

41 Treatment of Biliary and Esophageal Malignant Obstruction by Self-Expandable Nitinol Stents (Endocoil, Esophacoil)

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We report our experience with self-expandable nitinol coil stents (InStent, Inc.) in the treatment of malignant biliary and esophageal obstruction. This coil stent, being made of a flat tightly wound wire, resists tissue ingrowth and, as it does not incorporate into the mucosa, it can be removed endoscopically. The stent is inserted in a small diameter and after being located in the stricture area it self-expands while applying radial force till achieving its original configuration.

37 biliary stents were inserted endoscopically through a jumbo endoscope for the treatment of inoperable pancreatic and choledochal tumors. Short term complications occurred in 3 patients: 2 stents were removed because of failure of expansion and one stent was removed because the patient had a severe pancreatitis and was operated. In a long term follow-up no tissue ingrowth were observed. 7 stents were plagued due to sludge or tissue overgrowth and plastic stents were placed in them.

33 esophageal stents were inserted fluoroscopically in the treatment of proximal and distal esophageal tumors and gastric tumors. In a follow-up of 40 weeks (mean implant time – 14 weeks) stents remained fully opened, no tumor ingrowth or pain were observed. Complication occurred in 4 patients: 2 stents migrated into the stomach and were removed endoscopically without trauma, 2 stents broke after a period of 2–4 weeks leaving the main part of the stent still functioning in place. As a result of this last two cases a recall was done for the esophageal stents and a new design has been released recently, having a polymer coating.

We conclude that the self-expandable nitinol coil stent, having a tightly wound coil, resist tissue ingrowth and allows easy endoscopic procedure to relieve inoperable malignant strictures.

42 Endoscopic Balloon Sphincteroplasty (EBS) for Bile Duct Stones: Efficacy and Follow-Up in the First 90 Patients

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Since papillotomy accounts for the major morbidity/mortality associated with ERCP, we have previously proposed sphincteroplasty (EBS) as a safe and effective alternative for small to medium sized bile duct (BD) stones (<20 mm). We now report the efficacy and complications of EBS in a series of 90 patients.

Patients and Methods: EBS was considered for BD stones up to 20 mm in 90 patients, 24 post cholecystectomy, (mean age 64, range 19–89, 66 female, 24 male), of whom 17 were under 40 yrs. Stone size ranged from 3–20 mm (mean 10 mm, max 8). EBS was performed using a balloon tipped catheter (Microvasive) over a 0.21 guidewire inflated across the papilla (60 sec × 2) to a diameter of 10 mm allowing access for stone retrieval. Median follow-up was 10 months (range 0.5–20).

Results: Using EBS alone, the bile duct was cleared in 70 patients (76%). Mechanical lithotripsy was used to remove large stones (15–20 mm) in 13 (15%). Of the 20 EBS "failures" (24%) papillotomy was required to clear the duct in 7 (9%). A pigtail stent was inserted in 13 (15%) to maintain biliary drainage a) as a temporary measure because of doubt about residual stones >15 mm (n = 7, 9%), or b) as a definitive measure in elderly high risk patients with multiple stones >15 mm (n = 6, 6.5%). ERCP was repeated in 14 (16%) for stent removal ± replacement or repeat EBS-duct clearance (n = 4). There was no papillary haemorrhage, while uncomplicated pancreatitis was observed in 4 patients (5%).

Conclusion: EBS is a safe and effective sphincter preservation technique for the management of BD stones up to 20 mm in size, which significantly reduces the need for papillotomy.

43 A Randomized Study of Endoscopic Hemostatic Clipping (EHC) versus Endoscopic Variceal Ligation (EVL)

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Aim Assess the efficacy of Endoscopic Hemostatic Clipping & Endoscopic Variceal Ligation in the acute and elective treatment of esophagogastric varices. In our experience, combination of these techniques with low-volume sclerotherapy, might enhance the eradication of varices. **Patients** Twenty consecutive patients with variceal bleeding (median age 51.3 years range 23–70), were randomized to receive either EVL or EHC (5EVL and 3EHC patients were treated during acute bleeding). All patients but one (alcoholic cirrhosis) had a post-hepatic cirrhosis. Both groups were comparable for Child Score (median 8.1EVL, 8EHC), Varix size (median 3.EVL & EHC) and Pre-treatment trans-

fusional requirements (median 2.2EVL, 1.3EHC). Gastric varices were present in 4 EVL & 3 EHC patients; one patient in each group presented with active gastric variceal bleeding. **Methods** The Stiegmann Goff endoscopic ligator and the Olympus HX-3L Clip Fixing Device were used. Varices were clipped or ligated at the bleeding site first, or, when the procedure was elective, as close as possible to the esophagogastric junction. Two to three mls of 1% Aetoxisclerol were injected intravariceally 1–2 cms cephalad to the clipped/ligated site. **Results** Hemostasis was achieved in all cases of acute variceal bleeding. In both groups, obliteration of varices was possible in 19/20 pat (10/10 EHC pat. & 9/10 EVL pat.) after 2 sessions (range 1–4 EVL, 1–3 EHC). One patient (EVL) withdrew. A median of 4.4 clips (range = 3–6), 2.5 ligations (range = 2–3) and 13 mls of 1%.

Aetoxisclerol (range 9–18 mls) per session, were necessary. Gastric varices were obliterated in all patients; this was performed during active bleeding in one patient in each group. Clips stayed longer (median 4 weeks, range 2–6 weeks) on site than ligations (median 1 week, range 1–2 weeks, p < 0.001). No significant ulcerations were observed after clipping. During the 12 month follow-up, 5 EHC patients and 2 EVL patients had a single incident of rebleeding. Three patients died (2EHC, 1 EVL); one (EHC) during acute bleeding & two of hep. failure (EHC & EVL). **Conclusion** In this study, two different techniques of mechanical obliteration of varices appear to be effective; combination with sclerotherapy might enhance the result.

44 Prospective, Randomised Comparison of Ligation and Sclerotherapy for Oesophageal Varices. Preliminary Results

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Introduction. Since the second half of seventies, endoscopic sclerotherapy is considered the most effective treatment for oesophageal varices. However this technique has a significant percentage of complications (20–40% according to different authors). Endoscopic ligation was introduced in 1986 by Stiegmann and Goff as an alternative technique for the treatment of oesophageal varices and the results, according to the literature shows a good efficacy compared to sclerotherapy. In this prospective study we report our preliminary results of comparison between the two technique.

Methods. From January till November 1993 we have recruited 37 consecutive patients with oesophageal varices who had recently bled to treat by elastic binding or injective sclerotherapy. The choice of treatment was randomised. Sclerotherapy was performed with 1% polydocanol solution and mixed technique. The elastic binding was performed with the kit distributed by Bard Company. After the varices eradication was obtained the patients have been endoscopically controlled every 3 months.

Results. In those patients submitted to ligation, we obtained the variceal obliteration in 17 cases (85%), with a mean number of sessions of 4.0 (range 3–6) and a mean number of O-rings of 30.7 (range 18–59). In the group submitted to sclerotherapy we achieved variceal obliteration in 14 patients (82.4%) with a mean number of sessions of 3.9 (range 3–5). No any patient in the ligation group developed complication of clinical relevance. In those patients submitted to sclerotherapy 5 developed oesophageal stenosis which required several dilatation sessions, 1 a pleurisy after the first sclerotherapeutic session and one a cardiac ulcer which persisted 6 months after the treatment. 1 patient in each group had an episode of rebleeding before the end of treatment, and 3 patients in the sclerotherapy group had an episode of rebleeding during the follow up.

Conclusions. This our early experience, even if limited by the little number of treated cases, have shown us a very good tolerability of ligation treatment compared to sclerotherapy, an almost complete absence of complications and very good results in order to achieve variceal obliteration. The long term follow up will allow us to evaluate if the results of elastic binding are superimposable to those of sclerotherapy.

45 Endoscopic Therapy in Chronic Pancreatitis

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Interventional endoscopy represents a nonsurgical, organ preserving therapy in chronic pancreatitis (CP). A prospective study was conducted between January 1992 and October 1993 to evaluate the technical feasibility and clinical outcome of pancreatic endoscopy in CP. 42 patients with recurrent attacks of upper abdominal pain and relapsing inflammatory crises presenting for endoscopic retrograde cholangiopancreatography (ERCP) were included into the study. 12 women and 30 men were examined. Pancreaticojejunostomy had already been accomplished in one patient and endoscopic sphincterotomy (EST) in two patients. Percutaneous drainage of pseudocysts had been achieved in two patients and had been combined once with another EST. ERP revealed dilation of the Wirsung's Duct (WD) in 41 patients ranging from 4 to 30 mm (mean 10.9 mm). 26 patients had stenoses accompanied by

prestenotic dilation in 16 cases, 25 ductal concretions, 11 a disruption of WD, 11 pseudocysts corresponding to the duct, and 7 parenchymal concretions obstructing the outflow. The initial diagnosis of CP had to be corrected in five patients: twice there was a tumor stenosis and acute pancreatitis. Sclerosing pancreatitis was found once. In two patients CP was diagnosed, but there was no evidence of obstruction of WD and intervention was done without. Endoscopic therapy was indicated in 35/42 patients (83%). The interventions included 32 EST, 10 stentings, 4 stone extractions by balloon and 24 times short-time nasopancreatic drainage. 18 sessions of extracorporeal shock wave lithotripsy (ESWL) were necessary in 12 patients with pancreatic duct stones or parenchymal calculi. Endoscopic therapy was technically successful in 30 of 35 cases (85%). Technical failure was due to one 90 degree angle in the proximal WD, 3 disruptions and one stenosis that could not be passed with the guidewire. These settings were further complicated by extensive parenchymal calculi in three cases and duct stones in one patient. No postinterventional pancreatitis was observed. The only complication resulted in one papillary bleeding, that was stopped by sclerosing therapy. In conclusion, endoscopic therapy of CP with obstruction succeeded in 75%. It led to immediate relief of pain in all successfully treated patients. Nevertheless, 30% of the patients had to have reintervention within one year for stent occlusion or recurrent pain. 2/35 patients underwent pancreaticojejunostomy for definite relief of pancreatic obstruction.

46 Endoscopic Sphincterotomy (ES) Applied for Acute Biliary Pancreatitis (ABP) Prevents Further Attack of this Disease. A Prospective Follow-Up Study

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Background: Endoscopic sphincterotomy is relatively new method of treatment of ABP and our knowledge concerning its effectiveness for preventing the recurrence of this disease has not been evaluated as yet.

Material and methods: In 1983–1993 two hundred and eighty patients with ABP were treated. One hundred seventy-eight patients were treated by urgent endoscopic sphincterotomy (ES group) whereas remaining one hundred two patients were managed conventionally (CM group) according to study protocol. Both groups were comparable to age, sex, and predicted severity of ABP.

Two hundred sixty-three patients (who survived the acute phase of the disease) were subsequently followed-up in one-year intervals. Follow-up examination consisted of physical examination, laboratory tests and US. In selected cases patients were hospitalized and CT and/or ERCP were performed if needed. Special attention was paid to ABP recurrence with regarding to previously performed sphincterotomy and/or cholecystectomy.

Results: Follow-up data were obtained from 201 (76%) patients out of 263. Mean observation period was 49 (range: 2–132) months.

Results concerning the recurrence of APB are shown in the table:

	ABP recurrence		p (Fisher)
	ES	no ES	
Cholecystectomy	0/102	2/49 (4%)	0.104
No cholecystectomy	0/ 33	8/17 (47%)	0.000
Total	0/135	10/66 (15%)	0.000

Conclusion: In acute biliary pancreatitis endoscopic sphincterotomy effectively prevents the recurrence of the disease even in those with gallbladder stones left in situ.

47 Regional Specificities in the Phenotypes of Neuroendocrine Cells in the Human Anal Canal: Evidence for the Presence of a Metaplastic Neuroendocrine Cell Population

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Little is known about chemical phenotypes of neuroendocrine cells in the human anal canal, the endocrine-like cells and Merkel cells. The presence, morphology and distribution of neuroendocrine cells was investigated with a panel of antisera and antibodies for neural markers, biogenic amines and neuropeptides by the sensitive streptavidin-biotin-peroxidase immunocytochemistry. Coexistence patterns of neurochemically characterized neuroendocrine cells were examined by double immunofluorescence cytochemistry.

In the colorectal zone, endocrine-like cells were immunoreactive for chromogranin A (CGA), serotonin (5-HT), pancreastatin (PST), peptide tyrosine tyrosine (PYY), glucagon-like peptide-1 (GLP-1), and somatostatin (SOM). Coexistence patterns of endocrine-like cell types with CGA and GLP-1 were heterogeneous. In the anal transitional zone (ATZ), endocrine-like cells were immunoreactive for CGA, 5-HT and PST. Furthermore, six new types of

endocrine-like cells were characterized by their chemical phenotypes; namely PYY-, GLP-1-, protein gene product 9.5 (PGP)-, calcitonin gene-related peptide (CGRP)-, neurotensin (NT)- and SOM-immunoreactive cells. All endocrine-like cells types in the ATZ were immunoreactive for CGA. In the squamous zone and perianal skin, CGA-immunopositive Merkel cells were also immunoreactive for CGRP, PST and PGP.

Neuroendocrine cells in the anal canal exhibit epithelial zone-related diversities in their neurochemical phenotypes, morphology, distribution and coexistence, which may indicate specific regulatory functions. In the epithelium of the ATZ, which is regarded as metaplastic, endocrine-like cells expressed phenotypes characteristic of the neuroendocrine cells of the colorectal zone and the squamous zones, indicating a metaplastic origin of these cells.

48 Profuse Peptidergic Innervation of the Human Anal Canal: A Pathogenic Factor for Anorectal Diseases?

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Anorectal disorders like anal fissures or hemorrhoids have a very high prevalence and incidence and are regarded as chronic inflammations. Neuropeptides in the peripheral nervous system are not only regulators of physiological functions but may also be involved in the feedforward exacerbation of chronic inflammations. However, little is known about neuropeptides in anal nervous systems. We investigated the pan-neural and neuropeptidergic innervation of the human anal canal by different immunohistochemical techniques.

The general innervation, as assessed by staining for protein gene product 9.5 (PGP), was ubiquitously abundant in all regions and neuropeptidergic nerve fibres formed region-specific subsets. The pan-neural and neuropeptidergic innervation was particularly dense in the haemorrhoidal plexus, where haemorrhoids develop. In the dermis of the squamous zones, unusual distribution patterns of nerve fibres, consisting of concentrated nerves, were encountered and referred to as areas of high nerve fibre density. These nerves were especially rich in proinflammatory peptides like substance P (SP) and calcitonin gene-related peptide (CGRP). It appeared that areas of high nerve fibre density were increased in tissues of anal fissures.

Our results indicate a close connection between the anal nervous systems and anal disorders. In particular, sprouting of sensory peptidergic (SP/CGRP) nerve fibres may be a pathogenic factor of anal fissures, inflammation and pruritus. Neuropeptide agonists and -antagonists may be exploited in the human anal canal as topospecific antiinflammatory agents in anal inflammatory disease and pruritus.

49 Nitric Oxide Synthase (NOS)-Containing Neurons in the Small and Large Intestine of Rats and Guinea Pigs

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Nitric Oxide (NO) is a novel transmitter molecule which in the gut is implicated in muscle relaxation. NO is produced from L-Arginine by the action of NOS, an enzyme dependent upon CA⁺⁺, calmodulin and NADPH for its function. NO synthesizing neurons can be identified either by NADPH-diaphorase histochemistry or by immunohistochemistry using antibodies against NOS. The aim of this study was to visualize enteric neurons expressing NOS-immunoreactivity (IR), their distribution and innervation pattern in rat and guinea pig small intestine and colon. Animals were sacrificed and segments of jejunum, ileum and colon were opened, pinned flat on balsa wood and fixed in 4% paraformaldehyde. Each specimen was processed as whole mounts: the mucosa was removed and the submucosa peeled apart from the muscle layer. In some preparations the circular muscle was separated from the longitudinal layer. Submucosa, circular and longitudinal muscle were incubated 48 hrs with a new, specific anti-NOS rabbit polyclonal antibody (dilution: 1 : 250). NOS-IR was detected with similar innervation patterns both in the small intestine and colon of rats and guinea pigs. NOS-IR was localized to nerve fibers in the muscle layer and in ganglion cells of the myenteric and, to a lesser extent, submucous plexuses. The vast majority of NOS-labeled myenteric neurons showed typical features of Dogiel type I neural cells having lamellar dendrites and a single long processes. A dense network of fibers was seen in the internodal strands and secondary branches of the myenteric plexus while they were less abundant in the tertiary component. NOS-IR innervation of the circular muscle was markedly denser than that observed in the longitudinal layer both in the small intestine and colon. In addition, NOS-IR nerve fibers formed a dense network in the deep muscular plexus. The NOS-IR nerve supply of the submucosa was much less dense than that of the muscle. In conclusion, NO, which plays an important role in muscle relaxation and synaptic transmission, is produced in a subpopulation of neurons in the mammalian enteric nervous system. These