was used for matching. For the time to event data analysis, the Kaplan–Meier curve and log-rank test were used.

Results
Main cohort
A total of 246 eligible patients were identified. After excluding 32 patients in whom follow-up was less than 30 days, the EUS-GE group consisted of 107 patients (50%) and the duodenal stenting group included 107 patients (50%) (see Fig.1s and Table1s in the online-only Supplementary Material).

Baseline characteristics are shown in ▶Table 1. Pancreatic cancer-induced GOO was more frequent in the duodenal stenting group than in the EUS-GE group (65.4 % vs. 46.7%; P = 0.009). With regard to disease manifestations, peritoneal carcinomatosis was present more frequently in the EUS-GE group (41.1 % vs. 25.2%; P = 0.020), while the presence of ascites did not significantly differ between the two groups (29.0 % vs. 22.4%).

Technical success of EUS-GE and duodenal stenting was 94 % (95%CI 90%–99%) vs. 98% (95%CI 96%–100 %), respectively. Clinical success was 90% (95%CI 84%–96%) with EUS-GE and 77% (95%CI 68%–85%) with duodenal stenting. Stent dysfunction occurred less frequently after EUS-GE (3%; 95%CI 0–6%) than after duodenal stenting (30%; 95%CI 14%–46%).

Propensity score matching analysis
Propensity score matching allocated 88 patients in each group (1:1), resulting in a total of 176 patients. No significant differences in baseline characteristics were found between the two groups (▶Table1). The overall characteristics of the propensity score-matched cohort included a mean age of 66 years (SD

![Fig. 2 Stepwise approach to endoscopic duodenal stenting. a Endoscopic image: malignant duodenal stenosis. b Endoscopic image: traversing the stricture with a double-lumen catheter and a guidewire. c Fluoroscopic image: contrast injection through the catheter to determine the length of the stricture, relation to the papilla, and preferable size of the stent. d Fluoroscopic image: advancing the self-expandable metal stent over the guidewire across the stricture. e Fluoroscopic image: the stent was been deployed with the waist located in the middle of the stent confirming adequate position. f Endoscopic image: proximal side of the uncovered stent deployed proximally to the stricture.](image-url)
11.5), the majority being female (52.3%), and the underlying disease being pancreatic cancer (56.8%), while peritoneal metastasis and ascites were present in up to a third of patients.

Technical success was achieved in 83/88 (94%; 95% CI 89%–99%) EUS-GE patients and in 86/88 (98%; 95% CI 95%–100%) duodenal stenting patients, with no significant difference between the two groups ($P=0.44$) (▶Table 2). Clinical success rate was higher after EUS-GE (80/88; 91%; 95% CI 85%–97%) than after duodenal stenting (66/88; 75%; 95% CI 66%–84%; $P=0.008$). Per-protocol clinical success was 96% (95% CI 92%–100%) after EUS-GE and 77% (95% CI 68%–86%) after duodenal stenting, which was a significant difference ($P<0.001$). Median time to clinical success was shorter after EUS-GE (1 day [IQR 1–2]) than after duodenal stenting (2 days [IQR 2–3]; $P<0.001$). Median length of hospitalization was similar between the two groups, at 4 days (IQR 2–10.8) after EUS-GE vs. 4 days (IQR 1–9.5) after duodenal stenting.

Median follow-up was 85 days (IQR 43–157) in the EUS-GE group and 57 days (IQR 27–169.5) after duodenal stenting. Kaplan–Meier analysis showed higher probability of dysfunction-free survival for EUS-GE (hazard ratio 27.4, 95% CI 4.2–282; $P<0.001$) with a 6-month probability of remaining recurrence free of 100% compared with 65.0% with duodenal stenting (▶Fig. 3). Both recurrent GOO rates and stent dysfunction-free survival rate by Kaplan–Meier analyses revealed a significantly higher stent dysfunction rate after duodenal stenting compared with EUS-GE.

AEs occurred in 9/88 patients (10.2%; 95% CI 3.8%–16.7%) after EUS-GE and in 18/88 patients (20.5%; 95% CI 11.9%–29.0%) after duodenal stenting, and were similar between the two groups ($P=0.09$). The AEs in the EUS-GE group consisted of infectious complications (aspiration pneumonia [$n=1$; 1.1%] or cholangitis [$n=3$; 3.4%]), bleeding ($n=1$; 1.1%), and post-procedural pain ($n=4$; 4.5%); atrial fibrillation ($n=1$; 1.1%), and stent migration ($n=1$; 1.1%). Aspiration pneumonia occurred in four patients who were under general anesthesia with tracheal intubation, and in

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**Table 1 Main and matched cohort: baseline characteristics.**

<table>
<thead>
<tr>
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<th>Main cohort</th>
<th>Matched cohort</th>
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<tbody>
<tr>
<td></td>
<td>EUS-GE (n=107)</td>
<td>Duodenal stenting (n=107)</td>
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<tr>
<td>Age, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Mean (SD)</td>
<td>66 (11.8)</td>
<td>67 (11.2)</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>54 (50.5)</td>
<td>58 (54.2)</td>
</tr>
<tr>
<td>Follow-up duration, median (IQR), days</td>
<td>90.5 (44–177)</td>
<td>50 (27–126)</td>
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<tr>
<td>Primary disease, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pancreatic cancer</td>
<td>50 (46.7)</td>
<td>70 (65.4)</td>
</tr>
<tr>
<td>• Biliary tract cancer</td>
<td>15 (14.0)</td>
<td>7 (6.5)</td>
</tr>
<tr>
<td>• Gastric cancer</td>
<td>12 (11.2)</td>
<td>8 (7.5)</td>
</tr>
<tr>
<td>• Duodenal cancer</td>
<td>10 (9.3)</td>
<td>10 (9.3)</td>
</tr>
<tr>
<td>• Other</td>
<td>20 (18.7)</td>
<td>12 (11.2)</td>
</tr>
<tr>
<td>Disease stage, n (%)</td>
<td>n=104</td>
<td>n=106</td>
</tr>
<tr>
<td>• Local invasion</td>
<td>34 (32.7)</td>
<td>45 (42.5)</td>
</tr>
<tr>
<td>• Liver metastases</td>
<td>20 (19.2)</td>
<td>17 (16.0)</td>
</tr>
<tr>
<td>• Peritoneal metastases</td>
<td>14 (13.5)</td>
<td>8 (7.5)</td>
</tr>
<tr>
<td>• Diffuse metastatic</td>
<td>36 (34.6)</td>
<td>36 (34.0)</td>
</tr>
<tr>
<td>Disease manifestations, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Ascites</td>
<td>31 (29.0)</td>
<td>24 (22.4)</td>
</tr>
<tr>
<td>• Peritoneal carcinomatosis</td>
<td>44 (41.1)</td>
<td>27 (25.2)</td>
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EUS-GE, endoscopic ultrasound-guided gastroenterostomy; IQR, interquartile range.
one patient under deep sedation. The severity of AEs was not significantly different between EUS-GE and duodenal stenting (Table 2). Median survival after EUS-GE was 85 days (43–157) vs. 57 days (18.5–130.5) after duodenal stenting.

**Discussion**

This study reports the first propensity score-matched comparison between EUS-GE and endoscopic duodenal stenting in malignant GOO, and contains, to the best of our knowledge, the largest comparative cohort published to date. Our data indicate that, while technical success was similar between the two groups, EUS-GE showed higher clinical success, superior long-term stent patency, and similar AE rates compared with duodenal stenting.

To date, two smaller unmatched retrospective studies compared EUS-GE with duodenal stenting in malignant GOO [13, 14]. A recent meta-analysis included an additional three abstracts resulting in a total of 659 patients published in the literature [21]. None of these studies used propensity score matching in an attempt to correct for confounders such as the type of underlying malignancy, peritoneal carcinomatosis, or the presence of ascites.
In the current study, clinical success rates, using an intention-to-treat analysis, were significantly higher after EUS-GE than after duodenal stenting. Similar clinical success rates of EUS-GE were recently reported in a retrospective analysis of 19 centers including 267 patients (Table 3) [22]. Clinical success rates of duodenal stenting were slightly lower compared with previous large studies on this topic, which may be related to the relatively high incidence of peritoneal carcinomatosis in our study (Table 3) [23–25]. When comparing only technically successful procedures (per-protocol analysis) in our study, the benefit of EUS-GE with regard to clinical success was even more striking. EUS-GE has several features that may explain this superior clinical benefit. First, the short length of the LAMS (1.5 cm) is likely to facilitate food passage into the small intestine better than the longer duodenal stent (6–12 cm). Second, the LAMS in EUS-GE is placed some distance away from the tumor and expands to its full diameter, whereas compression due to tumor ingrowth, and may lead to more severe AEs such as peritonitis and perforation, even requiring salvage surgery. Yet our study showed that, in the hands of endoscopists who have received adequate training in expert high-volume settings, EUS-GE is a safe procedure [30]. Indeed, in our series, AEs associated with

### Table 3 Overview of largest series on endoscopic ultrasound-guided gastroenterostomy and endoscopic enteral stenting.*

<table>
<thead>
<tr>
<th>First author, year [ref.]</th>
<th>Design, geographic area</th>
<th>Patients, study dates</th>
<th>Treatment and technical details</th>
<th>Efficacy, %</th>
<th>Safety, AEs, %</th>
<th>Long-term outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current study</td>
<td>Retrospective, multicenter Europe (3)</td>
<td>n = 107 2015–2021</td>
<td>EUS-GE Freehand EC-LAMS</td>
<td>Tech. success: 94.4  Clin. success: 89.7</td>
<td>12.1  Follow-up: 91 days (IQR 44–177) Recurrence: 3.1 %</td>
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<td>Tringali, 2014 [25]</td>
<td>Prospective, multicenter Africa (1), Australia (1), Europe (3), North America (1), South America (1)</td>
<td>n = 106 2009–2011</td>
<td>UCSEMS</td>
<td>Tech. success: 99.1  Clin. success: 84.5</td>
<td>25.0  Follow-up: 47 days (range 0–195) Recurrence: 17.6 %</td>
<td></td>
</tr>
<tr>
<td>Current study</td>
<td>Retrospective, multicenter Europe (3)</td>
<td>n = 107 2015–2021</td>
<td>UCSEMS</td>
<td>Tech. success: 98.1  Clin. success: 76.6</td>
<td>17.8  Follow-up: 50 days (IQR 27–126) Recurrence: 29.3 %</td>
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</table>

* Studies describing treatment of malignant gastric outlet obstruction with either EUS-GE or endoscopic enteral stenting comprising > 100 cases were selected. Prospective studies were preferred over retrospective studies when available. AEs are reported using the definition of the current study.
EUS-GE were not more frequent nor more severe than after duodenal stenting.

The choice of therapy for frail patients with malignant GOO remains a matter of debate and will only finally be resolved once the results from adequately powered randomized controlled trials become available. Currently, based on the outcomes of previously underpowered randomized studies comparing duodenal stenting with surgical gastroenterostomy, duodenal stenting is advocated for use in patients with a prognosis of less than 2–6 months or a poor performance status (World Health Organization [WHO] performance score ≥ 3), whereas surgical gastroenterostomy has been advised in fitter patients with a better prognosis [6, 7]. The findings of our study suggest that EUS-GE may offer a valuable alternative to the currently employed options: EUS-GE is similar to duodenal stenting as a minimally invasive option that provides rapid symptom relief but has low morbidity and early hospital discharge, yet provides an anastomosis that achieves surgical-technical success and AEs rates. The higher clinical success, shorter time to clinical success, and lower GOO recurrence suggest that EUS-GE should be preferred over duodenal stenting when adequate expertise is available.

Our study has certain limitations. The retrospective design introduces confounders. However, by using propensity score matching analysis, we have tried to overcome these limitations, allowing a fair comparison between the two techniques. Although data regarding most important confounders such as etiology, presence of ascites, and (peritoneal) metastases could be reliably collected retrospectively, others, such as WHO performance scale, could not. However, overall post-procedural survival was not different between the two groups after matching, reducing the concern of different baseline frailty.

Finally, despite the promising outcomes of the EUS-GE group, generalizability of these results outside tertiary academic centers with specific expertise in interventional EUS remains difficult. Moreover, to date, the procedure includes an off-label use of the LAMS. In conclusion, this study showed that in patients with malignant GOO, EUS-GE and duodenal stenting displayed similar technical success and AEs rates. The higher clinical success, shorter time to clinical success, and lower GOO recurrence suggest that EUS-GE should be preferred over duodenal stenting when adequate expertise is available.

References

Conflict of interest
RLJ van Wanrooij is a consultant for Boston Scientific. M Bronswijk is a consultant for Taewoong – Priom Medical. W Laleman is Co-Chair of the Boston Scientific Therapeutic Biliopancreatic Endoscopy group, and is a consultant for Boston Scientific and Cook. H van Malenstein is a consultant for Boston Scientific. P Fockens is a consultant for Olympus and Cook Medical. SW van der Merwe is Co-Chair of the Boston Scientific Therapeutic Biliopancreatic Endoscopy group and Chair of the Portal Hypertension group for Cook; he is also a consultant for Cook, Boston Scientific, and Pentax. RP Voermans is a consultant for Boston Scientific and has received research grants from Boston Scientific and Taewoong – Priom Medical. The remaining authors declare that they have no conflict of interest.


