Endoscopic Management of Ulcer Disease

David Fleischer\textsuperscript{a}

\textit{Division of Gastroenterology, Georgetown University,}\n\textit{Washington, D.C.}\n
(Received February 25, 1994; sent for revision July 15, 1994; accepted August 22, 1994)

Endoscopy has revolutionized the management of digestive diseases in general and ulcer disease in particular. It allows the physician to view the pathologic process directly, and with biopsy and cytology techniques, to obtain histological samples. Endoscopy helped to usher in the field of minimally invasive therapy and endoscopic treatment of bleeding ulcers and is now a standard form of treatment. This overview is divided into three parts: first, the current diagnostic and therapeutic endoscopic management of ulcer disease will be addressed; second, some of the current work that should have future applications in the same area will be discussed. Finally, some conceptual ideals that look further beyond future applications will be addressed.

CURRENT APPLICATIONS

Diagnostic endoscopy

Esophagogastroduodenoscopy (EGD)\textsuperscript{b} or upper endoscopy is used with increasing frequency either as a replacement for upper GI radiographs (upper GI series), as a complementary study for the evaluation of “ulcer” symptoms or for upper GI bleeding. In addition to the fact that EGD is more sensitive than upper GI X-rays, it also allows the physician to sample tissue (for example, biopsies, cytology or \textit{Helicobacter pylori}). It is also common to use EGD for follow-up evaluation of gastric ulcers.

Therapeutic endoscopy

There currently is little application of endoscopy to the management of primary ulcer disease; rather, endoscopy has mainly been used for the management of complications of ulcer disease (bleeding, obstruction or perforation). There are some proposed endoscopic managements of the primary disease, and that will be addressed with future applications. Most commonly, endoscopy is used for the diagnosis and therapy of bleeding ulcers. The endoscopic options are shown in Table 1 [1].

At an NIH Consensus Conference in 1989, it was concluded that endoscopic therapy was beneficial in the management of bleeding ulcers [2]. The panelists concluded that multipolar electrocoagulation, heater probe, Nd:YAG laser and injection therapy all might be of benefit. They did not feel that topical therapies, Argon laser or monopolar electrocautery should be utilized.

Evidence that the multipolar electrocoagulation (MPEC) is of benefit comes from two studies. The first study included 44 patients with evidence of upper GI bleeding. MPEC treatment resulted in significant improved hemostasis, reduction in transfusion requirements, decreased need for urgent surgery and shorter periods of hospitalization [3].

\textsuperscript{a}To whom all correspondence should be addressed: Division of Gastroenterology, Georgetown University Hospital, 3800 Reservoir Road, NW, Washington, D.C. 20007. Tel: (202) 678-8741; Fax: (202) 784-3957.

\textsuperscript{b}Abbreviations used: EGD, esophagogastroduodenoscopy; MPEC, multipolar electrocoagulation; EUS, endoscopic ultrasonography; LIFS, laser induced fluorescent spectroscopy.
Table 1. Endoscopic treatment for gastrointestinal bleeding

A. Topical:
   1. Tissue adhesives
   2. Collagen
   3. Clotting Factors
   4. Ferromagnetic tamponade

B. Injection:
   1. Sclerosing agents
   2. Vasoconstricting agents

C. Mechanical:
   1. Clips
   2. Balloons

D. Thermal:
   1. Electrocoagulation
   2. Heat probe
   3. Laser
   4. Cryotherapy

E. Combination

Whereas the first study had evaluated MPEC for the treatment of active bleeding and lesions, the second study looked at nonbleeding visible vessels in ulcers. MPEC treatment reduced rebleeding, and the need for urgent surgery, transfusion requirements, length of hospitalization and hospital costs were also lowered in the treated group [4].

Heater probes have also been useful for ulcer hemostasis [5]. Randomized trials have shown significant benefit. In a study from Scotland, patients with active bleeding or visible vessel were randomized to medical/surgical treatment or heater probe medical treatment. The latter reduced rebleeding rates [6].

One hundred and thirty-seven patients with severe upper GI bleeding were prospectively evaluated in a study from China [7]. The patients treated with heater probe had better outcomes than those treated with alcohol injection or those in a medical treatment group. A study from UCLA compared medical treatment, MPEC and heater probe treatment. The latter two groups had reduced bleeding rates, transfusion requirements and the need for urgent surgery [8].

Although Nd:YAG laser is not commonly employed for endoscopic management of GI bleeding, good efficacy has been reported with that form of treatment. Twelve randomized, controlled trials compared laser treatment with other forms of therapy. In the large majority of trials, there has been significant benefit from laser therapy [9-20].

The NIH Consensus Conference rated injection therapy as very promising, but at the time of the Conference in 1989, only a few studies had been performed. Subsequent to that meeting, injection therapy has become a procedure that is commonly employed. Panes and colleagues [37] compared injection therapy with medical treatment in a group of patients, and there was a significant reduction in rebleeding rates, transfusion requirements and need for urgent surgery. Chung and associates [24] randomized patients with actively bleeding ulcers into injection therapy or medical therapy. Transfusion requirements and need for urgent surgery were reduced in the injection group [21]. Several other controlled trials yielded similarly favorable results [22-25].

The choice of endoscopic therapy is largely dictated by the endoscopist's personal preference. There is a consensus that endoscopic therapy is effective and safe for the
management of bleeding peptic ulcers. The studies quoted above attest not only to the efficacy of endoscopic therapy but also to its safety. The most serious complication, perforation, occurs in one percent or less of treatments.

There has been a debate about which ulcers are most amenable to treatment. The endoscopic appearance of the ulcer affects that decision. Table 2 shows the prognostic implications of the endoscopic appearance of the ulcer at the time of endoscopy [26].

It can be appreciated that the endoscopic finding is a relevant factor in determining whether or not to institute endoscopic therapy. There is a general consensus that an ulcer with a clean base should not be treated. There is divergence of opinion as to whether or not a nonbleeding visible vessel should be treated, since approximately one half rebleed and one half do not.

There are some limitations to endoscopic therapy. Some limitations exist because the situation is clinically difficult. If the patient is hemodynamically unstable or cannot be sedated, these present clinically difficult problems. Other situations are technically difficult. In some cases, the problem is access, either because there is overlying blood or the bleeding point is at a spot where endoscopic access is difficult (e.g., just inside the bulb). In other cases, the situation is technically difficult because our current therapies are ineffective. Often times, bleeding in the posterior duodenum is from a branch of the gastro-duodenal artery, and if the size of the vessel is greater than 1 mm, endoscopic therapies may be ineffective. Finally, sometimes the problem is conceptually difficult. What should be done in the case of rebleeding or if a bleeding source is not obvious after evaluation?

Current research is addressing the limitations of endoscopic therapy with the hopes that solutions to these problems might emerge. Some examples of potential solutions are as follows. Use of an endoscopic Doppler might allow better definition of flow below the surface of a nonbleeding visible vessel. Kohler and Riemann demonstrated the benefit of endoscopic Doppler application [27]. An approach to dealing with the vessel that is "too large" involves the use of endoscopic clips or sutures.

Endoscopic therapy has also been used for gastric outlet obstruction. Benjamin et al. described the use of endoscopic balloon dilation for pyloric stenosis secondary to scarring from previous ulcer disease [28]. A series of balloons that can be used endoscopically now exist for this application.

The conventional wisdom is that surgery is and should be the management of a perforated ulcer. Traditionally, that surgery has been via an open laparotomy. However, there are some reports of either laparoscopic or endoscopic sewing to close off a perforation.

FUTURE APPLICATIONS

It is interesting to speculate how some of the newer diagnostic technologies that are being applied to gastrointestinal endoscopy might be utilized for the management of ulcer disease:

| Endoscopic findings       | Risk of continued bleeding (%) | Incidence of findings (%) |
|---------------------------|--------------------------------|---------------------------|
| Spurting artery           | 85%                            | 8%                        |
| Visible vessel (nonbleeding) | 51%                          | 26%                       |
| Overlying clot            | 41%                            | 18%                       |
| Central red/black spot    | 5%                             | 12%                       |
| Clean base                | 0%                             | 36%                       |

Table 2. Prognostic implication of appearance of ulcer at the time of endoscopy
Diagnostic applications

With the advent of electronic endoscopes, a digitized image was created [29]. With an electronic endoscope as opposed to a fiberoptic endoscope, the creation of a digital image allows it to be combined with computer technology. Yamaguchi et al. utilized this principle in determining the three-dimensional gastric ulcer size [30]. Tsuji et al. used digitized endoscopy for the analysis of mucosal blood hemoglobin distribution [31].

Endoscopic ultrasonography (EUS) is employed in the evaluation of digestive diseases. It is commonly used to stage gastrointestinal malignancies. However, it would be possible to use EUS to help distinguish between benign and malignant ulcers or to better understand ulcer healing. Laser induced fluorescent spectroscopy (LIFS) is another technology that might be applied to better understand gastric physiology. Its primary application in the digestive tract to date has been to characterize benign versus malignant polypoid disease. However, it would also be possible to use similar principles to study mucosal hemodynamics [32].

Therapeutic applications

Many pioneers of gastrointestinal endoscopy have realized that if the endoscope can deliver the investigator to the pathologic process then therapy should be possible. Joffe and Sankar describe the endoscopic vagotomy and antrectomy [33]. Using contact Nd:YAG laser therapy, they demonstrated, in a canine model, that if the G cells of the antrum were destroyed with the laser and the pathway to the vagal nerves interrupted then acid secretion could be reduced. This procedure was carried out completely via endoscopy.

Another advance in the area of minimally invasive therapy is the field of endo-organ surgery. With this technique, multiple access ports are created between the abdominal wall of the stomach using modified gastrostomy ports [34]. This would allow for the introduction of instruments into the stomach (and esophagus and small bowel) for management of GI conditions. Endo-organ funduplications have been carried out as well as techniques for managing major gastrointestinal hemorrhage.

With the appreciation that H. pylori is likely involved in the pathogenesis of some ulcers, some investigators have speculated about the endoscopic eradication of H. pylori. Others have raised the possibility of other endoscopic approaches which may be beneficial in ulcer healing. These have included photostimulation, the endoscopic delivery of medical therapy, injection treatment of a healing factor or even molecular modulation.

BEYOND FUTURE APPLICATIONS

The parallel in convergent technologies that exist both within medicine and other areas have led to incredible speculations. Application of the work that is being done in the areas of computer science, defense systems, space technology and entertainment can all have applications for medicine in general and the management of ulcer disease in specific. The applications of robotics, telepresence and virtual reality may all have a role in the management of ulcer disease [35]. Conceivably, a robotic endoscope could be swallowed by the patient and guided to the site of the bleeding ulcer where robotic therapy could be delivered. By telepresence technology, the surgeon or endoscopist in one city might operate on a patient with an ulcer residing in another city. And finally in the application of virtual reality technology, the treating physician may “fly” into the cell and alter the sodium-potassium-ATPase pump which regulates acid secretion.

It can be seen that endoscopy is very important in the management of ulcer disease. The ulcer can be precisely localized and characterized. In situations where bleeding occurs, a wide range of endoscopic therapies are available, many of which have been
proven to be safe and effective. The potential to develop even more helpful diagnostic and therapeutic measures may be possible with several of the new technologies that are being applied to that task.

REFERENCES
1. Fleischer, D. Endoscopic therapy of UGI bleeding in man. Gastroenterology. 90:217-234, 1986.
2. Therapy for gastrointestinal bleeding. In: Geenen, J., Fleischer, D., and Waye, J., eds. Techniques in Therapeutic Endoscopy. New York: Gower; 1992, pp. 12.
3. Asaki, S. Tissue solidification in coping with digestive tract bleeding: Hemostatic effects of local injection of 99.5% ethanol. Tohoku J. Exp. Med. 134:223-227, 1981.
4. Asaki, S., Nishimura, T., Satoh, A., Asaki, S., Nishimura, T., Satoh, A., and Goto, Y. Endoscopic control of gastrointestinal hemorrhage by local injection of absolute ethanol: a basic assessment of the procedure. Tohoku J. Exp. Med. 1940:339-352, 1983.
5. Asaki, S., Sato, H., Nishimura, T., Ohkubo, S., Yamagata, R., Ito, R., Saito, Y., Miyazaki, S., and Yaginuma, N. Endoscopic assessment of the esophagogastric junction (The Mallory-Weiss syndrome). Gastrointest. Endosc. 32:318-323, 1986.
23. Chiozzini, G., Bortoluzzi, F., Pallini, P., Betetto, G., Constantini, R., Costa, F., Vitalba, A., and Saggiono, A. Controlled trial of absolute ethanol vs. epinephrine as injection agent in gastroduodenal bleeding [Abstract]. Gastroenterology 98:A31, 1990.
24. Chung, S.C.S., Leung, J.W.C., Steele, R.J.C., Crofts, T.J., and Li, A.K. Endoscopic injection of adrenaline for actively bleeding ulcers: a randomized trial. Brit. Med. J. 296:1631, 1988.
25. Chung, S.C.S., Leung, J.W.C., Lo, K.K., So, L.Y.S., and Li, A.K.C. Natural history of the sentinel clot: an endoscopic study [Abstract]. Gastroenterology 98:A31, 1990.
26. Cunningham, J. Gastric telangiectasias in chronic hemodialysis patients: a report of six cases. Gastroenterology 81:1131-1133, 1981.
27. Kohler, R. and Riemann, J.F. Endoscopic Doppler: evaluation of bleeding gastroduodenal ulcers. Scand. J. Gastroenterology 27:51, 1991.
28. Benjamin, S.B., Cattau, E.L., and Glass, R.L. Balloon dilation of the pylorus: therapy for gastric outlet obstruction. Gastrointest. Endosc. 28:253-254, 1981.
29. Sivak, M.V. and Fleischer, D.E. Colonoscopy with a videoendoscope: preliminary experience. Gastrointest. Endosc. 30:1-5, 1984.
30. Yamaguchi, M., Okazaki, Y., Yanai, H., and Takemoto, T. Three-dimensional determination of gastric ulcer size with laser endoscopy. Endosc. 20:263-266, 1988.
31. Tsuji, S., Sato, N., Kawana, S., and Kamada, T. Functional imaging for the analysis of the mucosal blood hemoglobin distribution using electronic endoscopy. Gastrointest. Endosc. 34:332-336, 1988.
32. Yakshe, P.N., Bonner, R.F., Cohen, P., Leon, M.B., and Fleischer, D.E. Laser-induced fluorescence spectroscopy may distinguish colon cancer from normal human colon. Am. J. Gastro. 35:184, 1989.
33. Leung, F.W., Slodownik, E., Jensen, D.M., Van Deventer, G.M., and Guth, P.H. Gastroduodenal mucosal hemodynamics by endoscopic reflectance spectrophotometry. Gastrointest. Endosc. 33:284-288, 1987.
34. Joffe, S. and Sankar, M. Endoscopic vagotomy and antrectomy. Lasers Tokyo '81. Tokyo, 1981.
35. Larson, D.E., Burton, D.D., Schroeder, K.W., and DiMagno, E. Percutaneous endoscopic gastrostomy. Indications, success, complications, and mortality in 314 consecutive patients Gastroenterology 93:48, 1987.
36. Satava, R.M. Robotics, telepresence, and virtual reality: a critical analysis of the future of surgery. Minimally Invasive Therapy 1:357, 1992.
37. Panés, J., Viver, J., Forné, M. Randomized comparison of endoscopic microwave coagulation and endoscopic sclerosis in the treatment of bleeding peptic ulcers. Gastrointest. Endosc. 37:611-616, 1991.