decreased odds for the presence of erosive esophagitis (odds ratio [OR], 0.11; 95% confidence interval [CI], 0.04–0.30) after adjusting for age, gender, and body mass index. The authors concluded that upper endoscopy was associated with a low diagnostic yield in patients with refractory GERD symptoms.

Comment. The American Society for Gastrointestinal Endoscopy guidelines recommend upper endoscopy as a diagnostic test for "GERD symptoms that are persistent or progressive despite appropriate medical therapy" (Gastrointest Endosc 2007;66:219–224). However, there are no recommendations stated regarding the role of repeat endoscopic examinations as a management tool for refractory GERD patients.

Studies have demonstrated that up to 70% of patients with GERD have normal endoscopic findings, most likely owing to prior use of PPI therapy (DDAS 2007;25:172–174; Gut 2004;53:1024–1031). There is a paucity of evidence to suggest that normal endoscopic findings might change over time, particularly in GERD patients on PPI therapy. For example, in a retrospective study examining whether Barrett's esophagus developed over time in a cohort of 500 patients with GERD and normal index endoscopic examination, none of the 400 patients with nonerosive disease developed erosive esophagitis or Barrett's esophagus during a mean of 3.5 endoscopic examinations that were performed over the course of 5 years. (APT 2006;25:83–91). However, in the cohort with 103 patients with erosive esophagitis at baseline or subsequent examinations, 5 (1%) were subsequently found to have Barrett's esophagus, suggesting either replacement of normal squamous epithelium with intestinal metaplasia after erosive esophageal injury, or nondetected intestinal metaplasia during initial examinations when erosive disease was present. In addition, none of the 169 Barrett's esophagus patients had normal index endoscopic examinations within a mean retrospective time period of 4.5 years (95% CI, 0%–2%). There are few data supporting repeat endoscopic examinations in patients with GERD and continuing symptoms if the index endoscopic examination was normal, unless there is a high suspicion for EoE and biopsies were not previously obtained.

A prior study by Fass et al examined the role of endoscopy and ambulatory pH monitoring comparing patients who were PPI responders (using once daily dosing) with PPI nonresponders. (Am J Gastroenterol 2009;104:2005–2013). The study included 24 patients in the PPI failure group and 23 patients in the PPI responder group. Endoscopy was normal in 63% of PPI failure patients and 76% of PPI success patients. Only grades A and B erosive esophagitis were observed in the PPI failure group (25%) and PPI success group (4%; $P = .1$) None of the patients had grades C or D erosive esophagitis. Short-segment Barrett's esophagus was seen in 3 (12%) of the PPI failure and 5 (22%) of the PPI success patients ($P = .5$). With regard to results of the pH monitoring studies, there was no difference in patients manifesting abnormal duodenogastroesophageal reflux while on PPI therapy (82% of PPI success patients and 67% of PPI failure patients; $P =$ NS). However, significantly more GERD symptoms in the PPI failure group were associated with acid reflux (64%) compared with DGER (41%; $P < .05$), suggesting that refractory symptoms were more likely related to acid reflux events. The findings of this study also support the practice of increasing PPI therapy to twice daily in refractory GERD patients rather than repeat upper endoscopic examination.

Finally, the major reason for repeat examination might be to examine for the presence of EoE, particularly in a GERD patient with dysphagia. A recent cost-effectiveness analysis (Gastroenterology 2010;138:S176–S177) examined the role of endoscopic biopsy for EoE in patients with refractory GERD symptoms on PPI therapy. Based on a literature review, the prevalence of EoE was 7% in GERD patients without dysphagia, and up to 15% in refractory GERD patients with dysphagia symptoms (Clin Gastroenterol Hepatol 2009;7:420–426; Am J Gastroenterol 2007;102:2627–2632). Using standard costs and probabilities, endoscopic with biopsy for EoE was not a cost-effective approach in patients with refractory GERD without dysphagia, but was within the acceptable threshold when the prevalence of EoE in refractory GERD exceeded 15%. Therefore, repeat biopsy for EoE should only occur in the setting of a high clinical suspicion and the appropriate clinical symptoms.

In summary, a growing body of literature suggests that a repeat endoscopic examination in a patient with refractory GERD symptoms on PPI therapy will be associated with a low diagnostic yield. In patients demonstrating erosive esophagitis on index examination, repeat EGD may be indicated to document healing and exclude underlying intestinal metaplasia. Gone are the days when >50% of patients receiving H_2-receptor antagonists as first-line GERD therapy manifested erosive changes that could be considered diagnostic for GERD. The superior healing capabilities of the PPIs have reduced the utility of the endoscopic examination as a diagnostic test for GERD. Instead, performance of ambulatory esophageal pH monitoring and esophageal manometry should be considered to help guide further management for these refractory GERD patients.

LAUREN B. GERSON, MD, MSc
Division of Gastroenterology and Hepatology
Stanford University School of Medicine
Stanford, California

TO DRAIN OR NOT TO DRAIN: THAT IS THE QUESTION

Van der Gaag NA, Rauws EAJ, van Eijck CHJ, et al. **(Academic Medical Center, Amsterdam, The Nether-**

lands). Preoperative biliary drainage for cancer of the head of the pancreas. N Engl J Med 2010;362:129–137.

Pancreatic cancer remains the 4th leading cause of cancer related deaths in the United States (N Engl J Med 2010;362:170–172). Cancer of the pancreatic head or periampullary region commonly presents as jaundice secondary to obstruction of the bile duct from tumor encasement. The only potentially curative option for pancreatic cancer is operative resection. In patients with biliary obstruction who are considered candidates for resection, biliary drainage is often performed before surgery. This practice is based on the argument that preoperative biliary drainage (PBD) may translate into improved surgical outcomes by restoring metabolic abnormalities associated with obstructive jaundice (J Gastrointest Surg 2009;13:814–820). However, to date, the evidence supporting PBD in this particular setting is equivocal (Pancreas 2010;39:119–126; Cochrane Database Syst Rev 2008;CD005444; Cochrane Database Syst Rev 2007;CD006001; Gastrointest Endosc 2002;56:529–534).

In this study by van der Gaag et al (N Engl J Med 2010;362:129–137), the authors address this issue by comparing PBD with early surgery for patients with cancer of the pancreatic head. In this multicenter, prospective, randomized, controlled trial, the authors randomly assigned 202 patients with biliary obstruction and with no evidence of distant disease or local vascular involvement, to undergo either PBD for 4–6 weeks followed by surgery, or surgery alone within 1 week after diagnosis. The biliary drainage procedure of choice was endoscopic retrograde cholangiopancreatography (ERCP) with plastic stent placement. Percutaneous transhepatic cholangiography with stent placement was performed as a salvage procedure in case of a failed ERCP. The primary outcome was the rate of serious complications within 120 days after randomization. The secondary outcomes were mortality and length of hospital stay. The study was designed to conduct a noninferiority test of the primary outcome with the null hypothesis that surgery alone was inferior to PBD followed by surgery. The participating centers in the study performed ≥10 cancer resections of the pancreatic head per year. The endoscopists performing the endoscopic procedures were experienced clinicians. All complications were reviewed and adjudicated by a committee in a blinded fashion. Sample size calculations for the primary outcome were based on a previously published meta-analysis by the authors (Ann Surg 2002;236:17–27). Statistical analysis involved an intention-to-treat analysis with comparison of the proportion of patients with serious complications in the cases versus the controls.

Of the 200 enrolled patients, 102 patients were randomized to PBD followed by surgery 4–6 weeks later, and 94 patients were randomized to early surgery. Adequate biliary drainage was achieved in 75% of patients on the first endoscopic attempt; after a second attempt, either endoscopic or percutaneous, adequate drainage was achieved in 94% of patients. The mean time to surgery was 5.2 weeks in the PBD group and 1.2 weeks in the group randomized to early surgery. Overall serious complications were reported in 39% of patients in the early surgery group and 74% of patients in the PBD group; relative risk of serious complications in the early surgery group versus the PBD group was 0.5 (95% confidence interval [CI], 0.41–0.71). ERCP-related complications including pancreatitis, perforation, bleeding, and cholangitis were seen in 46% of patients. Surgery-related complications were reported in 37% of patients in the early surgery group and in 47% of patients in the PBD group (relative risk, 0.79; 95% CI 0.57–1.11). There was no difference in the overall mortality and length of hospital stay between the 2 groups. The authors conclude that routine PBD in patients undergoing surgery for cancer of the pancreatic head increases the rate of complications.

Comment. Operative resection remains the only curative option for pancreatic cancer. With increasing surgical procedural volumes at specialized centers, mortality rates from surgery have improved in the past 20 years to rates of ≤5% (Pancreas 2010;39:119–126); however, pancreaticoduodenectomy is still associated with high morbidity rates, estimated at 40%–60% (J Gastrointest Surg 2009;13:814–820), with postoperative complications including anastomotic leak, hemorrhage, delayed gastric emptying, impaired wound healing, sepsis, pneumonia, and renal failure.

In an effort to improve the morbidity and mortality associated with this procedure, researchers have attempted to identify potential risk factors for adverse outcomes. Cholestasis from biliary obstruction is considered to be 1 such risk factor. This is based on the recognition that cholestasis promotes a proinflammatory state, may impair cellular immune responses (Am Coll Surg 1995;181:567–581), and leads to hepatic dysfunction resulting in impaired blood clotting function (J Gastrointest Surg 2009;13:814–820). Hence, preoperative biliary decompression to reduce cholestasis is routinely practiced before pancreaticoduodenectomy, particularly if a delay between the diagnosis and surgery is foreseen. In addition, other factors contributing to the decision to perform preoperative biliary drainage include patient symptoms such as cholangitis and severe pruritis, delay in staging workup, and/or surgeon preferences.

Several studies have attempted to determine whether preoperative biliary drainage actually improves outcome after operative resection. Much of the available information has been derived from data from retrospective studies. Only a small number of prospective, randomized trials addressing this question have been performed (Pancreas 2010;39:119–126). A majority of these trials have