Update on Small Bowel Endoscopy
Simon K. Lo, MD

Double-balloon enteroscopy is a novel full-function endoscopic technique to allow physicians to view the entire small intestine in real time. Both diagnostic and therapeutic procedures can be performed within the small bowel without open surgery.

Comprehensive, real-time view

One balloon is attached to the distal end of the scope and the other is attached to a transparent overtube. When inflated with air, the balloons can grip a section of the small intestine and pleat it over the endoscope. Sequential shortening of the small intestine over the endoscope enables a comprehensive examination of the entire small intestine.

Cedars-Sinai Medical Center and five other tertiary care centers (University of Chicago, Mayo-Scottsdale, Stanford, Virginia Mason and California Pacific) have accumulated a large volume of experience using this technique. As a result, these medical centers have collaborated to publish their early findings. This technology is now available in most countries, particularly in Japan and Germany.

Novel approaches from Digestive Diseases Week

At the 2007 Digestive Diseases Week (DDW), leading-edge technological advances in small-bowel endoscopy were introduced, including:

The Single Balloon Enteroscope System, developed by Olympus. It is similar to the double-balloon system, except that it does not use a balloon at the tip of the enteroscope, and both the overtube and balloon use silicone instead of latex.

The Endo-Ease® developed by Spirus. The small bowel overtube is equipped with a spiraling rubber ridge, similar in design to a corkscrew, to promote advancement of the endoscope and pleating of intestinal folds. To date, less than 100 patients have been studied outside of the United States, but the product has not yet been used on post-abdominal surgery patients.

A modification of the double-balloon system from Israel. This disposable system attaches onto a standard long endoscope and is thought to be effective at going a long distance in the small bowel.

As data emerges, so too will choices

While there is not yet sufficient data to tell if any of the recently introduced modalities will be contenders with double-balloon enteroscopy, the next three to four years will no doubt bring many comparative studies that look at safety, distance, patient acceptance and effectiveness at delivering diagnoses and therapy. It is entirely possible that one of these technologies will emerge as the new standard of care, or that preferred long and short techniques may emerge.

It also will be interesting to see how these systems will be utilized relative to the small bowel wireless capsule. Currently in the US – and many other parts of the world – capsule endoscopy is used as a screening tool followed by a more thorough examination with the double-balloon system or surgical exploration. With all the current emerging technologies, will this continue to be a two-step process or will one tool emerge that can do both? This – and much more – will most likely be determined over the next few years.

Dr. Lo is Director of the Pancreatic and Biliary Diseases Program and Director of GI Endoscopy at Cedars-Sinai.
E-mail: simon.lo@csbs.org
Gastric Electrical Stimulation Provides a New Option for Obese Patients with Type II Diabetes

Edy E. Soffer, MD

**Satiety signals are the key**
One of the evolving alternative treatments for obese diabetics is the application of electrical stimulation to the stomach. Since satiety signals from the stomach – derived from food-related distension and contraction of the stomach muscles – are a major factor in the process of meal termination, enhancing gastric contractions can be used to amplify satiety signals. This, in turn, can result in reduced food intake, weight loss and improved glycemic control.

**Gastric stimulation proves to be a simple process**
This concept is currently being tested both abroad and in the US. The Tantalus™ System is a gastric electrical stimulation system that delivers gastric contractility modulation signals in synchrony with gastric slow waves. The system consists of pairs of electrodes sutured to the wall of the stomach and connected to an implantable pulse generator (IPG) positioned in the abdominal wall.

The IPG serves a dual role:
1. It records electrical and mechanical signals from the stomach that are incorporated into a novel algorithm for automatic eating detection.
2. Once the onset of a meal is detected, the IPG is programmed to automatically deliver electrical stimulation to the gastric wall muscle, thus precluding constant stimulation (between meals or during sleep) or the need for patient activation.

In an ongoing study of obese patients with diabetes implanted with the Tantalus System in Europe, it was found that obese patients with Type II diabetes – rather than those with Type I diabetes – had the best response. Patients in the study showed weight loss as well as improvement in glucose control and reduction in HbA1c.

**Cedars-Sinai studies this new obesity protocol**
A Phase I safety and feasibility study for this novel therapy was recently completed at Cedar-Sinai, one of only two medical centers in the US to conduct the study. A multi-medical center study is planned to begin in the very near future, enrolling obese subjects with poorly controlled Type II diabetes.

Dr. Soffer serves as a consultant to the manufacturer of the Tantalus System.

Case Study: Chronic Epigastric Pain, Weight Loss and a Dilated Pancreatic Duct

Simon K. Lo, MD

A 73-year-old, Japanese-American woman was referred to Cedars-Sinai for evaluation and treatment of symptomatic chronic pancreatitis. The patient presented with mild, chronic abdominal discomfort that became significant over the course of a few months. She lost 10 percent of her body weight over those same months. The patient was known to have a dilated pancreatic duct for several years. While an earlier CT scan revealed some calcification in the body of the pancreas, it was unclear if the calcification was in the pancreatic parenchyma or in the peri-pancreatic vasculature.

**Clinical investigations**
The patient was initially scheduled for an endoscopic retrograde cholangiopancreatography (ERCP) and possible endoscopic pancreatic therapy. After discussion with the patient, we decided to investigate the pancreatic condition first with an endoscopic ultrasound study to determine whether symptoms were the result of chronic pancreatitis, and to make certain that the pancreatitis had not evolved into a cancer with a secondary pancreatic ductal obstruction.

The endoscopic ultrasound found a small nodule within a dilated duct of Wirsung in the head of the pancreas. The main pancreatic duct was diffusely dilated throughout the entire pancreas (figure 1). No pancreatic calcification was noted. Based on the EUS findings, we then proceeded with an ERCP, which showed an ill-defined filling defect/short stricture at the head of the pancreas. The pancreatic sphincter was slightly generous but without a wide-mouth appearance or mucus plug. Next, a cholangioscopy using a new technology called SpyGlass™ (Boston Scientific) was done to examine the filling defect. SpyGlass utilizes a miniature 6,000-pixel, fiber-optic probe that attaches to a camera head. The probe is inserted through a single-use access and delivery catheter that can be steered in four directions to access and inspect the treatment area. This exam identified a fish egg/herring roe appearance and frond-like lesions in the ducts in the head of the pancreas. No other main duct lesion was seen beyond that point.

To support our tentative diagnosis of intraductal papillary mucinous neoplasms (IPMN) and to exclude a cancer at the base of the frond-like lesions, we took biopsies using through-the-scope “spybite” forceps. The biopsies confirmed our clinical and endoscopic suspicion of IPMN (figure 2). There was no cancer in the tissue specimens. As a result, the patient is being actively evaluated for surgical resection.
Challenges in diagnosis

IPMN is often confused with chronic pancreatitis. However, it can present with acute pancreatitis or without any physical signs or symptoms. It can occasionally present as a large solid or complex cystic mass in the pancreas. An isolated dilated pancreatic side branch due to an IPMN is increasingly being referred for EUS evaluation of a pancreatic cyst. Considered a rare disease a few years ago, IPMN was first described as mucinous ductal ectasia by some Japanese doctors. IPMN is now increasingly seen in this country and has been found in patients of virtually all ethnicities.

IPMN is a small, flat tumor in its early stage and is very difficult to detect unless it is directly visualized on a pancreatoscopy. An isolated dilated pancreatic duct or mucus passage through the pancreatic sphincter may be the first clue to its presence. It is a slow-growing lesion with minimal space occupation and therefore produces no symptoms or clinical signs in most cases. It is often discovered accidentally on abdominal ultrasound, CT or MRI as unexplained cysts, dilated pancreatic duct or chronic pancreatitis. It can produce symptoms and findings of acute relapsing pancreatitis and even classical chronic pancreatitis. In its late stage, an IPMN may evolve into a cancer and may become a large complex cystic mass. A cancer is often associated with fistula formation with extrusion of mucus through the stomach or duodenum (figure 3). Most of the complaints and findings are probably caused by the copious production of thick mucus and secondary congestion of the pancreatic duct (figure 4). Interestingly, colonic and other gastrointestinal cancers seem to be associated with this condition. A colonoscopy and upper endoscopy should be performed in any patient discovered with this condition.

Suggestive findings of IPMN include cystic dilation of one or multiple pancreatic side branches, ill-defined filling defects within a dilated pancreatic duct, or passage of mucus from the pancreatic sphincter. Some endoscopists consider it pathognomonic to have a wide open pancreatic sphincter filled with a mucus globule (figure 5). The truly definitive diagnosis is made on direct visualization of villous fronds or a positive biopsy.

IPMN and malignancy

Managing this condition is based on a number of variables, including its location, size and histology within the pancreas. Frequently, IPMN is an incidental finding, but in the main duct as many as 30 percent of cases are associated with cancer at the time of discovery. The management recommendations have been evolving, with the previous recommendations dominated by either partial or total pancreatectomy in all cases. A recently published guideline recommended resection of all main duct IPMN regardless of symptoms because of a roughly 70 percent incidence of associated malignancy (Tanaka M, et al., International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. Pancreatology 2006;6:17-32).

Likewise, all symptomatic side branch IPMN should be considered for resection unless there are other clinical restrictions such as co-morbidities or very advanced age. Asymptomatic side branch IPMN has a much lower malignant potential than its main duct counterpart and can be managed conservatively with periodic surveillances.
Surveillance for Post-operative Recurrence in Crohn’s Disease

Andrew Ippoliti, MD

Nearly 75 percent of patients with Crohn’s disease will undergo surgery during the course of their disease. Unfortunately, these patients are at high risk for clinical recurrences, 30 percent at one year and 70 percent by two years. This leads to repeat surgery in nearly half these patients. Thus, these patients are in a high risk group and an aggressive approach to post-operative management is warranted.

Many studies have examined potential risk factors for recurrent Crohn’s disease or surgery. Smoking, fistulizing or penetrating disease phenotype, extent and location of disease are often cited risks. However, the overall likelihood of recurrences is so high that all patients with resective surgery and an anastomosis should be aggressively managed.

There are three elements to the management of this group of patients:
1) Maintenance medication
2) Endoscopic surveillance
3) Treatment of endoscopic recurrence

Maintenance

There are three types of medications that have been tested as maintenance medication to prevent recurrence: immunomodulators, 5-aminosalicylates (5-ASAs), and imidazole antibiotics. Controlled clinical trials have not demonstrated substantial long term efficacy for any of these medications. 5-ASAs are the best tolerated group long term but several trials have failed to demonstrate significant benefit vs. placebo. Ornidazole, 1 gm a day, was effective in preventing recurrences at one year but was associated with frequent drop-outs due to side effects. The immunomodulators, 6-mercaptopurine, azathioprine, and methotrexate, are often prescribed for this purpose based on their greater potency as an immune response modifying drug and their role as maintenance therapies in other immune disorders. There is some evidence for efficacy in this role, although a recent controlled trial demonstrated modest but statistically significant benefit for 6-MP 50 mg daily.

Another factor that influences gastroenterologists and patients is that some or all of these medications were tried and failed to prevent the initial operation. Nonetheless, it is still common practice to either prescribe one of the above medications or wait to see what happens.

Surveillance

Given the limitations of prophylactic therapies, an endoscopic surveillance program permits the detection of endoscopic recurrences at a pre-clinical state. In Rutgeerts’ study, patients with endoscopic recurrence at three months post-resection were four times more likely to have a clinical recurrence at 12 months than those without endoscopic recurrence. The Rutgeerts’ endoscopic scoring system can be easily applied for evaluation of anastomotic findings at colonoscopy (table 1). The colonoscopy should be done at six or 12 months post-op and repeated annually. The timing, six or 12 months, can be determined by the severity of the condition pre-operatively.

Wireless capsule (WCAP) endoscopy is also a valuable tool for surveillance. Its value in this role has been documented and is most useful for patients with inaccessible anastomoses, i.e. beyond the reach of the enteroscope or colonoscope. In addition, WCAP may demonstrate small bowel ulceration proximal to the anastomosis that was not apparent at the time of surgery.

Treatment of recurrence

Identification of endoscopic recurrence justifies the use of biologic therapies to both heal and prevent future recurrences. Although anti-TNF therapies have not been tested in this role, it is likely that their efficacy would be at least as good as with symptomatic disease. The predictive value of significant endoscopic recurrence and the high likelihood of clinical recurrence in this group justify this form of therapy. Rutgeerts’ scores of 2 or greater should either be treated directly or should warrant a WCAP to evaluate the rest of the small bowel.

In summary, an aggressive endoscopic surveillance approach should be taken in Crohn’s patients following resective surgery. It is important for gastroenterologists to be proactive rather than reactive with these high-risk patients.

Dr. Ippoliti is Director of Administration and Clinical Affairs in Cedars-Sinai’s Division of Digestive Diseases. E-mail: Andrew.Ippoliti@cshs.org

Selected articles


Rutgeerts’ Endoscopic Scoring System

<table>
<thead>
<tr>
<th>Score</th>
<th>Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>i0</td>
<td>No lesions</td>
</tr>
<tr>
<td>i1</td>
<td>&lt;5 aphthous lesions</td>
</tr>
<tr>
<td>i2</td>
<td>&gt;5 aphthous lesions with normal mucosa between the lesions, skip areas of larger lesions, or lesions confined to the ileocolonic anastomosis (that is, &lt; 1 cm in length)</td>
</tr>
<tr>
<td>i3</td>
<td>Diffuse aphthous ileitis with diffusely inflamed mucosa</td>
</tr>
<tr>
<td>i4</td>
<td>Diffuse inflammation with larger ulcers, nodules and/or narrowing</td>
</tr>
</tbody>
</table>