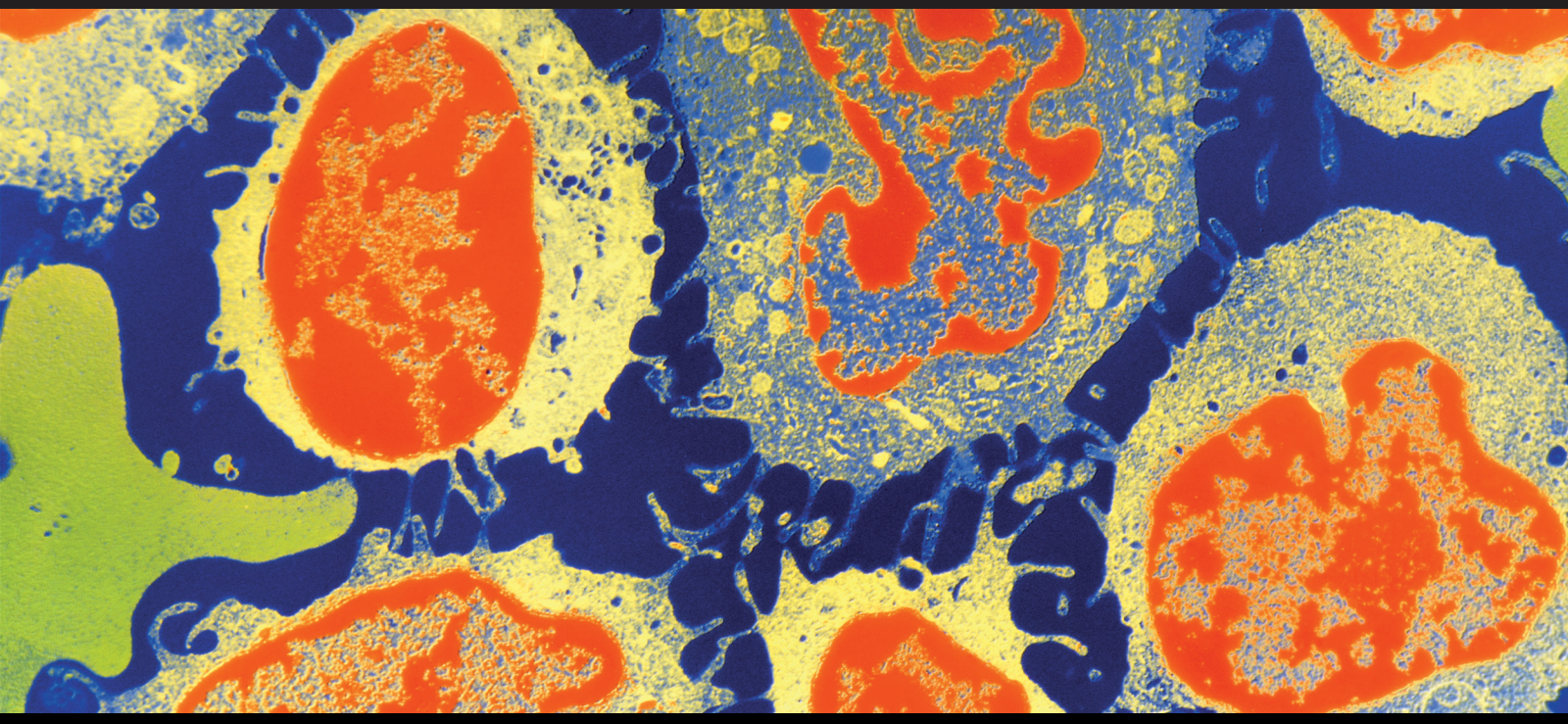
Journal of Oncology

Endoscopic Oncology

Guest Editors: Everson L. A. Artifon, Takao Itoi, Jose G. de la Mora-Levy, and Juan Vila



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Editorial Board

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Editorial
Endoscopic Oncology

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Endoscopy has evolved from a purely diagnostic tool to a highly selective minimally invasive therapy to treat both benign and malignant conditions. Thus, endoscopic treatment has become the mainstay of therapy for many oncological diseases in the gastrointestinal tract. The aim of this endoscopic treatment can be merely palliative as it is shown in the study by N. S. Ding et al. and in the study by Figueroa-Barojas et al. Ding et al. describe the outcomes of self-expandable metal stents (SEMS) deployment for managing 94 patients with malignant gastroduodenal outlet obstruction. The authors achieved an improvement in gastric outlet obstruction score in 90% of patients with a low rate of complications (5%) and a short hospital stay of only 3 days. On the other hand, Figueroa-Barojas et al. applied radiofrequency ablation to 25 unresectable malignant biliary strictures in 20 patients achieving a significant increase in the mean bile duct diameter of 3.5 mm at the expense of secondary postprocedural pain in 5 patients, one of them with development of pancreatitis.

But the endoscopic treatment for oncological diseases can be also applied with a curative aim. In the study by K. Ohata et al., the authors examine the efficacy and safety of endoscopic submucosal dissection (ESD) for treatment of 608 cases of colorectal neoplasms including adenomatous polyps and lesions with malignant superficial invasion. The authors divided patients into two groups: patients with lesions between 2 and 4.9 cm in size and patients with lesions bigger than 5 cm, showing an equal efficacy in resection of both groups (99.2% and 99% resp., $P = 0.8$), although complications were significantly more common with ESD for larger lesions (4.1% versus 9.9%, $P = 0.03$).

Endoscopy has also improved its diagnostic role in gastrointestinal diseases by means of supporting techniques such as chromoendoscopy with colorant staining or newly developed electronical advances such as narrowband imaging (NBI). In the study by E. Ide et al., the diagnostic yield of chromoendoscopy with Lugol's staining is compared with the diagnostic yield of NBI to detect high-grade dysplasia and intramucosal esophageal squamous cell carcinoma in 43 patients with achalasia. The authors found that both methods offer a similar sensitivity and negative predictive value.

Finally, in this special issue, a study by E. Balik et al. describing predictive parameters for failure in ERCP is included. In this study, previous hepatic biliary tract surgery, malignant infiltration of the ampulla, obstruction of gastroduodenal tract, and ulcerative duodenal disease significantly increased the failure rate.

Everson L. A. Artifon
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Clinical Study

Gastroduodenal Outlet Obstruction and Palliative Self-Expandable Metal Stenting: A Dual-Centre Experience

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Background. Self-expandable metal stents (SEMs) are increasingly being utilised instead of invasive surgery for the palliation of patients with malignant gastroduodenal outlet obstruction. *Aim*. To review two tertiary centres' experience with placement of SEMs and clinical outcomes. *Methods*. Retrospective analysis of prospectively collected data over 12 years. *Results*. Ninety-four patients (mean age, 68; range 28–93 years) underwent enteral stenting during this period. The primary tumour was gastric adenocarcinoma in 27 (29%) patients, pancreatic adenocarcinoma in 45 (48%), primary duodenal adenocarcinoma in 8 (9%), and cholangiocarcinoma and other metastatic cancers in 14 (16%). A stent was successfully deployed in 95% of cases. There was an improvement in gastric outlet obstruction score (GOOS) in 84 (90%) of patients with the ability to tolerate an enteral diet. Median survival was 4.25 months (range 0–49) without any significant differences between types of primary malignancy. Mean hospital stay was 3 days (range 1–20). Reintervention rate for stent related complications was 5%. *Conclusion*. The successful deployment of enteral stents achieves excellent palliation often resulting in the prompt reintroduction of enteral diet and early hospital discharge with minimal complications and reintervention.

1. Introduction

Malignant gastroduodenal obstruction is a late and severe complication that develops in up to 20% of patients with advanced carcinoma of the pancreas, stomach, or the duodenum [1–3]. Patients may present with nausea, vomiting, and weight loss with resultant impairment in quality of life [4]. Palliative interventional procedures, either surgical or endoscopic, offer a rapid nonpharmacological modality to improve symptoms as measured by the gastric outlet obstruction score (GOOS) [5].

Although surgery for established gastric outlet obstruction is technically successful in up to 90% of patients [6], it is often associated with a prolonged hospital stay and sometimes with poor function of gastroenterostomy [7].

Curative surgical resection is often not possible and palliative surgical bypass operations have been associated with high mortality and morbidity rates of up to 30% and 50%, respectively [8–10]. Even with the improvements in surgical care and laparoscopic techniques, the more recent reported rates of mortality and morbidity are 10% and 30%, respectively [11–13].

Self-expandable metal stents (SEMs) are devices that are used in the alimentary tract to help alleviate symptoms caused by oesophageal, gastroduodenal, biliary, and colonic malignancies [14, 15]. Endoscopic stent deployment for gastroduodenal obstruction, often performed under sedation, has been shown to be a safe alternative to surgical bypass. Up to 92% of patients can consume an enteral diet and up to 73% can tolerate solid or semisolid food following stent deployment [16].

Endoscopic therapy has the advantages of being a well-tolerated day stay or short stay procedure associated with a low complication rate and rapid symptom relief. It is effective in the majority of cases and often no further reintervention is necessary.

In this large dual-centre study, we report on our technical success and the clinical outcomes of patients with gastroduodenal outlet obstruction treated with SEMs.

2. Methods

A retrospective, nonrandomised study was performed using prospectively collected data in two tertiary care hospitals in Australia over a 12-year period. Patients over 18 years with symptomatic gastroduodenal obstruction who were not surgical candidates were included in the study. Patients with multiple lesions, intestinal ischaemia, and contraindication to gastrointestinal endoscopy were excluded.

All patients had been considered unsuitable for surgical intervention prior to referral and were unable to tolerate enteral nutrition at the time of referral. Without intervention, these patients would have required a nasogastric tube or venting gastrostomy to relieve obstruction. The diagnosis of obstruction was confirmed by endoscopy or barium studies prior to intervention. Patients with biochemical evidence of contemporaneous biliary obstruction underwent endoscopic (or, if not feasible, radiological) placement of a metal biliary stent prior to gastroduodenal stent insertion. All patients gave informed consent for the intervention.

We defined technical success as successful endoscopic and fluoroscopic placement of stent. Clinical success was defined as time to resumption and/or improvement of oral intake (defined by gastric outlet obstruction scoring system (GOOSS) score, with 0 = no oral intake, 1 = liquids only, 2 = soft foods, and 3 = solid food/full diet) and duration of patient survival. This information was collected after reviewing patient's clinical history.

Patients were discharged when able to tolerate at least a liquid/softened diet. Follow-up data were obtained by reviewing the medical records and by contacting the referring physician or the patient's general practitioner. Information obtained included the occurrence of complications and the need for reintervention, the type of diet that was tolerated, and the duration of survival.

2.1. Technique of Stent Insertion. SEMs are packaged in a compressed form for delivery and consist of various alloy mesh cylinders. They are available in various lengths and diameters. Once deployed, they are designed to exert self-expansive forces until they reach their maximum fixed diameter (Figure 1). To prevent migration, most SEMs have a proximal and/or distal flare.

During the first 7 years of our study, 60 or 90 mm long, 20 or 22 mm long outer diameters through the scope Wallstents (Boston Scientific Corporation, MA, USA) were used. During the last 5 years, predominantly newer WallFlex stents (60, 90, or 120 mm long, 22 mm body) were used (Boston Scientific Corporation, MA, USA). All stents were uncovered.

Stent placement was conducted under sedation or general anaesthesia and the identification of the structure was required endoscopically. A 0.035-inch (0.9 mm) guidewire was subsequently used to traverse the stricture under fluoroscopic guidance. The stent was then positioned across the stricture and deployed (Figure 2). The length of the stent used was determined by the endoscopist at the time of the procedure based upon the length of the stricture and the position of the distal and proximal ends of the stent in the anatomical shape of the duodenum. Contrast was injected immediately before and after stent insertion to estimate the tumour length and to confirm that the guidewire was within the small bowel lumen.

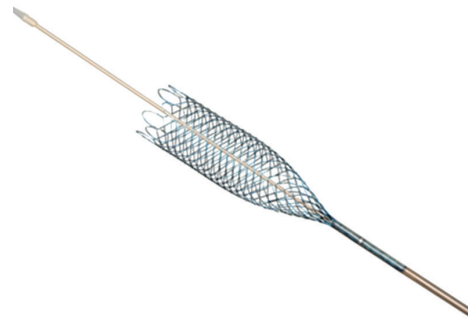


Figure 1: Self-expandable metal stent (courtesy of Boston Scientific Corporation).

Table 1: Patient characteristics.

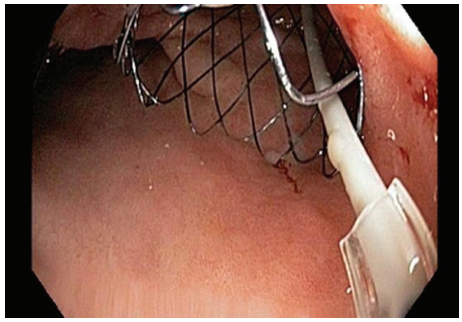
	Male	Female	Total
Number	43	51	94
Mean age (range) (years)	69 (28–92)	68 (40–93)	68 (28–93)
Tumour type			
Pancreatic			45 (48%)
Gastric			27 (29%)
Cholangio carcinoma/metastatic carcinoma			14 (16%)
Duodenal adenocarcinoma			8 (9%)

3. Results and Discussion

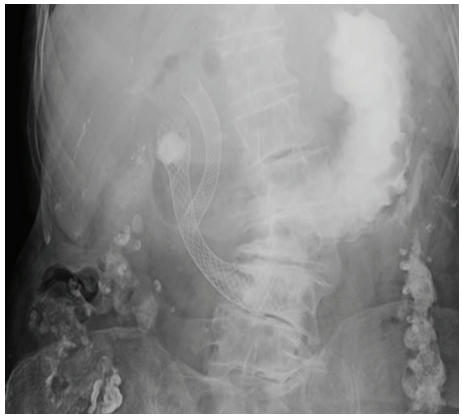
Between January 2000 and June 2012, 94 patients underwent enteral stent placement for malignant gastroduodenal obstruction. There were 51 females and 43 males with a mean age of 68 years (range 34–93 years) (Table 1). All patients had been deemed unsuitable for surgical gastroenterostomy prior to referral. 75% required a nasogastric tube at presentation for suction and symptomatic relief, indicating advanced disease.

The primary diagnosis was gastric adenocarcinoma in 27 (29%) patients, pancreatic adenocarcinoma in 45 (48%), primary duodenal adenocarcinoma in 8 (9%), and cholangiocarcinoma and other metastatic diseases in 14 (16%) (Figure 3). The stent position was duodenal in 44 patients (47%), gastric in 40 (43%), and jejunal in 10 patients (10%).

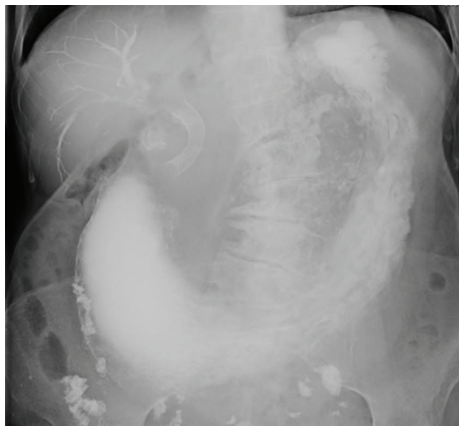
Enteral stent placement was technically successful in 89 (95%) patients and clinically successful in 84 (90%) with all of these showing improvement in gastric outlet obstruction score (GOOS) (Figure 4). There was a one-point improvement of GOOS in these patients. Fifty-six (60%) patients had



(a) Placement of WallFlex duodenal stent



(b) Preduodenal stent (note preexisting stent in the bile duct)



(c) 3 days after duodenal stent contrast in stomach showing prestenotic dilatation

Figure 2: Fluoroscopic and endoscopic view of deployed stent.

Wallstents inserted; thirty-three (35%) had WallFlex stents; and four (4%) patients had both.

The average length of stay was 3 hospital days (range 1–20). In 5 cases (5%), stent reinsertion was undertaken due to tumour ingrowth (Figure 5). This was seen in three patients with pancreatic adenocarcinoma and two with duodenal adenocarcinoma. These additional stents were all successfully deployed with an average time to restent of 3 months (range 1–5). No stent migration was noted.

Complications encountered were perforation in one patient and aspiration pneumonia in 5 patients. The perforation occurred in a 90-year-old patient with subsequent death; all the aspiration cases required prolonged hospital admission and administration of intravenous antibiotics.

Table 2: Survival outcomes after stent insertion.

Type of tumour	Median survival (months)	Average (months)	Range (months)
Pancreatic $N = 45$	2	4.21	0.5–49
Gastric $N = 27$	2	3.53	0.5–49
Cholangiocarcinoma $N = 12$	2	4.18	0.5–10
Duodenal adenocarcinoma $N = 8$	2	4.25	0.15–30
Breast (metastatic) $N = 2$	3	6.28	0.25–9

The average survival after stent placement was 4.25 months with a median survival of 2 months (0–49 months) (Figure 6). There were no significant differences in survival between patients with gastric or pancreatic cancers, with median survival of 2 months range (0.5–49) (Table 2).

Thirty-one patients (32.9%) survived less than one month after stent placement. The cause of death in this group was from metastatic disease and did not relate to stent failure from tumour ingrowth.

Following stent insertion, 84 (90%) of patients were able to recommence oral intake (either solids or liquids). In ten patients, no enteral feeding could be commenced. There was notably median survival of 2 weeks in this group.

4. Discussion

Patients with malignant gastroduodenal obstruction often have a limited life expectancy and will rapidly deteriorate from complications relating to obstructive symptoms and starvation [2]. Many of these patients are not surgical candidates due to poor nutrition and general health [3]. A surgical gastroenterostomy has a high success rate in bypassing their obstruction, but it is associated with a morbidity of up to 40% and occasional mortality [13, 17, 18] whilst extending the hospital stay by at least 2 weeks [6].

This study demonstrates that in patients with malignant gastroduodenal obstruction who are unsuitable for surgery, endoscopic stent placement can result in rapid resolution of symptoms (reduction of GOOS score to at least 1). Importantly, oral intake can re-commence in up to 90% of patients.

A review article by Jeurnink et al. [19] published in 2007 demonstrated results comparable with our study, with clinical success rates of 89%, early major complications of 7%, and a reintervention rate of 18% (mostly due to tumour ingrowth). A mean hospital stay of 7 days was quoted with mean survival of 105 days. In this meta-analysis, surgery was favoured for younger patients due to the higher rate of re-intervention in the endoscopic group. Based on our lower reintervention rates (5% versus 18%), this conclusion may not be so strongly indicated.

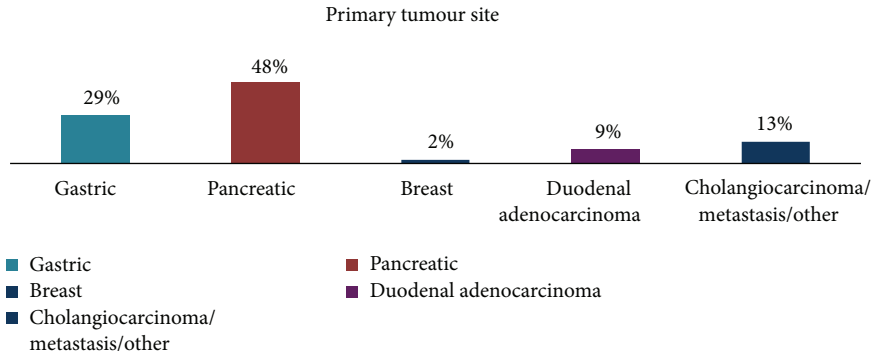


Figure 3: Graphical representation of underlying primary malignancy.

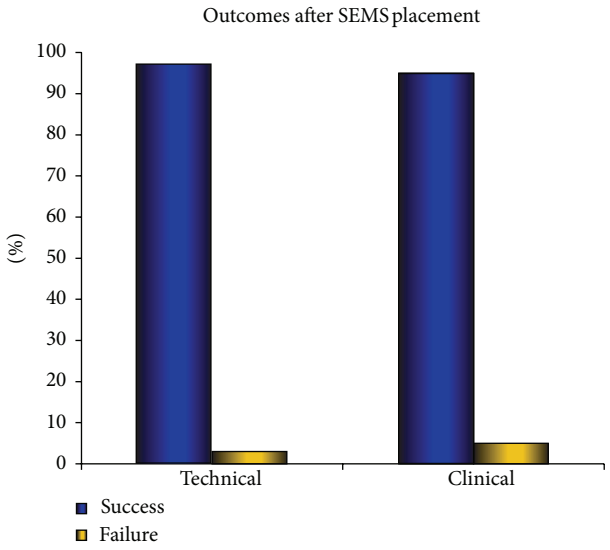


Figure 4: Graph showing clinical and technical success of stent placement.

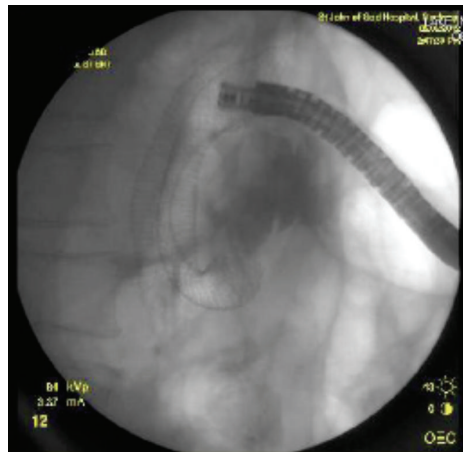


Figure 5: Tumour ingrowth treated with insertion of a second stent.

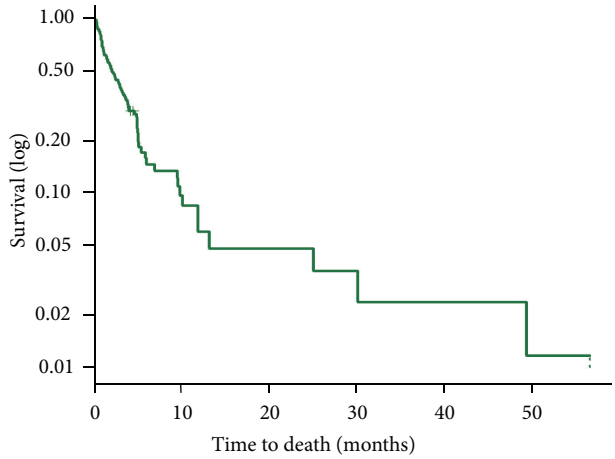


Figure 6: Kaplan-Meier plot of patient survival after stent insertion.

The major shortcomings of all previous endoscopic studies have been the small numbers of patients involved. Our study reports on the largest cohort of patients undergoing gastroduodenal stenting for malignant obstruction examined to date. Furthermore, our study differentiated between patients according to the underlying malignancy and the location of obstruction, information which is lacking in many other studies. We demonstrated no significant difference in survival between gastric and pancreatic cancers, with a median of 127 days seen in each group. This is in contrast to 2006 report which showed that survival was shorter in stented patients with pancreatic cancer [20].

We note that stenting is not seen as effective in helping overcome obstruction from gastric cancer as opposed to pancreatic cancer often due to the location of the stenosis within the body of the stomach that does not allow for good expansion and often stent migration [21]. These factors may have led to a referral bias with less gastric cancers referred to our service for stenting. It was also seen that stenting in patients with gastric cancers had a decreased life expectancy. One possible explanation may be that these patients present later for intervention and hence portend a worse outcome.

In our study, we utilised two different stents from the same company (Boston) as these were the only two stents that were approved for the treatment of malignant gastroduodenal

obstruction during the majority of our study period (up until 2011). All cases were undertaken by three experienced endoscopists (David Devonshire, Sina Alexander, and Michael P. Swan) with special interest and training in the insertion of gastroduodenal stents.

Restenting occurred in 5 patients as a result of tumour ingrowth. This takes place through the wall of the stent and results in worsening gastroduodenal obstruction. All these patients all had successful reinsertion of stents and subsequent 1 month of increased life. Two of the patients with stent reinsertion had concurrent chemotherapy. The studies collecting data looking at concurrent systemic chemotherapy with stenting have not shown that chemotherapy in addition to stenting increases life expectancy [18, 20].

A potential weakness of our study is that patients were not prospectively randomised to either SEMs or surgery. However, a randomised study would be difficult to conduct as most patients with advanced disease are not surgical candidates. In fact, none of the patients in our cohort were deemed to be surgical candidates and many were referred to us by various surgical units.

Examining the best quality published surgical data [13, 17], the clinical success rate for surgery in cases of malignant gastroduodenal obstruction is lower (72%) and is associated with a higher complication rate (33%). This is despite the fact that patients who are offered surgery are often younger [17], have early stage disease, and have less comorbidity. In nonrandomised trials, these same selection biases may also lead to a perception of improved survival for those undergoing surgery. Despite this, whilst our study supports the association of stent placement with more favorable short-term results, perhaps younger patients with increased likelihood of longer survival will be better served undergoing surgical bypass to avoid the potential need for reintervention. This may be especially relevant as chemotherapeutic modalities improve over time, improving patient survival rates.

5. Conclusion

This study reports on a large cohort of patients to demonstrate the clinical effectiveness of SEMs in achieving rapid symptomatic relief in patients with advanced gastroduodenal obstruction. When enteral stenting is undertaken by experienced endoscopists, SEMs have a high success rate with few complications, short hospitalisation and reduced need for reinterventions.

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Review Article

Endoscopic Submucosal Dissection for Large Colorectal Tumor in a Japanese General Hospital

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Background and Aims. Endoscopic submucosal dissection (ESD) is not widely used in large colorectal lesions because of technical difficulty and possible complications. We aimed to examine the efficacy and safety of ESD for large colorectal neoplasms. *Patients and Methods*. During the past 5 years, 608 cases of colorectal neoplasm (≧20 mm) were treated by ESD. They were divided into Group A (20–49 mm, 511 cases) and Group B (≧50 mm, 97 cases). *Results*. The average age, lesion size, and procedure time were 67.4 years, 30.0 mm, and 60.0 min in Group A, and they were 67.1 years, 64.2 mm, and 119.6 min in Group B. En bloc resection rates were 99.2% and 99.0% ($P = 0.80$), and complication rates were 4.1% and 9.9% ($P = 0.03$). Complications in Group A consisted of perforation (2.7%), bleeding (1.2%), and ischemic colitis (0.2%). Those in Group B were perforation (8.2%) and bleeding (1.0%). Two cases in Group A and none in Group B required emergency surgery for perforation. *Conclusions*. There was no difference in efficacy between Groups A and B. Complications were more frequent in Group B, but all perforations in Group B were successfully managed conservatively. ESD can be effective and safe for large colorectal tumors.

1. Introduction

More than 20 years have passed since the introduction of endoscopic mucosal resection (EMR) to the treatment of digestive tract tumors, and the endoscopic treatment is now widely performed for early digestive tract cancers including stomach esophageal, and colon cancers [1–4]. More recently, endoscopic submucosal dissection (ESD) has been developed as a new technique [5], and an en bloc endoscopic resection of large lesions and lesions with ulcer scars has become possible [6].

ESD is a minimally invasive treatment and enables the en bloc resection for early colorectal neoplasm. However, it is not widely used in the large neoplastic lesions because of technical difficulty and complications. It has been reported that the tumor size of 50 mm or large is an independent risk factor for complications [7].

We aimed to examine the safety, efficacy and complications of ESD for large colorectal neoplasms (larger than 20 mm) in a nonacademic hospital in Japan, retrospectively.

2. Patients and Methods

We have treated 608 cases of colorectal neoplasm (size ≧20 mm) from July 2007 to December 2012.

All cases were carried out with 1 expert and/or 5 novice endoscopists who had performed under expert's supervision. We have treated 608 cases of colorectal neoplasm (size ≧20 mm) from July 2007 to December 2012. We divided the cases into two groups by size: Group A (lesion size: 20–49 mm) and Group B (lesion size ≧50 mm) (Table 1). Written informed consent was obtained from all patients. We evaluated tumor size, macroscopic type, histology, procedure time, en bloc and curative resection rates, and complications (Table 1).

2.1. Procedure of ESD. Details of the procedure have been described elsewhere [8–11]. In brief, normal saline was preinjected into the submucosal layer of the colon to avoid subsequent injections of sodium hyaluronate solution into an inappropriate layer. Sodium hyaluronate (0.5%) was then injected to make a good protrusion of the targeted mucosa.

Table 1: Clinical characteristics of 608 colorectal ESDs divided into 2 separate groups.

	Group A (20–49 mm)	Group B (≧50)
Total ESDs	511	97
Age, y.o., mean ± SD	67.4 ± 10.3	67.1 ± 11.7
Tumor size, mm, mean ± SD	30.0 ± 7.50	64.2 ± 16.0
Tumor location		
Cecum	67	17
Right colon	254	49
Left colon	169	18
Rectum	88	30
Macroscopic type		
LST-G	205	80
LST-NG	260	13
Protruded	40	4
Recurrent	6	0
Histology		
Adenoma	289	43
Mucosal cancer	120	28
SM1 cancer	39	8
SM2 cancer	20	10
Serrated or nonneoplastic lesions	43	2
En bloc resection rate, %	99.2	99.0
Curative resection rate, %	94.7	88.7
Procedure time, min, mean ± SD	60 ± 35.3	119.6 ± 60.0
Complication, no. (%)		
Immediate perforation	13 (2.5%)	8 (8.2%)
Delayed perforation	1 (0.2%)	0 (0%)
Bleeding	6 (1.2%)	1 (1.0%)
Others	1 (0.2%)	

ESDs: endoscopic submucosal dissections, LST-G: granular -type laterally spreading tumor, SD: standard deviation, SM1: submucosal invasion less than 1000 μm from the muscularis mucosae, and SM2: submucosal invasion 1000 μm or more from the muscularis mucosae.

By mixing a small amount of dye, the sodium hyaluronate can be distinguished easily from the noninjected area even after the preinjection of normal saline. A small amount of epinephrine was also mixed with sodium hyaluronate to diminish bleeding during the procedures.

A mucosal incision around the tumor was then made with either a dual knife (KD-650L/KD-650Q; Olympus) or a flex knife (KD-630L; Olympus). Before incising the entire circumference of the lesion, dissection of the submucosa was started from the area in which the mucosal incision was completed, prior to the flattening of the lifted area as the procedure progressed.

The principal knife used for the submucosal dissection was the same one as that used for the mucosal incision.

The operation time was recorded for all the procedures. A typical example is shown in Figure 1.

CO_2 insufflation was used instead of air insufflation. Since CO_2 is absorbed more rapidly than air, it reduces the patient's discomfort due to an increase in gas in the intestine associated with a prolonged procedure, and if it should leak into the abdominal cavity due to perforation, it is absorbed relatively quickly.

ESD was performed under conscious sedation in the endoscopy room.

2.2. Histological Assessment. The specimens, fixed by formalin, were cut into 2 mm slices. They were examined microscopically for histological type, depth on invasion, lateral resection margin, and vertical resection margin. Histological assessments were based on the Japanese classification of cancer of colon and rectum and the Vienna classification [12–14]. Resections were considered tumor free when the lateral and vertical margins of a specimen were both negative for tumor cells independent of its histological features. A curative resection was achieved when both the lateral and the vertical margins of the specimen were free of cancer, and there was no SM invasion deeper than SM1, lymphatic invasion, vascular involvement, and poorly differentiated component. An adenoma with unknown lateral margin was also considered to be a curative resection provided that such adenoma met all of the other criteria.

2.3. Statistical Analysis. All statistical analyses were performed by using JMP software version 8.0 (SAS Institute, Cary, NC, USA). Some variables in this study were described as mean (SD). The P value was 2 sided, and $P < 0.05$ was used to determine statistical validity.

3. Results

For the 608 cases, 511 cases (84.0%) were assigned to group A, and 97 cases (16.0%) were assigned to Group B (Table 1).

3.1. Clinicopathological Characteristics. The average age and the lesion size were 67.4 years and 30.0 mm in Group A, and 67.1 years, 64.2 mm respectively, in Group B.

Histologically, of the 511 tumors, there were 289 tubular adenomas (56.6%), 120 mucosal cancers (23.5%), 39 SM1 cancers (7.6%), 20 SM invasions 1000 μm or more from the muscularis mucosae (SM2) or deeper (3.9%), and 43 serrated or nonneoplastic lesions (8.4%) in Group A.

Macroscopic types included 260 nongranular-type LSTs (50.9%), 205 granular-type LSTs (40.1%), 40 protruded (7.8%), and 6 recurrent (1.2%) in Group A.

On the other hand, of the 97 tumors, there were 43 tubular adenomas (44.3%), 28 mucosal cancers (28.9%), 8 SM1 cancers (8.2%), 10 SM invasions 1000 μm or more from the muscularis mucosae (SM2) or deeper (10.3%), and 2 serrated or nonneoplastic lesions (2.1%) in group B.

Macroscopic types included 13 nongranular-type LSTs (13.4%), 80 granular-type LSTs (82.5%), 4 protruded (4.1%), and 0 recurrent (0%) in Group B.

Tumor locations included 67 in the cecum (13.1%), 254 in the right colon (49.7%), 169 in the left colon (33.1%), and 88 in the rectum in Group A, and there were 17 in the cecum

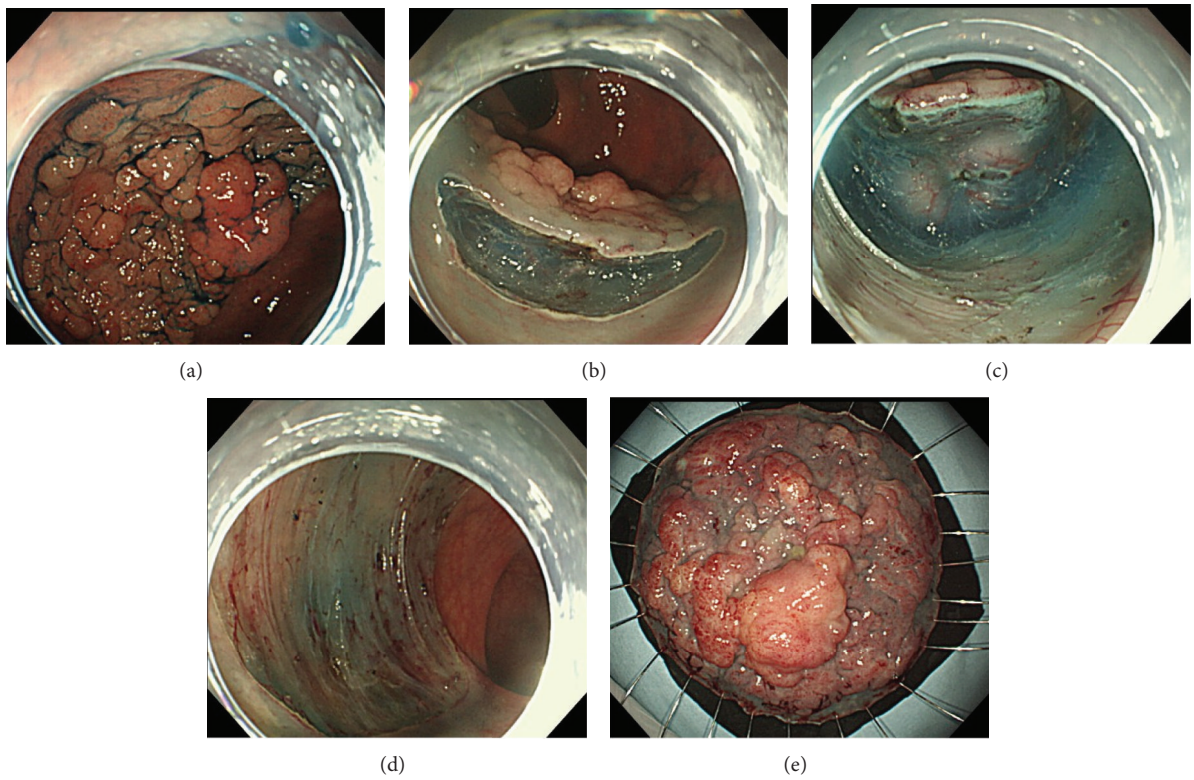

Figure 1: ESD for a 6.5 cm LST-G of the rectum: 6.5 cm LST-G is observed in the rectum. Initial mucosal incision after submucosal injection at the oral side of the lesion. The body position was changed to allow the lesion to hang by gravity and, thus, to facilitate insertion of the endoscope into the submucosal layer. After the completion of ESD: about a 1/2 circumferential mucosal defect is observed: resected specimen.

(17.5%), 49 in the right colon (50.5%), 18 in the left colon (18.6%), and 30 in the rectum (30.9%) in Group B.

3.2. Clinical Outcomes of Colorectal ESD. The mean procedure time was 60 ± SD minutes in Group A, and it 119.6 ± SD minutes in Group B ($P < 0.0001$). The en bloc resection rate and the curative resection rate were 99.2% and 94.7% in Group A, and the 99.0% and 88.7% in Group B ($P = 0.80$ and $P = 0.12$). There were statistically significant differences in the mean procedure time among 2 Groups ($P < 0.0001$).

3.3. Complication Rate. Complications in Group A were 14 perforations (2.7%), 6 bleedings (1.2%), and 1 ischemic colitis (0.2%). In Group B were 8 perforations (8.2%) and 1 bleeding (1.0%) ($P = 0.03$).

Perforations during actual ESD procedures occurred in 13 patients (92.9%) in Group A and in 8 patients (100%) in Group B. Delayed perforations occurred in another 1 patient (7.1%) in Group A.

One delayed perforation and 1 immediate perforation required emergency surgery in Group A, but none in Group B.

4. Conclusions

While esophageal or gastric neoplastic lesions undergoing endoscopic treatment are mostly early cancers, their colorectal counterparts are mostly benign (adenomatous). In addition, precise diagnostic techniques, including magnifying endoscopy, were established early on, facilitating the differentiation of adenomas from carcinomas and, preoperative estimation of the site and extent of the submucosal invasion with high-level accuracy [15, 16]. Based on the established preoperative diagnostic techniques, large lesions have been shown to be completely curable by divided endoscopic mucosal resection (EMR), which is currently performed worldwide. However, there are many lesions for which en bloc resection by ESD is desirable, such as large, depressed lesions untreatable by snare EMR, lesions strongly suspected of slight SM invasion before surgery, and lesions with fibrosis. Therefore, ESD, which has become a common technique for treating esophageal and gastric cancers, has recently come into use for the treatment of colorectal cancers. However, because ESD is associated with a high level of technical difficulty due to organ characteristics, and with frequent complications, colorectal ESD should be performed in high-volume endoscopy centers.

In our institution, a general hospital, the number of endoscopic procedures was so high that we had performed 608 colorectal ESDs up until December 2012.

In 2010, Saito et al. [7] analyzed the results of more than 1,000 colorectal ESDs in 10 centers specialized for endoscopic treatment in Japan, and they reported that, in the 4 most experienced centers performing more than 100 colorectal ESDs, intraoperative perforation, delayed perforation, and postoperative bleeding occurred in 4.1%, 0.2%, and 1.1% of

the patients, respectively. In the present study, intraoperative perforation, delayed perforation, and postoperative bleeding occurred in 3.5%, 0.2%, and 1.1% of the patients, respectively, which were compared favorably with the results for the above mentioned centers that are specialized in endoscopic treatment. In addition, the en bloc resection rate, the curative resection rate, and the procedure time in our hospital were 99.2%, 93.8%, and 73.0 min, respectively. These results were very favorably compared with those (89.0%, 89.7%, and 117 ± 91 min, resp.) in the 4 most experienced centers.

ESD, if performed under the supervision of an expert even in a general hospital, has become a safe treatment modality. Because Saito et al. reported that a tumor size ≥50 mm was an independent risk factor for the development of complications, we evaluated the outcome of the treatment for Group A cancers (with a tumor size of 20–49 mm) and Group B (with a tumor size ≥50 mm) cancers in this study, and we found that the perforation rate was significantly higher and the procedure time was significantly longer for group B than for Group A cancers. However, all perforations were successfully managed conservatively, requiring no emergency surgery.

Similar to the study of Saito et al., ESD for large colorectal neoplasms ≥5 cm was technically more difficult than that for their smaller counterparts, and it was associated with a high incidence of complications, all of which were successfully treated conservatively. Considering a procedure time of about 2 hours and the invasiveness of the surgery, it is necessary to further study the possibility of using ESD as a treatment option. In particular, extensive rectal lesions may require colostomy, giving a marked advantage to ESD. The present study led us to consider that, in a general hospital like ours, colorectal ESD can be performed relatively safely after training by, and under the supervision of, an experienced specialist.

Although further studies involving more patients are needed, colorectal ESD seems to be a relatively safe and effective treatment for large (larger than 20 mm) superficial colorectal tumors.

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Research Article

Endoscopic Detection of Early Esophageal Squamous Cell Carcinoma in Patients with Achalasia: Narrow-Band Imaging versus Lugol's Staining

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Chromoendoscopy with Lugol's staining remains the gold standard technique for detecting superficial SCC. An alternative technique, such as narrow-band imaging (NBI), for "optical staining" would be desirable, since NBI is a simpler technique and has no known complications. In this study, we compare NBI without magnification and chromoendoscopy with Lugol's staining for detecting high-grade dysplasia and intramucosal esophageal squamous cell carcinoma (SCC) in patients with achalasia. This was a prospective observational study of 43 patients with achalasia referred to the Gastrointestinal Endoscopy Unit of the Hospital of Clinics, São Paulo, University Medical School, Brazil, from October 2006 to February 2007. Conventional examinations with white light, NBI, and Lugol staining were consecutively performed, and the suspected lesions were mapped, recorded, and sent for biopsy. The results of the three methods were compared regarding sensitivity, specificity, accuracy, positive predictive value, negative predictive value, positive likelihood value, and negative likelihood value. Of the 43 patients, one was diagnosed with esophageal squamous cell carcinoma, and it was detected by all of the methods. NBI technology without magnification has high sensitivity and negative predictive value for detecting superficial esophageal squamous cell carcinoma, and it has comparable results with those obtained with Lugol's staining.

1. Introduction

Achalasia is a chronic esophageal motility disorder associated with esophageal retention of foods and fluids, bacterial overgrowth, and impaired clearance of regurgitated gastric contents [1]. These factors usually lead to chronic inflammation of the esophageal mucosa, which potentially increases the risk of hyperplasia, dysplasia, and esophageal cancer [2, 3].

Esophageal squamous cell carcinomas in achalasia patients have been investigated previously. In a large cohort followup study, Wychulis et al. [4] analyzed 1,318 patients and found a 7-fold increased risk of esophageal squamous cell carcinomas in achalasia patients compared to the general population. Despite some contradictory data [5–7], achalasia is generally accepted as a condition associated with an increased risk for developing esophageal squamous cell carcinoma [8, 9].

Chromoendoscopy with Lugol's staining remains the gold standard technique for detecting superficial esophageal squamous cell carcinoma [10, 11]. Although Lugol's staining is a simple and low-cost method, instillation of its solution may lead to complications, such as hypersensitivity to iodine, laryngitis, and pneumonitis, as well as frequent painful sensations and nausea [12–15]. Kondo et al. [15] demonstrated a significant reduction in retrosternal discomfort with the use of sodium thiosulfate. An alternative technique such as narrow-band imaging for "optical staining" would be desirable,

especially because it is a simpler technique and has no known complications.

Narrow-band imaging technology may be useful for detecting squamous cell carcinomas of the pharynx and esophagus. Muto et al. [16] and Yoshida et al. [17] observed morphological pattern changes in intrapapillary capillary loops. These patterns can be useful for diagnosing squamous cell carcinomas and even to predict lesion extension.

Various reports of early-stage pharyngeal and esophageal squamous cell carcinomas identified with narrow-band imaging technology can be found in the literature. Without using imaging magnification, Muto et al. [16] diagnosed a superficial squamous cell carcinoma of the pharynx, which appeared as a small and well-defined brownish area. Watanabe et al. [18], who also used narrow-band imaging without magnification, found six pharyngeal squamous cell carcinomas, and Goda et al. [19] found an esophageal squamous cell carcinoma that was not identified by conventional endoscopy (obscure lesion). Recently, our group demonstrated that narrow-band imaging performs as well as Lugol's chromoendoscopy for the detection of esophageal squamous cell carcinoma in patients with head and neck cancer [20].

The aim of this study was to compare narrow-band imaging technology with Lugol's staining during endoscopic examination of the esophagus for the detection of high-grade intraepithelial neoplasias and superficial squamous cell carcinomas in patients with esophageal achalasia.

2. Materials and Methods

2.1. Design. This was a cross-sectional study, and esophageal mucosal examination was analyzed in a sequential approach divided into three phases. The first phase was with white light, the second phase was with narrow-band imaging, and the final phase was with Lugol's staining. At the end of each phase, abnormal findings were documented.

The patients were submitted to an endoscopic procedure, and it was performed under conscious sedation with midazolam and fentanyl. Only one senior endoscopist (Edson Ide) performed all of the endoscopic procedures.

At the first phase, any residues or exudates were removed through water instillation. The esophagus was, then, analyzed with white light. If there were lesions, they were mapped using the anterior, posterior, right, and left esophageal walls and the distance up to anterior incisors as references.

The second phase involved the use of narrow-band imaging assessment of the esophageal mucosa. At this moment, brownish areas were identified as lesions suspected of being neoplasia, compared to "normal" mucosa, which is green independent of changes in surface or vascular texture.

In the third phase, Lugol's staining was performed by spraying 20cc of a 2% Lugol's solution at esophageal mucosa. After the staining, white-colored areas were suspected of being neoplasia, in contrast with brown or brownish "normal" areas.

The operator took biopsies of every suspicious lesion detected by any phase of the study. Biopsies were only performed after Lugol's staining was completed, and, after mucosal examination and biopsy, a volume of 20cc of a 0.5% sodium thiosulfate solution was instilled to remove Lugol's solution in order to reduce spasm and pain. Complications due to Lugol's solution were registered including laryngitis, chemical pneumonitis, hypersensitivity, and anaphylactic shock.

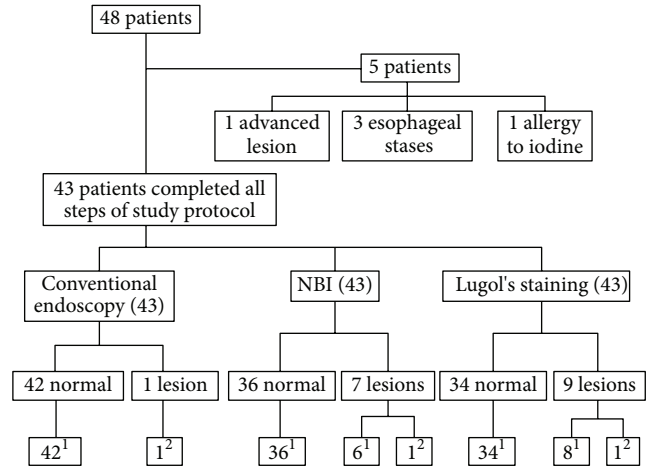


Figure 1: Flowchart of the study protocol. [1]Total patients without squamous cell carcinoma ($n = 42$); [2]total patients with squamous cell carcinoma ($n = 1$). NBI: Narrow band imaging.

The size and macroscopic shape of the lesions were evaluated according to the Paris Classification [21] for superficial esophageal lesions. Topography was divided into cervical (up to 5 cm of cricopharyngeus muscle), thoracic, and abdominal esophagus.

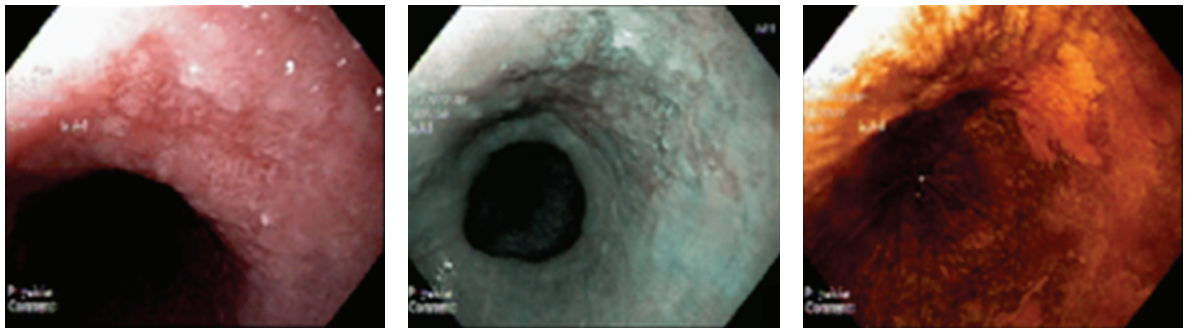
2.2. Patients. From October 2006 to February 2007, 48 consecutive patients with achalasia were referred to the Gastrointestinal Endoscopy Unit of a tertiary academic center for early esophageal cancer detection. These patients usually participate in a surveillance protocol, which consists of upper gastrointestinal endoscopy with associated esophageal Lugol's staining every 3 years.

Inclusion criteria were indications to take part in the surveillance protocol for patients with achalasia, despite any treatment (e.g., pharmacologic, endoscopic dilation, and surgical cardiomyotomy) they had undergone previously. Exclusion criteria were as follows: clinical conditions that prevented upper gastrointestinal endoscopy examination or Lugol's staining; previous history of allergic reaction to iodine; esophageal stasis that could not be cleared by endoscopic procedures; and endoscopic detection of an ulcerated, infiltrative, or stenotic lesion.

All participants provided written informed consent. This study was approved by the Ethics Committee of the University of São Paulo Medical School.

2.3. Endoscopy System. An Exera II Evis 180 GIF180 videogastroscope (Olympus, Tokyo, Japan) with high resolution (1,080 dpi), 1.5-fold magnification, and narrow-band imaging technology was used.

2.4. Histology. Histology was performed by a senior pathologist, who was aware of the endoscopic suspicion of esophageal



(a) (b) (c)

Figure 2: Esophageal lesion with flat morphology (0-IIb according to Paris Classification). (a) Conventional examination. (b) Narrow-band imaging. (c) Lugol's staining.

Table 1: Correlation between endoscopic findings and histopathologic examination by hematoxylin and eosin staining.

Method	Negative endoscopic findings	Positive endoscopic findings	Histopathologic examination		
			Squamous cell carcinoma (*in situ*)	Esophagitis	Normal
Conventional	42	1	1	—	—
Narrow-band imaging	36	7	1	5	1
Lugol's	34	9	1	8	0

squamous cell carcinoma. Biopsy specimens were immersed in formaldehyde for fixation and stained with hematoxylin and eosin. The lesions were classified in accordance with the Revised Vienna Classification [22]. In the absence of lamina propria invasion, noninvasive neoplastic lesions were divided into two groups based on the degree of intraepithelial neoplasia: low grade and high grade.

High-grade dysplasia, intraepithelial carcinoma, and carcinoma *in situ* were considered equivalent entities [21]. Whenever the lamina propria of the mucosa was invaded, the lesion was referred to as intramucosal carcinoma.

In this study, only findings of high-grade intraepithelial neoplasia (carcinoma *in situ)* and intramucosal carcinoma of squamous cells were considered true positives for esophageal squamous cell carcinoma [22].

2.5. Statistical Analysis. Values and 95% confidence intervals were calculated for sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and positive and negative likelihood ratios.

3. Results

Of the 48 patients enrolled, five were excluded: one because he had an advanced malignant esophageal lesion that was easily detected by conventional endoscopy, three because they had esophageal stasis, and one because of a prior history of allergy to iodine. Of the remaining 43 patients, there were 14 men and 29 women. The median age was 59 years.

The 43 patients underwent all stages of the protocol of investigation for this study (Figure 1). Narrow-band imaging and Lugol's staining found seven and nine suspected lesions, respectively. Conventional endoscopy revealed one superficial lesion with a flat morphology (0-IIb according to Paris Classification), which was also detected by narrow-band imaging and Lugol's staining (Figure 2). This lesion proved to be an esophageal neoplasia (squamous cell carcinoma *in situ*), sized 15 mm in diameter, and was located in the thoracic esophagus.

Of the seven lesions found by narrow-band imaging, histopathology revealed that one was normal mucosa, five were esophagitides, and one was squamous cell carcinoma *in situ*. Of the nine lesions found by Lugol's staining, histopathology revealed that eight were esophagitides and one was squamous cell carcinoma *in situ*. The same squamous cell carcinoma was found in one patient (Table 1).

The performance of narrow-band imaging was similar to that obtained by Lugol's staining. Sensitivity and negative predictive value were 100% for both methods, and the specificity was 85.7% (75.1%–96.3%) for narrow-band imaging and 81% (69.1%–92.8%) for Lugol's staining. Diagnostic performances for conventional endoscopic examinations, narrow-band imaging, and Lugol's staining are presented in Table 2.

In the Lugol's staining group, there were no cases of chemical laryngitis or hypersensitivity to iodine. No complications were reported with conventional or narrow-band imaging procedures.

4. Discussion

The present study selected patients with achalasia as an increased-risk group for esophageal squamous cell carcinoma. These patients usually present with delayed esophageal emptying, and they report worsening of these symptoms due to development of an obstructive tumor at late stages [23]. Without surveillance, esophageal carcinoma is usually diagnosed in advanced stages with poor prognosis [24].

Table 2: Comparison of the performance across methods (95% confidence interval) (%).

	Conventional examination	Narrow-band imaging	Lugol's
Sensitivity	100 (100-100)	100 (100-100)	100 (100-100)
Specificity	100 (100-100)	85.7 (75.1–96.3)	81 (69.1–92.8)
PPV	100 (100-100)	14.3 (−11.6–40.2)	11.1 (−9.4–31.6)
NPV	100 (100-100)	100 (100-100)	100 (100-100)
Accuracy	100 (100-100)	86 (75.7–96.4)	81.4 (69.8–93)
PLR	n/c	7	5.3
NLR	0	0	0

PPV: positive predictive value; NPV: negative predictive value; PLR: positive likelihood ratio; NLR: negative likelihood ratio; n/c: non calculable.

The Lugol's staining technique is based on the presence of large amounts of glycogen in the squamous epithelium, which stains intensely with iodine; in contrast, dysplastic and carcinoma cells contain little or no glycogen, which results in no staining [15, 25–27]. Thus, upper gastrointestinal endoscopy with Lugol's staining is still considered the best method for the diagnosis and delimitation of superficial esophageal squamous cell carcinoma [27–29].

However, Lugol's solution irritates the mucosa and may lead to retrosternal chest pain and discomfort, because of its alcoholic nature. Its utilization is limited by other factors, namely, hypersensitivity to iodine and the risk of chemical esophagitis, laryngitis, and bronchopneumonia. Several authors have reported necrosis and injury to the esophageal and gastric mucosa caused by hypersensitivity to Lugol's solution [30, 31]. Furthermore, esophageal chromoendoscopy with Lugol's staining significantly increases the length of the examination period [32].

Narrow-band imaging enhances the visualization of superficial capillaries, as well as mucosal surface structure, and has an effect similar to that of chromoendoscopy. Moreover, narrow-band imaging does not have the limitations of Lugol's staining chromoendoscopy and could be considered as a potential alternative method for the detection of esophageal squamous cell carcinoma.

Few studies have evaluated the capacity of narrow-band imaging without magnification to detect esophageal squamous cell carcinoma. Watanabe et al. [18] found that narrow-band imaging was more likely 2 folds than conventional white-light evaluation to detect pharyngeal squamous cell carcinoma. In a multicenter study that compared narrow-band imaging with conventional white-light evaluation, the accuracy was 90.2% and 55.3%, respectively ($P < 0.0001$) [33]. When Lugol's staining chromoendoscopy was compared with narrow-band imaging with image magnification, the sensitivity was the same (92.3%), but narrow-band imaging had a higher specificity (91.7% versus 72.2%) [34].

In our study, we compared Lugol's staining with narrow-band imaging technology without magnification. Many medical centers do not have the resources for magnification; therefore, the aim of this study was to determine whether narrow-band imaging alone would suffice to detect small and superficial neoplasias of the esophagus. Narrow-band imaging and Lugol's staining identified one esophageal neoplasia that was also detected by conventional white-light examination. Both methods had 100% sensitivity and negative predictive value. Although narrow-band imaging without magnification had a higher specificity for detecting early squamous cell neoplasias in the esophagus, it was similar to Lugol's staining: 85.7% (75.1%–96.3%) and 81% (69.1%–92.8%), respectively. In a study of patients with head and neck squamous cell carcinomas employing the same methodology, Ide et al. observed similar results when they compared narrow-band imaging without magnification with Lugol's staining [20]. Lee et al. and Takenaka et al. [33, 34] found that the sensitivity of narrow-band imaging for detecting esophageal squamous cell carcinoma and high-grade intraepithelial neoplasia was 90.9% (58.7%–99.8%), the specificity was 95.4% (90.3–98.3%), and the accuracy was 95.1% (90.1%–98.0%).

Narrow-band imaging without magnification and Lugol's staining had equivalent performances; this indicates that narrow-band imaging is a potential surveillance method for patients with esophageal achalasia.

Our study has limitations in its methodology. A sequential approach was adopted in which the standard endoscopy, narrow-band imaging, and the Lugol's staining were employed by the same operator in the same patient. This setting might have affected the results since the operator possessed prior information after each phase of endoscopic procedure. However, the sequential approach seems to be the best strategy for daily practice. Furthermore, this methodology was used in similar studies [31, 33, 34].

In conclusion, the results obtained with narrow-band imaging technology without magnification were comparable with those obtained with Lugol's staining for the screening of esophageal squamous cell carcinoma in patients with achalasia. Although narrow-band imaging does not have the risks and technical difficulties associated with Lugol's staining, larger multicenter studies are necessary in order to analyze the cost and benefits of this technology and to determine whether narrow-band imaging could replace Lugol's staining for screening of early-stage esophageal squamous cell carcinoma.

Authors' Contribution

E. Ide and F. Maluf-Filho contributed equally to this study; E. G. de Moura, P. Sakai, and I. Cecconello made the decision to submit the application; F. Maluf-Filho, D. M. Chaves, and R. Sallum designed the research; E. Ide, Maluf-Filho, and E. G. de Moura performed the research; and F. O. Carneiro and M. S. V. Frazão wrote the paper.

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Clinical Study

Parameters That May Be Used for Predicting Failure during Endoscopic Retrograde Cholangiopancreatography

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Aim. Endoscopic retrograde cholangiopancreatography (ERCP) is frequently used for the diagnosis and treatment of hepatic, biliary tract, and pancreatic disorders. However, failure during cannulation necessitates other interventions. The aim of this study was to establish parameters that can be used to predict failure during ERCP. *Methods*. A total of 5884 ERCP procedures performed on 5079 patients, between 1991 and 2006, were retrospectively evaluated. *Results*. Cannulation was possible in 4482 (88.2%) patients. For each one-year increase in age, the cannulation failure rate increased by 1.01-fold ($P = 0.002$). A history of previous hepatic biliary tract surgery caused the cannulation failure rate to decrease by 0.487-fold ($P < 0.001$). A tumor infiltrating the ampulla, the presence of pathology obstructing the gastrointestinal passage, and peptic ulcer increased the failure rate by 78-, 28-, and 3.47-fold, respectively ($P < 0.001$). *Conclusions*.Patient gender and duodenal diverticula do not influence the success of cannulation during ERCP. Billroth II and Roux-en-Y gastrojejunostomy surgeries, a benign or malignant obstruction of the gastrointestinal system, and duodenal ulcers decrease the cannulation success rate, whereas a history of previous hepatic biliary tract surgery increases it. Although all endoscopists had equal levels of experience, statistically significant differences were detected among them.

1. Introduction

ERCP is a frequently used procedure for the diagnosis of biliary tract and pancreatic disorders. Following the first endoscopic cannulation of the ampulla of Vater by McCune, increasing experience and the technological developments in the field have enabled diagnostic and therapeutic uses of the procedure via interventions, such as sphincterotomy, biopsy of the biliary tract, extraction of calculi from the biliary tract, and stent placement, to provide temporary or permanent cures for biliary and pancreatic disorders [1–7]. Side-viewing endoscopes, supportive equipment, and improvements in visualization have helped to establish the current ERCP standards. However, difficulties imposed by the anatomy of the biliary tract and pancreas as well as the need for both an endoscopist and an endoscopy nurse with certain degrees of experience have made ERCP the most complicated, the most difficult to learn, the most interventional, and the most therapeutic of all endoscopic procedures [8]. Although the complication rates of ERCP are higher than those of other endoscopy procedures, they are markedly low compared to surgical interventions performed on the biliary tract and pancreas. The morbidity rate following ERCP is 4–15.9% (pancreatitis, 1.3–15.9%; perforation, 0.08–1.1%; bleeding, 0.76–2.3%; cholangitis, 0.57–5.01%; cholecystitis, 0.11–0.68%), whereas the mortality rate is between 0 and 1% [9, 10].

The success of ERCP involves the cannulation of the biliary tract and obtaining a cholangiogram because cannulation is the first step for both diagnostic and therapeutic interventions [11]. Failure during cannulation renders the ERCP unsuccessful and gives rise to various consequences, including cholangitis and pancreatitis, which may require

interventions, such as percutaneous transhepatic cholangiography (PTC) and surgery, with higher morbidities [12].

2. Methods

Our study involved the retrospective evaluation of 5884 ERCP procedures performed on 5079 patients by 4 experienced endoscopists at the Surgical Endoscopy Unit in the Department of General Surgery, Istanbul University Faculty of Medicine, between 1991 and 2006. The aim of the study was to establish the factors that could be used to predict cannulation failures. The cases were evaluated (with the help of a computer) with regard to the following:

(1) age,

(2) gender,

(3) the presence of periampullary diverticula,

(4) previous upper abdominal surgery,

(5) the success of the cannulation,

(6) the final diagnosis,

(7) the endoscopist,

(8) any additional findings obtained during endoscopy.

The main criterion for the success of ERCP was the cannulation of the biliary tract. The data were statistically evaluated via single- and multiple-variable analyses using SPSS 13.0 to establish factors that could be used for predicting failure during ERCP.

3. Results

A total of 5884 ERCP procedures were performed on 5079 patients at the Surgical Endoscopy Unit in the Department of General Surgery, Istanbul University Faculty of Medicine, between 1991 and 2006. The procedure was performed two or more times on 688 patients. Of these 688, 197 were cases where the first intervention had failed. The age of the patients ranged between 8 and 98 years, and the mean age was estimated to be 56.2 years. The reasons for performing the ERCP procedure were as follows: jaundice in 2454 (48.3%), abdominal pain in 1906 (37.5%), cholangitis in 304 (6%), biliary fistula in 268 (5.3%), followup in 108 (2.1%) patients, and rare reasons in 39 (0.8%) patients. The rare reasons included elevated hepatic enzyme levels, pruritus, cholestatic enzyme elevation, melena, vomiting, and pancreatic fistula.

Cannulation, which is considered to be an indicator of a successful procedure, was possible in 4482 (88.2%) patients, while the papilla could not be cannulated in 597 (11.8%) patients. A diverticulum was detected in 660 (13%) patients. A precut incision was performed in 1017 (20%) patients. A total of 873 (17.2%) patients previously had upper abdominal surgery. *Endoscopist 1* performed 2000 (39.4%), *endoscopist 2* performed 1084 (21.3%), *endoscopist 3* performed 1052 (20.7%), and *endoscopist 4* performed 943 (18.6%) of the ERCP procedures.

The ECRP results were classified into 11 groups and are shown in detail in Table 1.

Table 1: ERCP diagnosis.

Final diagnosis	*n*	%
Biliary tract stones	952	18.7
Malignant obstruction of the biliary tract	778	15.4
Normal ERCP	661	13
Unsuccessful ERCP	597	11.7
Stones in the gall bladder and in the biliary tract	593	11.6
Gall bladder stones	515	10.2
Enlarged biliary tract	508	10.1
Biliary fistula	187	3.7
Benign obstruction of the biliary tract	139	2.7
Cystic disease of the biliary tract	29	0.6
Others	120	2.3
Total	5079	100

Of the 4482 ERCP procedures where cannulation was possible, a papillotomy was performed in 3791 (84.5%). While 1377 of the procedures involved the extraction of calculi from the biliary tract, a stent was placed in the biliary tract in 507. Of the 597 patients for whom ERCP had failed, the procedure was repeated for 197 (32%) of them. A second ERCP was performed in 138 (70%) of these 197 patients.

The data that were collected with regard to age, gender, the presence of periampullary diverticula, previous upper abdominal surgery, biliary tract cannulation, the endoscopist, and any additional findings obtained during endoscopy were evaluated with regard to their influence on the cannulation success rate using single- and multiple-variable analyses.

The mean age for the cases where a successful cannulation could not be performed was 60.37 (±14,15). In the patients for whom a successful cannulation was conducted, the mean age was 56.66 (±16,248). This difference was statistically significant ($P < 0.001$).

When the success of the cannulation was evaluated with regard to gender, ERCP was found to have been successful in 1919 (86.8%) of the 2212 male patients and 2563 (89.4%) of the 2867 female patients. The cannulation success rate was significantly higher in women than in men (Fisher's exact test, $P = 0.004$).

When the influence of duodenal diverticula on the cannulation success rate was evaluated, it was found that cannulation was successful in 592 (89.7%) of the 666 cases where a diverticulum was present. In contrast, cannulation was successful in 3890 (88%) of the 4419 cases where a diverticulum was not present. A statistical analysis showed that the presence of duodenal diverticula does not influence the cannulation success rate (Fisher's exact test, $P = 0.215$).

Of the 873 patients with a history of upper abdominal surgery, the ampulla was cannulated in 822 (94.2%) cases. Of the 4206 cases with no such history, the ampulla was cannulated in 3660 (87%) patients. The cannulation success rate in patients with a history of upper abdominal surgery was significantly higher (Fisher's exact test, $P < 0.001$).

Previous surgical interventions were examined in detail using 6 different subgroups consisting of Billroth II gastric resection or Roux-en-Y gastrojejunostomy, hepatic resection,

Table 2: Distribution of cannulation success rates for each previous upper abdominal surgery intervention subgroup (chi-square test, $P < 0.001$).

Surgical history	Cannulation		Total
	Yes	No	
None	552 (13.1%)	3665 (86.9%)	4217 (100%)
Billroth II/R-Y gastrojejunostomy	10 (62.5%)	6 (37.5%)	16 (100%)
Hepatic resection	1 (10%)	9 (90%)	10 (100%)
Hydatid cyst surgery	4 (6.1%)	62 (93.9%)	66 (100%)
Cholecystectomy	20 (3.2%)	614 (96.8%)	634 (100%)
Biliary tract exploration	8 (7%)	107 (93%)	115 (100%)
Others	2 (9.5%)	19 (90.5%)	21 (100%)
Total	597 (11.8%)	4482 (88.2%)	5079 (100%)

Table 3: Distribution of cannulation success rates for each endoscopist (chi-square test, $P < 0.001$).

Endoscopist	Cannulation		Total
	Yes	No	
Endoscopist 1	262 (13.1%)	1738 (86.9%)	2000 (100%)
Endoscopist 2	91 (8.4%)	993 (91.6%)	1084 (100%)
Endoscopist 3	108 (10.3%)	944 (89.7%)	1052 (100%)
Endoscopist 4	136 (14.4%)	807 (85.6%)	943 (100%)
Total	597 (11.2%)	4482 (88.2%)	5079 (100%)

Table 4: Distribution of cannulation success rates for each endoscopists in cases where a second ERCP was performed after a failed first ERCP (chi-square test, $P = 0.428$).

Endoscopist	Cannulation		Total
	No	Yes	
Endoscopist 1	33 (35.5%)	60 (64.5%)	93 (100%)
Endoscopist 2	9 (23.7%)	29 (76.3%)	38 (100%)
Endoscopist 3	10 (27.8%)	26 (72.2%)	36 (100%)
Endoscopist 4	7 (23.3%)	23 (76.7%)	30 (100%)
Total	59 (29.9%)	138 (70.1%)	197 (100%)

hydatid cyst surgery, cholecystectomy, biliary tract interventions, and so forth. A statistical analysis of these subgroups showed that the cannulation success rates in patients with Billroth II gastric resection or Roux-en-Y gastrojejunostomy were significantly lower, whereas they were significantly higher in the other groups ($P < 0.001$; Table 2). When the success rates of the four endoscopists were evaluated, *endoscopist 2* was found to be more significantly successful than the other endoscopists ($P < 0.001$; Table 3). Because each endoscopist had performed at least 943 endoscopy procedures, all of the endoscopists were considered experienced, and no comparisons were made with regard to experience. The cannulation was successful in the second ERCP attempt in 70% of the 197 patients for whom the first ERCP had failed. When the success rates of the endoscopists performing the second ERCP were evaluated, it was found that *endoscopist 4*, who had the lowest cannulation success in the first ERCP, had achieved the highest cannulation rate in the repeated ERCP procedure in the patients for whom cannulation could not be performed in the first ERCP attempt. However, this difference was not statistically significant ($P = 0.428$; Table 4).

The distribution of the cannulation success rates with regard to the additional findings was as follows: 9.5% ($n = 7$) in 74 periampullary tumors infiltrating or distorting the ampulla, 23.6% ($n = 13$) in 55 obstructive disorders preventing gastrointestinal passage (obstructive antrum tumor, pyloric stenosis, etc.), and 84% ($n = 27$) in 38 peptic ulcer patients. Cannulation was performed in 90% ($n = 4387$) of the 4855 patients in whom no additional findings were detected. In the patients with the additional aforementioned findings, the cannulation success rate was significantly lower (chi-square test, $P < 0.001$).

The factors that were found to produce significant differences in the single-variable analysis (i.e., age, gender, a history of upper abdominal surgery, any additional findings obtained in endoscopy, and the endoscopist) were reevaluated in a multiple-variable analysis. Multiple-variable logistic regression analysis was performed using the backward LR method. While the female gender was found to be advantageous for cannulation success rates in the single-variable analysis, the multiple-variable analysis did not reveal a statistically significant difference with regard to gender ($P = 0.386$). It was found that the cannulation failure rate increased by 1.01-fold for every one-year increase in age ($P = 0.002$). In addition, a history of previous hepatic biliary tract surgery caused the cannulation failure rate to decrease by 0.487-fold ($P < 0.001$). A tumor infiltrating the ampulla, the presence of a pathology obstructing the gastrointestinal passage, and peptic ulcer increased the failure rate by 78-, 28-, and 3.47-fold, respectively, ($P < 0.001$). In the single-variable analysis, *endoscopist 2* was the most successful. In the multiple-variable analysis, the most successful endoscopist was *endoscopist 3*.

Accordingly, having *endoscopist 1* instead of *endoscopist 3* perform the ERCP increased the failure rate by 0.684-fold ($P = 0.004$), whereas having *endoscopist 2* perform the procedure decreased the failure rate by 0.55-fold ($P < 0.001$). No difference between *endoscopist 1* and *endoscopist 4*, who appeared to be the least successful in the single-variable analysis, was detected in the multiple-variable analysis ($P = 0.386$). The confidence intervals and relative risks in the multiple-variable analyses are shown in Table 5.

4. Discussion

Success during ERCP implies the cannulation of the biliary tract and obtaining the cholangiogram because cannulation is the first step for both diagnostic and, if necessary, therapeutic interventions [11]. It should also be noted that cannulation failure renders ERCP unsuccessful and may lead to serious consequences. These include cholangitis and pancreatitis and may necessitate interventions with higher morbidities, such as PTC and surgery [12].

There are few studies in the medical literature regarding age and cannulation success rates during ERCP. Lobo et al. [13] indicated that the frequency of periampullary diverticula

Table 5: Distribution of the predicted relative risk (PRR) and confidence intervals (CIs) for the factors influencing cannulation in the multiple-variable analysis (logistic regression using the backward LR method).

		PRR	95% confidence interval	
			Minimum	Maximum
	Factors			
$P = 0.002$	Age	1.01	1.004	1.016
$P = 0.386$	Gender	1.086	0.901	1.309
$P < 0.000$	History of previous upper abdominal surgery	0.467	0.357	0.663
	Additional findings			
$P = 0.000$	Periampullary tumor infiltrating the ampulla	78.060	35.426	172.001
$P = 0.000$	Problem in GIT passage	29.190	15.413	55.282
$P = 0.001$	Peptic ulcer	3.457	1.687	7.085
	Endoscopist			
	Endoscopist 1			
$P = 0.000$	*Endoscopist 2*	0.550	0.419	0.722
$P = 0.004$	*Endoscopist 3*	0.684	0.529	0.883
$P = 0.389$	*Endoscopist 4*	0.897	0.700	1.149

increases significantly in patients over 75 years of age, and they found that cannulation success rates decrease significantly due to diverticula that increase with age. When evaluating our data, increasing age was found to be a risk factor for successful cannulation in the single-variable analysis. In the multiple-variable analysis, the failure rate was found to have increased by 1.01-fold for each one-year increase in the patient's age.

There is also no data regarding the impact of gender on the cannulation success rate. In a Japanese study by Fukatsu et al., the success of ERCP was reported to be lower in women [11]. Although the cannulation success rate was found to be significantly lower in the single-variable analysis in our series, gender was not found to be a factor influencing the failure of ERCP in the multiple-variable analysis.

The relationship between duodenal diverticula and the cannulation success rate has been investigated in detail. There are different views regarding the effect of duodenal diverticula on cannulation. Lobo et al. [13] determined that the frequency of duodenal diverticula increases with age and decreases the cannulation success rate. They found that the success of treating intradiverticular papillas was significantly lower than that of juxtadiverticular papillas. In a study conducted on 400 patients, Boix et al. [14] detected periampullary diverticula in 131 (32.8%) patients. They classified these diverticula according to the location of the papilla: Type 1 refers to the group where the papilla is inside the diverticulum, Type 2 implies that the papilla is on the border of the diverticulum, and Type 3 means that the diverticulum is close to the papilla. Boix et al. reported that periampullary diverticula do not adversely affect cannulation. However, they concluded that cannulation is more difficult in Type 1 diverticula, and hemorrhagic complications following a sphincterotomy increase in periampullary diverticula. Fukatsu et al. [11] found a 15% frequency of duodenal diverticula in their series, and they did not consider this to be a factor influencing the cannulation success rate. In our series, duodenal diverticula were detected in 666 (13.1%) of the 5079 patients. A single-variable analysis suggested that the presence of duodenal diverticula does not influence the cannulation success rate. However, the diverticula were not classified in our study.

Adhesions due to previous upper abdominal surgery, gastrointestinal diversions, and gastrointestinal obstructions are also factors that affect the cannulation of the papilla during ERCP. In the series by Choudari et al. [15], Billroth I or II interventions, Roux-en-Y gastrojejunostomy, gastric outlet obstruction, and narrowing of the duodenum have been listed as reasons for ERCP failure. In a study by Baron et al. [16], Billroth II surgery, gastrojejunostomy, hepaticojejunostomy, Whipple surgery, and gastrointestinal obstructions or narrowing were reported to cause ERCP failure. In another study by Nordback and Airo [17], the ERCP success rate following gastric diversion was reported to be as low as 33%, and an inability to reach the duodenum was stated to be the most important reason. The worst results were detected in patients undergoing Billroth II surgery with a long jejunal loop. In addition, there are sources that indicate that the risk of perforation is high in patients with gastric diversion surgery since more endoscopic maneuverings are required [18]. In the study by Fukatsu et al. [11], a history of Billroth I surgery and left-lobe hypertrophy following a right hepatectomy were listed as factors influencing failure. Freemann and Guda [19] also indicated that Billroth II surgery and surgical obesity treatment increase the cannulation failure rate during ERCP. In our series, the ERCP success rate decreased to 37.5% in patients with Billroth II surgery and Roux-en-Y gastrojejunostomy, which is comparable to the findings reported in the literature. However, except for Billroth II and Roux-en-Y gastrojejunostomy interventions, the cannulation success rate was significantly higher in patients with a history of hepatic biliary tract surgery than in those with no surgical history. This group consisted of patients in whom postoperative complications (such as icterus and biliary fistula) had developed. Our interpretation of this finding is that ERCP is more successful in patients with such complications due to better endoscopist motivation or facilitated ERCP (as a result of a fixated stomach or duodenum, due to the presence of adhesions). Additionally, in the cases of malignant or benign pathologies that narrow or obstruct the gastrointestinal system, the cannulation success rate was low (23.6%) in our series, which was also comparable to the literature described above. In the patients in whom a duodenal ulcer was detected, the cannulation success rate was significantly lower than in those who did not have duodenal ulcer. In summary, while the cannulation failure rate decreased by 0.487-fold in patients with a history of hepatic biliary tract surgery, it increased by 28-fold in those with Billroth II surgery, Roux-en-Y gastrojejunostomy, and

(benign or malignant) narrowing or obstruction of the gastrointestinal system. Nevertheless, it increased by 3.457-fold in those with a duodenal ulcer.

We detected that the cannulation failure rate increased by 78-fold in patients where periampullary tumors infiltrated or distorted the ampulla of Vater compared to patients with no such pathology. In their published series, Fukatsu et al. [11] and Freemann and Guda [19] showed that malignant biliary tract obstructions decrease the cannulation success rate during ERCP.

In addition to the factors that contribute to failure, factors that increase the success of ERCP have also been investigated. Of these, most data are available regarding precut (or needle-knife) incisions. In many studies, it has been reported that, in cases where cannulation cannot be performed during ERCP, a precut incision increases the success rate [11, 16, 19, 20]. Some studies have even suggested that directly starting the procedure with a precut incision, without attempting cannulation with the standard technique, is safer and more efficient than in patients where this approach is not used [17]. Because precut incisions were not directly used in our series, it was not taken into consideration in this study. In addition to these factors, it has been reported that glucagon, cholecystokinin (or its analogues), and topical nitroglycerin can be used to increase the cannulation success rate; however, it has been found that they do not produce statistically significant increases [21–23]. Such pharmacological agents were not used on the patients in our series.

As endoscopic sonography has become available, it has begun to be used in ERCP procedures where cannulation cannot be performed. In a study by Gupta et al. [24], it was found that in the ERCP procedures where cannulation cannot be performed using the standard technique, endosonography decreases the need for drainage via PTC or surgical procedures. It was also emphasized that endosonography can be used to facilitate cannulation during ERCP. Endosonography is not used in our clinic.

Another factor that influences the ERCP success rate is the experience of the endoscopist. The success rate increases in direct proportion to experience. Although various sources have reported different figures, it has been suggested that, during his or her training, an endoscopist should have performed approximately 100–200 ERCPs with a successful cannulation rate of 85–90%, and at least 25 (preferably half) of these interventions should have been therapeutic procedures [25, 26]. In an American study by Verma et al. [27], the cannulation success rate increased from 43% to 80% after 350 ERCPs, whereas it was found to be more than 96% after 400 ERCPs. In our series, all of the endoscopists had experience with at least 3000 gastroscopy and colonoscopy procedures. The fewest number of ERCP procedures that an endoscopist had performed was 943. Therefore, all four endoscopists were considered to be experienced. However, the single-variable analysis showed that the highest cannulation rate was achieved by *endoscopist 2*, and this difference was statistically significant. However, in the cases where a second ERCP was performed after an unsuccessful first ERCP attempt, *endoscopist 4*, who seemed to be the least successful endoscopist in the single-variable analysis, was found to be the most successful, although this difference was not statistically significant. Despite the fact that all of the endoscopists were equally experienced, the multiple-variable analysis showed that the cannulation success rates were significantly higher for *endoscopist 2* and *endoscopist 3*.

Ramirez et al. [28] showed that when the same individual performs a second ERCP after a first failed attempt, the success rate increases from 87.5% to 95%. Our series showed that for failed ERCPs, the success rate was more than 95% when we performed a second ERCP.

5. Conclusions

We conclude that the patient gender and duodenal diverticula do not influence the cannulation success rate during ERCP. In contrast, Billroth II and Roux-en-Y gastrostomy surgeries, a benign or malignant gastrointestinal obstruction that prevents the passage of the endoscope, and duodenal ulcers decrease the cannulation success rate, whereas a history of previous hepatic biliary tract surgery increases the success rate. In addition, although all of the endoscopists had equal levels of experience, statistically significant differences were detected among them.

Conflict of Interests

Emre Balik, and the other coauthors have declared that no conflict of interests exists.

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Clinical Study

Safety and Efficacy of Radiofrequency Ablation in the Management of Unresectable Bile Duct and Pancreatic Cancer: A Novel Palliation Technique

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Objectives. Radiofrequency ablation (RFA) has replaced photodynamic therapy for premalignant and malignant lesions of the esophagus. However, there is limited experience in the bile duct. The objective of this pilot study was to assess the safety and efficacy of RFA in malignant biliary strictures. Methods: Twenty patients with unresectable malignant biliary strictures underwent RFA with stenting between June 2010 and July 2012. Diameters of the stricture before and after RFA, immediate and 30 day complications and stent patency were recorded prospectively. *Results*. A total of 25 strictures were treated. Mean stricture length treated was 15.2 mm (SD = 8.7 mm, Range = 3.5–33 mm). Mean stricture diameter before RFA was 1.7 mm (SD = 0.9 mm, Range = 0.5–3.4 mm) while the mean diameter after RFA was 5.2 mm (SD = 2 mm, Range = 2.6–9 mm). There was a significant increase of 3.5 mm (t = 10.8, DF = 24, P value = <.0001) in the bile duct diameter post RFA. Five patients presented with pain after the procedure, but only one developed mild post-ERCP pancreatitis and cholecystitis. Conclusions: Radiofrequency ablation can be a safe palliation option for unresectable malignant biliary strictures. A multicenter randomized controlled trial is required to confirm the long term benefits of RFA and stenting compared to stenting alone.

1. Introduction

Self-expanding metal stents (SEMS) have become the mainstay palliative treatment for malignant biliary obstruction in patients with a life expectancy greater than 3 months [1, 2]. Their use has improved bile duct patency beyond what was achieved with plastic stents; however, long-term patency continues to be an unresolved issue. SEMS can occlude from tissue ingrowth or overgrowth, benign epithelial hyperplasia or secondary to biofilm, and sludge formation within the lumen of the stent [3]. Up to 50% of patients will have stent occlusion in the first 6 to 8 months [4, 5]. Different design alternatives have been explored in an attempt to improve stent patency. Covered SEMS were designed to prevent tissue ingrowth; however, they are contra-indicated for hilar drainage, have higher migration rates, and might be associated with increased risks of pancreatitis and cholecystitis [6–11]. Another treatment strategy to prolong stent patency and eventual survival is photodynamic therapy (PDT). PDT showed promising results; however, it carries a high complication rate including cholangitis and photosensitivity requiring the patient to avoid direct exposure to light for 4–6 weeks [12–14].

Radiofrequency ablation (RFA) has been used for tumor ablation in the esophagus [15], rectum [16], and liver [17]. It utilizes heat to achieve contact coagulative necrosis of surrounding tissue. Within the bile duct it seems to lead to improved stent patency by decreasing tumor ingrowth and benign epithelial hyperplasia [18]. This technique has been widely used to treat primary and secondary liver cancer [17]; however, the experience in malignant biliary obstruction is limited. There have been animal studies to assess the power

and duration of treatment [19], but there is only one study assessing this procedure in humans [20]. We aimed to assess the safety and efficacy of this novel palliative technique prospectively.

2. Methods

Data on twenty patients were collected between June 2010 and July 2012. Inclusion criteria included patients with unresectable malignant biliary strictures, unresectable cholangiocarcinoma, or pancreatic cancer with biliary obstruction and a life expectancy greater than 3 months. Exclusion criteria included cardiac pacemaker, instability for endoscopy, uncorrected coagulopathy, and pregnancy. Patients were evaluated with comprehensive laboratory studies as well as cross-sectional imaging prior to RFA and 30-days post RFA. All patients underwent RFA with either plastic or metal stent placement. Our primary outcome measures were the safety and efficacy of RFA. For efficacy measures, diameters of the stricture before and after RFA were recorded, as well as data on stent patency after a month was collected. Immediate and 30-day complications and stent patency were also recorded. Our study's primary endpoints were success rate—efficacy of RFA in terms of biliary stricture dilation and safety profile with respect to frequency and intensity of adverse events. The study was approved by the institutional ethics review committee (http://www.clinicaltrials.gov/ identifier NCT01303159).

2.1. Technique of RFA. All procedures were performed under general anesthesia. Side viewing endoscopes TJF-160 and TJVF-160 (Olympus America, Center Valley, PA) were used for all procedures. All patients underwent biliary sphincterotomy. A cholangiogram was then performed to define stricture length and diameter (Figure 1). The Habib EndoHPB wire guided catheter (EMcision, Hitchin Herts, UK) was advanced over a wire at the level of the biliary stricture and ablation using a RITA 1500X RF generator (Angiodynamics, Latham, NY) set at 7–10 watts for a time period of 2 minutes was conducted (Figures 2, 3, and 4). A one-minute resting period after energy delivery was allowed before moving the catheter. Biliary stents were placed systematically after radiofrequency ablation (Figure 5). Immediate and 30-day complications as well as technical and intraprocedural difficulties were recorded. SAS 9.2 was used to conduct statistical analyses.

3. Results

Twenty patients (15 males) with a mean age of 65.3 years (range 45–86) were included in the study. A total of 25 malignant biliary strictures were treated with RFA. 11 patients had unresectable cholangiocarcinoma, 7 had unresectable pancreatic cancer, 1 had Intraductal papillary mucinous neoplasm (IPMN) with high grade dysplasia, and 1 had gastric cancer with metastatic tumor in the bile duct. Patient demographics are shown in Table 1. Deployment and application of the Habib EndoHPB catheter was successful in all 20 patients.

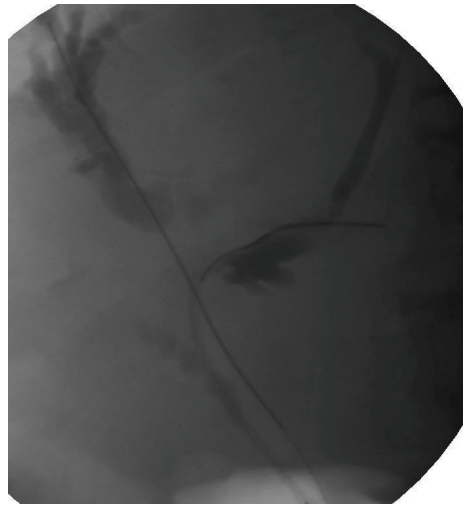

Figure 1: Fluoroscopic images of bile duct cancer at the confluence with a Bismuth III lesion.

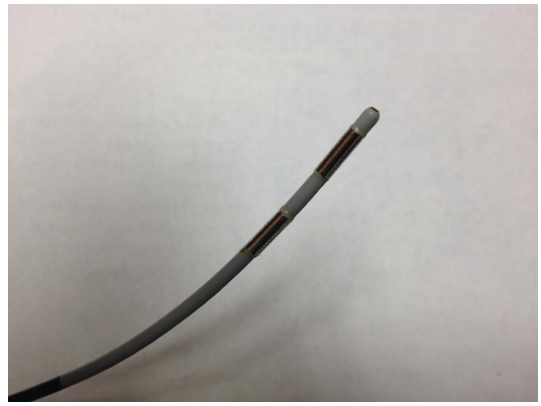

Figure 2: EndoHPB Probe for radio frequency ablation.

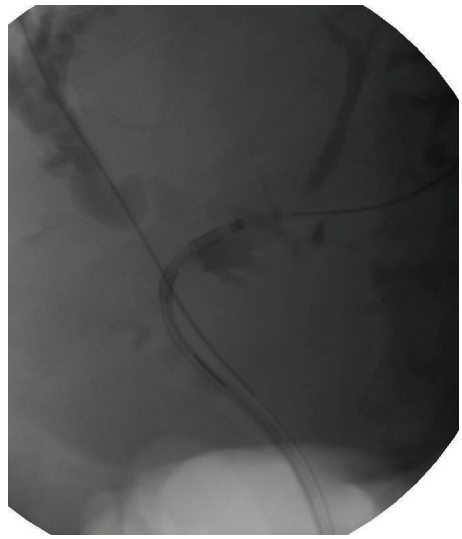

Figure 3: Application of radiofrequency at the level of the left hepatic duct.

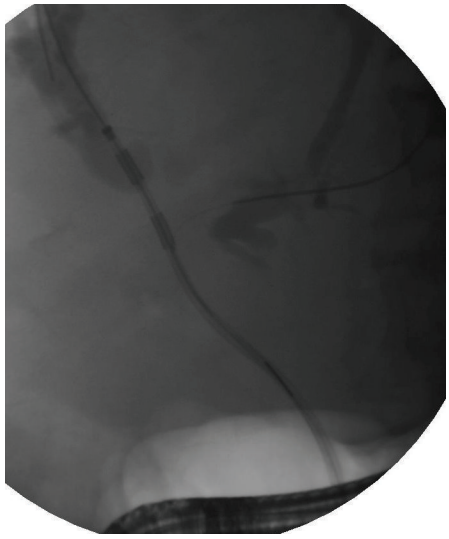

Figure 4: Application of radiofrequency ablation at the level of the right hepatic duct.

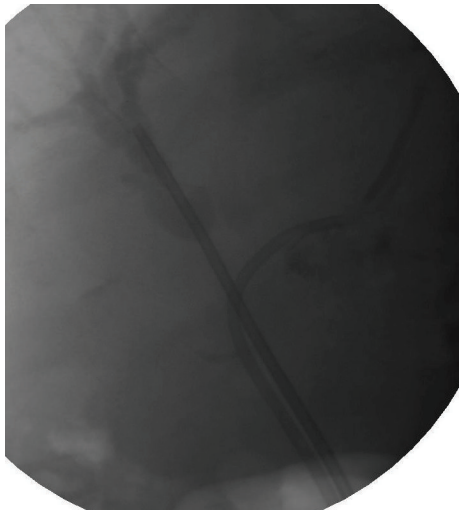

Figure 5: Placement of biliary stent posts radiofrequency application.

The median stricture length treated was 9.7 mm. The mean stricture length treated was 15.2 mm (SD = 8.7 mm, Range = 3.5–33 mm). The mean stricture diameter before RFA was 1.7 mm (SD = 0.9 mm, Range = 0.5 – 3.4 mm) while the mean diameter after RFA 5.2 mm (SD = 2 mm, Range = 2.6–9 mm). The before and after RFA treated stricture diameters were compared using paired t-test. There was a significant increase of 3.5 mm ($t = 10.8$, DF = 24, P value $\leq .0001$) in the bile duct diameter after RFA.

All patients were stented after the procedure. Patients undergoing repeated sessions of RFA received plastic stents. Patients receiving a single session of RFA were offered metal stents. Covered metal stents were placed for distal CBD strictures while uncovered metal stents were placed for hilar lesions. Covered self-expanding metal stents (SEMS) (Wallflex, Boston Scientific, Natick, MA) were used in 13 patients, 1 patient received an uncovered Wallflex SEMS and 6 patients received plastic stents. One of the patients with plastic stents received uncovered Wallflex stent at his second RFA session (Table 2).

Table 1: Patient demographics.

Number of patients	20
Age y, median (range)	65.3 (45–86)
Sex (male/female)	15/5
Disease:	
Cholangiocarcinoma	11
Pancreatic cancer	7
IPMN	1
Gastric cancer	1

Table 2: Treatment results.

Number of strictures treated	25
Mean stricture length (mm)	15.2 (SD = 8.7, range = 3.5–33)
Mean stricture diameter before RFA (mm)	1.7 (SD = 0.9, range = 0.5–3.4)
Mean stricture diameter after RFA (mm)	5.2 (SD = 2, range = 2.6–9)
Type of stent placed	
Uncovered SEMS*	1
Partially or fully covered SEMS	13
Plastic stents	6
Complications	
Pain	5
Mild after ERCP pancreatitis	1
Cholecystitis	1

*SEMS: self-expanding metal stent.

Three patients underwent choledochoscopy confirming tissue necrosis and ablation after RFA, one of them at three months after RFA just before his second session of RFA. Immediate and 30-day complications were collected for all patients. All stents were patent at day 30 for all patients. Five patients presented with pain after the procedure, but only one developed mild post-ERCP pancreatitis managed conservatively and cholecystitis which was drained percutaneously.

4. Discussion

Endoscopic biliary decompression has become the preferred palliation technique in unresectable malignant biliary obstruction. Long-term biliary drainage continues to be a challenge and modifications to stent design have not proven to be an effective solution [3, 4, 11]. SEMS have been shown to offer longer palliation than plastic stents but can occlude due to tumor growth, sludge or biofilm formation. In patients with cholangiocarcinoma, PDT has shown improvement in

overall survival; however, it is also associated with complications such as cholangitis, hemobilia, and photosensitivity (12.5–30%) [13, 14].

Initial experience with RFA comes from the Hammersmith team [20] and is very encouraging. In their study, they treated a total of 22 patients and demonstrated immediate and 30-day safety and 90-day biliary patency. They reported improved stricture after RFA treatment, with similar complication rates as in our study (1 asymptomatic biochemical pancreatitis, 2 cholecystitis) and one failure to decompress the bile duct, which eventually resulted in the patient's death [20].

Our study shows that RFA treatment of malignant biliary obstructions can be safe and effective. The complications described in animal models, including extension of the RFA burn into adjacent structures and difficult catheter reintroduction after treatment were not observed in this study [19]. The placement and application of the RFA probe was successful in 100% of our patients and there were no difficulties introducing other catheters after treatment for stent deployment. The coagulative necrosis induced by the probe has an immediate effect as confirmed by choledochoscopy and seems to be related to the intensity of the energy liberated by the probe in contact with the tumor; that is, the tighter the stricture, the more intense the contact and the amount of energy liberated.

Five of the patients had postprocedural complications with only one being severe (i.e., cholecystitis requiring percutaneous drainage); however we remained within the expected post-ERCP/stent placement complications rate. These complications are primarily attributed to ERCP and/or stenting post RFA. All complications resolved with medical management and none required surgery.

Radiofrequency ablation seems to be an efficient and safe treatment strategy in palliation of unresectable malignant biliary obstructions. A prospective study, preferably randomized control trial, is required to confirm the benefits of RFA on long-term biliary stent patency and survival rates.

Disclosure

P. Figueroa-Barojas, M. R. Bakhru, K. Ellen, J. Millman, A. Jamal-Kabani, and M. Gaidhane have no conflict of interests. N. A. Habib is the Chief Executive Officer and Founder of EMcision Limited, UK. M. Kahaleh has received a grant support from Boston Scientific, EMcision, Mauna Kea, and Xlumena Inc. He is a Consultant for Boston Scientific and Xlumena (http://www.clinicaltrials.gov/ identifier NCT01303159).

Authors' Contribution

P. Figueroa-Barojas, M.D., M. R. Bakhru, M.D., N. A. Habib, M.D., and K. Ellen contributed to the drafting of the paper and the critical revision for important intellectual content. J. Millman and A. Jamal-Kabani contributed to the acquisition of data and critical revision of the paper for important intellectual content. M. Gaidhane, M.D., M.P.H., contributed to the acquisition of data, statistical analyses, interpretation of data, critical revision of the paper for important intellectual content, and study coordination. M. Kahaleh, M.D., contributed to the study concept and design, acquisition of data, critical revision of the paper for important intellectual content, and study supervision.

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