Digestive Diseases and Sciences (2023) 68:4297–4300
https://doi.org/10.1007/s10620-023-08115-9

PROFILES AND PERSPECTIVES

DDS Perspective: If Gastroenterology Were a Dog, Would Endoscopy Be Its Tail? Has Therapeutic GI Endoscopy Learned to Wag the Dog?

Richard A. Kozarek[1,2]

Received: 19 August 2023 / Accepted: 14 September 2023 / Published online: 5 October 2023

I trained in the mid-1970s. A clinical gastroenterology fellowship was 2 years in length at that time, and unless you were engaged in bench research and/or continuing to work toward a PhD, you were presumed to have absorbed enough relevant information to practice independently: Ulcers were caused by too much acid and treated with antacids or a Sippy diet, reserving resective surgery and/or truncal, selective, or highly selective vagotomy for patients with complications or medical failures; inflammatory bowel disease was treated with sulfasalazine and steroids, less frequently with azathioprine or 6-mercaptopurine; refractory gastroesophageal reflux warranted elevation of the bed head and antacids, as histamine-2 receptor antagonists had yet to be introduced, with a steady pool of patients requiring esophageal bougienage for distal esophageal strictures; virtually all esophageal cancer was squamous cell carcinoma. What else did I "know" when I finished my training? Viral hepatitis was A, B, or non-A, non-B and chronic hepatitis was separated into chronic persistent and chronic active, the former a benign process and the latter with the potential to cause cirrhosis. Obstructive jaundice was a surgical disease or, in high-risk patients, treated with a percutaneous transhepatic biliary drain (PTBD). Almost everything I learned at the time was rudimentary or would be proven wrong.

Endoscopy, in turn, was primarily a diagnostic procedure, although we did remove colon polyps and applied it both diagnostically and prognostically to facilitate therapies to include esophageal dilation using Maloney or Hurst mercury-filled dilators or Eder-Puestow metal olives under fluoroscopic guidance. Additional therapeutics included placing plastic prostheses fashioned from Tygon tubing. The sole treatments for bleeding at the time of my fellowship was placement of a Sengstaken-Blakemore balloon to tamponade actively bleeding esophageal or fundal varices or infusing the stomach with ice water for bleeding ulcers in an attempt to induce vascular constriction.

Evolving Endotherapy

Allow me to delineate the three areas of technologic advancements that I believe were pivotal to the initial development of therapeutic endoscopy. Although not the first therapeutic innovation, from my perspective it was the development of multiple treatments for gastrointestinal (GI) bleeding that were adopted by general gastroenterologists and integrated into their practices that launched the field of therapeutic endoscopy. In our own unit, this started with the marketing of injection needles, using a variety of sclerosants that included sodium morrhuate and sodium tetradecyl sulfate, among others, to treat bleeding esophageal varices [1].

Although randomized, controlled trials have relegated most sclerosants as both less effective and associated with a higher rate of adverse events when compared to band ligation [2], a variety of injection solutions are still used to treat peptic ulcers [1, 3], Mallory-Weiss tears, and Dieulafoy lesions. These include various forms of cyanoacrylate (superglue) preparations to treat esophagogastric and ectopic enteral varices. However, it was the development of "coaptive" coagulation probes—bipolar and multipolar cautery and heater probes–that changed the equation for massive or recalcitrant peptic ulcer bleeding from surgical to endoscopic control [3]. Subsequent innovations came quickly: Nd-YAG laser, argon plasma coagulation, through-the-scope (TTS) and over-the-scope (OTSCs) clips [4], hemostatic powders [5], and most recently, self-assembling hemostatic peptides [6]. These techniques have been variably used and

A profile of Richard A. Kozarek is available at https://doi.org/10.1007/s10620-023-08116-8.

✉ Richard A. Kozarek
richard.kozarek@virginiamason.org

[1] Emeritus Executive Director, Digestive Disease Institute, Virginia Mason Medical Center, 1100 Ninth Ave, Seattle, WA 98101, USA

[2] Clinical Investigator, Center for Interventional Immunology, Benaroya Research Institute, 1201 Ninth Ave, Seattle, WA 98101, USA

have expanded the available treatments in our endoscopic quiver.

Endoscopy Therapy for GI Strictures

Dilating Balloons

Although various dilating balloons had been used for decades to treat achalasia, anatomic considerations historically limited most endoscopic therapy for GI stenoses other than those in the esophagus and distal colorectum. It took the development of endoscopically facilitated dilation balloons that required placement of a guidewire across a stenosis for gastroenterologists to be able to treat GI strictures fluoroscopically [7]. Realistically, the majority of these dilations could have been done by an interventional radiologist without our help, although the latter would invariably have required an additional procedure if the stenosis was first diagnosed endoscopically. Those balloons subsequently were designed to be passed through the endoscopic (TTS) and have further evolved as controlled/continuous radial expansion (CRE) balloons that can stretch or fracture a stricture with increments of balloon diameter up to a maximum of 5 mm. The latter technology has revolutionized the treatment of both esophageal and non-esophageal strictures to include benign anastomotic, pyloric, small bowel, and colonic stenoses, and there have been multiple reports confirming efficacy, with lower costs and fewer adverse events when compared to surgery [8–10].

Balloon dilation and radial incision of refractory benign stenoses [10] have also been applied for short refractory esophageal, anastomotic, pyloric, and Crohn's enteral stenoses. More recently, dilating balloons have played a bit part or have been abandoned altogether in the setting of per-oral endoscopic myotomy (POEM) for achalasia [11] and endoscopic pyloromyotomy for pyloric stenosis or gastroparesis.

Self-Expandable Metal Stents (SEMS)

Although SEMS were originally released in the luminal gut for unresectable esophageal malignancy [12], they quickly became an alternative to surgical gastrojejunostomy in the palliation of malignant gastric outlet obstruction [13, 14]. They have evolved from an uncovered mesh to a myriad of woven or braided metals, most commonly nitinol covered completely or in part most commonly with silicone [15]. Moreover, like dilating balloons, many SEMS have been mounted on shafts that fit through large channel gastroscopes or colonoscopes to allow concise placement under direct vision, often with concomitant fluoroscopy. Designed initially for malignancy, covered SEMS have also been utilized for refractory benign disease to include caustic esophageal strictures as well as recalcitrant Crohn's strictures in patients at high surgical risk [16].

Lumen-Apposing Metal Stents (LAMS)

In the continuously evolving field of treating GI luminal strictures, endoscopic ultrasound (EUS)–facilitated gastroenterostomy with a wide-flanged short-shaft LAMS has supplanted both enteral SEMS and laparoscopic gastrojejunostomy in many institutions for malignant and some benign gastric outlet obstructions. Both direct comparative studies and recent meta-analyses suggest comparable procedural success and survival as well as fewer adverse events and shorter hospitalization times compared with surgery and significantly fewer re-interventions when compared with enteral stent placement [17, 18].

LAMS have also been used with variable short- and long-term success for refractory anastomotic strictures, particularly those following Roux-en-Y gastric bypass and obstructing anastomotic colon strictures [19].

Biliary Endoscopic Sphincterotomy (ES)

If therapeutic endoscopy, other than colonoscopic polypectomy and esophageal dilation/prosthesis placement, was popularized with the treatment of upper GI bleeding and morphed into treating benign and malignant luminal stenoses throughout the GI tract, the most dramatic event from a personal perspective antedated both advances: the initial reports of endoscopic sphincterotomy in 1974 [20]. The latter procedure literally opened the door to the biliary tract, and later, the pancreas, allowing us to treat common bile duct symptoms that included biliary pain, obstructive jaundice, cholangitis, and recurrent biliary pancreatitis, as well as palliation of malignant obstructive jaundice [21]. Moreover, its application morphed into treating pancreatic duct strictures and stones in chronic pancreatitis and, in conjunction with EUS, treating the consequences of severe acute pancreatitis, including ductal disruptions and a smorgasbord of pancreatic fluid collections [22].

However, it was the innovation of laparoscopic cholecystectomy that led therapeutic endoscopy to supplant the surgeon in the management of common bile duct stones [23], and some of the more colorfully entitled editorials that I authored at the time focused on the interaction between laparoscopy and ERCP-sphincterotomy [24–26].

ES, now variably combined with large-diameter endoscopic balloon dilation (EBD), is not infrequently used in conjunction with the other previously described innovations in therapeutic endoscopy [27]. Procedure-related bleeding may require injection therapy with epinephrine, coaptive coagulation with bipolar cautery, balloon tamponade, and,

in refractory cases, placement of a covered biliary SEMS. Refractory stone disease is often temporized by placement of a plastic stent with subsequent procedures that may require mechanical (EHL) or laser lithotripsy (LL). Unresectable proximal or distal malignancy is now palliated primarily with SEMS to include LAMS inserted under EUS control through the stomach or duodenum.

Conclusion

It seems that we have come full circle, yet only scratched the surface of advances in therapeutic endoscopy, since I started my career. I failed to address the evolution of fiber endoscopes into videoscopes that can interface with a computer, image manager, report generator, and an evolving interface with artificial intelligence (AI). Nor have I discussed the simultaneous advancements in GI surgery and interventional radiology and our interdependence in caring for patients with GI disorders. Finally, I have failed to discuss a myriad of advances in endoscopic interventions: Percutaneous endoscopic gastrostomy, endoscopic approaches to obesity, endoscopic mucosal resection (EMR), and endoscopic submucosal dissection (ESD). However, if therapeutic advances in endoscopy are truly wagging the dog of gastroenterology, even a little, I can't wait for the "hair of the dog that bit me" almost 50 years ago.

References

1. Sarin SK, Kumar A. Sclerosants for variceal sclerotherapy: a critical appraisal. *Am J Gastroenterol.* 1990;85(6):641–649.
2. Stiegmann GV, Goff JS, Michaletz-Onody PA, Korula J, Lieberman D, Saeed ZA, Reveille RM, Sun JH, Lowenstein SR. Endoscopic sclerotherapy as compared with endoscopic ligation for bleeding esophageal varices. *N Engl J Med.* 1992;326(23):1527–1532.
3. Mullady DK, Wang AY, Waschke KA. AGA Clinical Practice Update on Endoscopic Therapies for Non-Variceal Upper Gastrointestinal Bleeding: Expert Review. *Gastroenterology.* 2020;159(3):1120–1128.
4. Sung JJ, Tsoi KK, Lai LH, Wu JC, Lau JY. Endoscopic clipping versus injection and thermo-coagulation in the treatment of non-variceal upper gastrointestinal bleeding: a meta-analysis. *Gut.* 2007;56(10):1364–1373.
5. Changela K, Papafragkakis H, Ofori E, Ona MA, Krishnaiah M, Duddempudi S, Anand S. Hemostatic powder spray: a new method for managing gastrointestinal bleeding. *Therap Adv Gastroenterol.* 2015;8(3):125–135.
6. de Nucci G, Reati R, Arena I, Bezzio C, Devani M, Corte CD, Morganti D, Mandelli ED, Omazzi B, Redaelli D, Saibeni S, Dinelli M, Manes G. Efficacy of a novel self-assembling peptide hemostatic gel as rescue therapy for refractory acute gastrointestinal bleeding. *Endoscopy.* 2020;52(9):773–779.
7. Kozarek RA. Hydrostatic balloon dilation of gastrointestinal stenoses: a national survey. *Gastrointest Endosc.* 1986;32(1):15–19.
8. Guo F, Huang Y, Zhu W, Wang Z, Cao L, Chen A, Guo Z, Li Y, Gong J, Li J. Efficacy and safety of endoscopic balloon dilation for upper gastrointestinal strictures of Crohn's disease. *Dig Dis Sci.* 2016;61(10):2977–2985.
9. Singh VV, Draganov P, Valentine J. Efficacy and safety of endoscopic balloon dilation of symptomatic upper and lower gastrointestinal Crohn's disease strictures. *J Clin Gastroenterol.* 2005;39(4):284–290.
10. Acar T, Aslan F, Acar N, Kamer E, Ünsal B, Hacıyanlı M. Role of endoscopic interventions and electroincision in benign anastomotic strictures following colorectal surgery. *Turk J Gastroenterol.* 2019;30(8):673–679.
11. Hasan A, Low EE, Fehmi SA, Yadlapati R. Evolution and evidence-based adaptations in techniques for peroral endoscopic myotomy for achalasia. *Gastrointest Endosc.* 2022;96(2):189–196.
12. Morgan R, Adam A. Use of metallic stents and balloons in the esophagus and gastrointestinal tract. *J Vasc Interv Radiol.* 2001;12(3):283–297.
13. Oh SY, Edwards A, Mandelson M, Ross A, Irani S, Larsen M, Gan SI, Gluck M, Picozzi V, Helton S, Kozarek RA. Survival and clinical outcome after endoscopic duodenal stent placement for malignant gastric outlet obstruction: comparison of pancreatic cancer and nonpancreatic cancer. *Gastrointest Endosc.* 2015;82(3):460–468.
14. Çağatay AK, Sayar S, Kılıç ET, Kahraman R, Öztürk O, Özdil K. The role of self-expandable metallic stents in the treatment of malignant strictures in all segments of the gastrointestinal tract. *Indian J Palliat Care* 2023;29(1):64–69.
15. Laasch HU. Current designs of self-expanding stents. In: Kozarek R, Baron T, Song HY, eds. New York: Springer; 2013.
16. Spaander MCW, van der Bogt RD, Baron TH, Albers D, Blero D, de Ceglie A, Conio M, Czakó L, Everett S, Garcia-Pagán JC, Ginès A, Jovani M, Repici A, Rodrigues-Pinto E, Siersema PD, Fuccio L, van Hooft JE. Esophageal stenting for benign and malignant disease: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2021. *Endoscopy.* 2021;53(7):751–762.
17. Chan SM, Dhir V, Chan YYY, Cheung CHN, Chow JCS, Wong IWM, Shah R, Yip HC, Itoi T, Teoh AYB. Endoscopic ultrasound-guided balloon-occluded gastrojejunostomy bypass, duodenal stent or laparoscopic gastrojejunostomy for unresectable malignant gastric outlet obstruction. *Dig Endosc.* 2023;35(4):512–519.
18. Boghossian MB, Funari MP, De Moura DTH, McCarty TR, Sagae VMT, Chen YI, Mendieta PJO, Neto FLP, Bernardo WM, Dos Santos MEL, Chaves FT, Khashab MA, de Moura EGH. EUS-guided gastroenterostomy versus duodenal stent placement and surgical gastrojejunostomy for the palliation of malignant gastric outlet obstruction: a systematic review and meta-analysis. *Langenbecks Arch Surg.* 2021;406(6):1803–1817.
19. Mizrahi M, Fahmawi Y, Merritt L, Kumar M, Tharian B, Khan SA, Inamdar S, Sharma N, Uppal D, Shami VM, Kashif MS, Gabr M, Pleskow D, Berzin TM, James TW, Croglio M, Baron TH, Adler DG. Luminal-apposing stents for benign intraluminal strictures: a large United States multicenter study of clinical outcomes. *Ann Gastroenterol.* 2021;34(1):33–38.
20. McHenry L, Lehman G. Approaching 50 years: The History of ERCP. In: Baron TH, Kozarek RA, Carr-Locke DL, eds. 3rd edn. Elsevier: Philadelphia; 2019; 1–6.
21. Solomon S, Baillie J. Indications for and contraindications to ERCP. In: Baron TH, Kozarek RA, Carr-Locke DL, eds. 3rd edn. Elsevier: Philadelphia; 2019; 54–58.
22. Vanella G, Bronswijk M, Arcidiacono PG, Larghi A, Wanrooij RLJV, de Boer YS, Rimbas M, Khashab M, van der Merwe SW. Current landscape of therapeutic EUS: changing paradigms in gastroenterology practice. *Endosc Ultrasound.* 2023;12(1):16–28.

23. Lyu Y, Cheng Y, Li T, Cheng B, Jin X. Laparoscopic common bile duct exploration plus cholecystectomy versus endoscopic retrograde cholangiopancreatography plus laparoscopic cholecystectomy for cholecystocholedocholithiasis: a meta-analysis. *Surg Endosc.* 2019;33(10):3275–3286.
24. Kozarek RA. Romancing the stones. *Gastrointest Endosc.* 1989;35(2):127–128.
25. Kozarek RA. Laparoscopic cholecystectomy: who does what, when and to whom? *Endoscopy.* 1992;24(9):785–787.
26. Kozarek RA. ERCP and laparoscopic cholecystectomy (the relationship is strained but they are still together for the children's sake). *J Clin Gastroenterol* 2001;33:183–184.
27. Li T, Hao LX, Lv C, Li XJ, Ji XD, Chen M, Liu C, Bie LK, Gong B. Long-term outcomes of endoscopic papillary large-balloon dilation (12–15 mm) with or without limited sphincterotomy for removal of bile duct stones. *Hepatobiliary Pancreat Dis Int.* 2023;22(4):392–398.