

Preop Biliary Drainage Not Helpful in Patients With Obstructive Jaundice

Preoperative Biliary Drainage for Cancer of the Head of the Pancreas.

Van der Gaag NA, Rauws EAJ, et al:

N Engl J Med 2010; 362 (January 14): 129-137

Delaying surgery to drain the biliary tree in patients with obstructive jaundice due to pancreatic cancer results in more complications.

Background: There has been a long-observed association between being severely icteric due to obstructive jaundice and having a more complicated postoperative course. Several trials in the past have indicated that preoperative transcutaneous biliary decompression does not reduce the subsequent surgical morbidity or mortality. There are fewer data available for endoscopic drainage.

Objective: To assess the value of performing endoscopic drainage along with a 4- to 6-week delay (to allow damage in the liver to heal) compared to immediate surgery on subsequent clinical outcome.

Design: Randomized controlled trial.

Participants: Icteric patients with suspected pancreatic cancer causing obstruction of the common bile duct.

Methods: Patients who could be randomized within 4 days of a CT scan were assigned to 1 of 2 arms: (1) preoperative endoscopic biliary drainage employing a plastic stent and a subsequent 4- to 6-week wait to allow any secondary damage in the liver to resolve; or (2) surgery alone within 1 week of the diagnosis. The primary outcome was the rate of serious complications within 120 days of randomization; the various complications were defined a priori. The secondary outcomes included mortality and length of hospital stay. The patients were seen 2, 6, and 12 weeks after hospital discharge. The complications were classified by an adjudication committee that was unaware of the group assignment. There was adequate generation of the randomization scheme and concealment of allocation. A non-inferiority sample size calculation indicated that 94 patients would be needed in each group. An interim analysis was planned halfway through the study.

Results: 202 patients were randomized, but 6 were subsequently excluded, leaving 94 in the early surgery arm and 102 in the preoperative biliary drainage arm. Approximately 90% to 95% of the patients in each arm had pancreatic cancer as the cause of the obstructive jaundice. The rate of serious complications was significantly higher in the preoperative biliary drainage group (75% vs 39%), mainly because of the large number of complications associated with the first drainage procedure. These patients were in the hospital for an average of 2 days longer. No difference was seen in the mortality rate.

Conclusions: Routine preoperative biliary drainage increases the rate of complications.

Reviewer's Comments: This trial validates the previous observation regarding the lack of utility of preoperative drainage for patients with obstructive jaundice. It also points out the danger of making policy decisions based on observations of association and assuming that the association is causative. (Reviewer-Ronald L. Koretz, MD).

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Keywords: Pancreatic Cancer, Obstructive Jaundice

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Know the Risk Factors for Screening, Surveillance Colonoscopy

Serious Complications Within 30 Days of Screening and Surveillance Colonoscopy Are Uncommon.

Ko CW, Riffle S, et al:

Clin Gastroenterol Hepatol 2010; 8 (February): 166-173

Complications with colonoscopy are rare. Risk factors for complications include polypectomy with cautery and preprocedure warfarin and clopidogrel.

Objective: To determine the risk of serious complications after colonoscopy for colorectal cancer screening.

Methods: This was a prospective cohort study of patients aged ≥ 40 years undergoing colonoscopy for screening, personal history of colorectal polyps, family history of polyps or colon cancer, or follow-up of screening abnormalities. Eighteen sites from the Clinical Outcomes Research Initiative National Endoscopic Database participated in the study. Endoscopy reports with specific fields had to be completed before they could be finalized (approximately 76% from community-based practices). A standardized telephone questionnaire was administered concerning complications when patients were contacted 7 and 30 days after the procedure. Hospital records were obtained in a percentage of patients to validate that serious complications occurred as described by patients. Eighty-five percent (18,271 of 21,375) of the enrolled population were contacted and followed up for 30 days. The primary outcome of the study was serious complications related to colonoscopy.

Results: Of 18,271 cases followed for 30 days, the incidence of complications at the time of colonoscopy was 12.9 per 1000 ($n=276$), of which 160 cases (7.5 per 1000) were related to respiratory depression and 105 (4.9 per 1000) were related to cardiovascular events (bradycardia or hypotension). Reversal medications (atropine, flumazenil, and/or naloxone) were administered in 62 patients (2.9 of 1000). Secondary outcomes included later complications. Gastrointestinal bleeding was the most common ($n=34$; 1.59 per 1000) while other complications included perforation ($n=4$; 0.19 per 1000), postpolypectomy syndrome ($n=2$; 0.09 per 1000), and diverticulitis ($n=18$; 0.84 per 1000; hospitalized patients, $n=5$; 0.23 per 1000). Twenty-eight complications (MI, angina, or stroke) were potentially related to colonoscopy (1.31 of 1000). Overall, there were 68 patients with later complications (possibly) related to colonoscopy (3.1 per 1000). Multivariate analysis revealed that an increased complication rate was noted with a polypectomy with cautery (OR, 6.71), >1 polyp removed with cautery (OR, 12), and preprocedure warfarin (OR, 2.88) or clopidogrel (OR, 2.69) but not ASA or NSAIDs. Three deaths were identified: end-stage liver disease, identified in the pretransplant evaluation; 1 aspiration pneumonia found 33 days later; and 1 death that occurred 3 days after colonoscopy but cause was unknown.

Conclusions: Complications associated with screening or surveillance colonoscopy are uncommon. During the procedure, respiratory and cardiovascular events are the most common complications. After the procedure, gastrointestinal bleeding is the most common complication. Risk factors include polypectomy with cautery and preprocedure warfarin and clopidogrel.

Reviewer's Comments: While this study demonstrates the relative safety of colonoscopy, it does point out the myriad of possible complications that can occur. As we see older, healthy patients requesting surveillance colonoscopy, we must always weigh the risks and benefits of the procedure. (Reviewer-Roy K.H. Wong, MD).

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Keywords: Complications, Colonoscopy, Screening, Surveillance

Print Tag: Refer to original journal article

BE Peaks in Caucasian Men at Age 50

Age- and Sex-Specific Yield of Barrett's Esophagus by Endoscopy Indication.

Rubenstein JH, Mattek N, Eisen G:

Gastrointest Endosc 2010; 71 (January): 21-27

The incidence of Barrett's esophagus increases steeply starting around age 30 and plateaus around age 50 years.

Background: Screening for Barrett's esophagus (BE) has been recommended. However, determining which patients need to be screened and at what age have yet to be determined.

Objective: To determine the age-specific yield of endoscopy for BE stratified by age and sex.

Design: Retrospective cross-sectional study.

Participants: 155,641 adult patients undergoing first endoscopy at a Clinical Outcomes Research Institute (CORI) site. Surveillance cases were excluded, and age, sex, and indications were recorded.

Methods: The CORI database, which was established to study use and outcomes of endoscopy, was used to mine data.

Interventions: Upper endoscopy.

Results: Among Caucasian patients, the risk of BE increases steeply from the third decade of life to middle adulthood. There was no difference in the yield of BE between middle-aged white women with GERD and white men without GERD.

Conclusions: The yield of endoscopy for the diagnosis of BE increases rapidly among white men with GERD and reaches a plateau at around age 50 years. Compared to white men without GERD, white women with GERD are at no increased risk.

Reviewer's Comments: It appears that the neoplastic change to BE typically occurs between 20 and 50 years, particularly in Caucasian men with GERD. The authors' suggestion to start screening men with reflux at age 50 years seems like a good place to start in the absence of controlled data and recent improvements in the treatment of dysplastic tissue in the esophagus. It makes no sense to screen women with GERD if their risk is no different than men without GERD. (Reviewer-J. Mark Lawson, MD).

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Keywords: Age, Sex, Endoscopic Indications, Barrett's Esophagus, Prevalence

Print Tag: Refer to original journal article

Retrograde-Viewing Device Improves Adenoma Detection

A Retrograde-Viewing Device Improves Detection of Adenomas in the Colon: A Prospective Efficacy Evaluation.

Waye JD, Heigh RI, et al:

Gastrointest Endosc 2010; 71 (March): 551-556

The use of a retrograde-viewing device, the Third Eye Retroscope, increases the detection rate of adenomas.

Background: Attention has now been focused on higher adenoma detection rates for screening colonoscopies. The Third Eye Retroscope (TER) may improve polyp detection.

Objective: To evaluate the utility of a retrograde-viewing device for the detection of polyps.

Design: Open-label, prospective, multicenter study evaluating colonoscopy with the TER in combination with a standard colonoscope.

Participants: 249 patients (aged 55 to 80 years) presenting for screening or surveillance colonoscopy.

Methods: 14 experienced endoscopists at 4 university hospitals, 2 ambulatory surgery centers, 1 community hospital, and a physician's office participated in this study. Standard colonoscopy preparation was performed, and a TER device was used in the working channel of the colonoscope. Simultaneous viewing of the images from the forward and retrograde views was performed. For each polyp, it was noted whether the polyp could be seen with the colonoscope view alone or whether it could be seen with the colonoscope only after it was detected with the TER. Polyps seen with both modalities or those seen first with the TER but then easily visualized with the forward view were not considered additional polyp detection.

Interventions: Colonoscopy with the TER.

Results: A total of 257 polyps were detected in 249 subjects with the colonoscope alone. The TER system detected an additional 34 polyps, for a 13.2% increase ($P < 0.0001$). The increased detection rate for adenomas ≥ 6 mm with TER was 25%. Interestingly, the additional detection rate for adenomas ≥ 10 mm with the TER was an impressive 33.3%. In 11.2% of patients, at least one additional polyp was detected with the TER; in 3% of cases, this was the only polyp found. The additional adenoma detection rate with the TER was 4.1% in the left colon and 14.9% for the right colon.

Conclusions: A retrograde-viewing device detected 13.2% more polyps than would have been found on forward-viewing colonoscopy alone.

Reviewer's Comments: There is a nice editorial accompanying this paper that points out the 4 key variables for polyp detection in colonoscopy: instrument angle of view, withdrawal time, bowel preparation, and tip deflection technique. I suspect, as the editorialist noted, that the endoscopist who was willing to spend extra time with careful tip deflection (particularly in the right colon) might be able to achieve similar results as those found in this study without the added expense of this new device. Many gastroenterologists, including myself, routinely retroflex in the ascending colon to view this area more carefully. Comparison of the TER technique with routine colonoscopy with careful tip deflection technique and perhaps standard retroflexion in the right colon should be able to answer this interesting question. (Reviewer-J. Mark Lawson, MD).

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Keywords: Retrograde-Viewing Device, Adenomas

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Be Aware of Propofol-Related Complications

Incidence of Sedation-Related Complications With Propofol Use During Advanced Endoscopic Procedures.

Coté GA, Hovis RM, et al:

Clin Gastroenterol Hepatol 2010; 8 (February): 137-142

Propofol can be used safely for advanced endoscopic procedures when administered by trained professionals. Independent predictors of the need for airway modification with the use of propofol include male gender, increased BMI, and ASA score of ≥ 3 .

Objective: To determine the incidence of sedation-related (SR) complications (primarily airway modification [AM]) associated with the use of propofol.

Design/Methods: This was a prospective study of patients undergoing advanced endoscopic procedures (ERCP, endoscopic ultrasound (single-balloon or spiral overtube-assisted small-bowel enteroscopy)). These procedures were performed with a certified registered nurse anesthetist (CRNA) using propofol alone or in conjunction with opiates and/or a benzodiazepine. The primary outcome was the need for AM during the procedure, although other outcomes were measured (pO₂, hypotension, and/or need to terminate the procedure due to sedation). AM was defined as a chin lift maneuver or the need for nasopharyngeal airway, modified mask airway, bag-mask ventilation, or endotracheal intubation. Continuous monitoring of ECG, heart rate, pulse oximetry, nasal capnography, and blood pressure was performed.

Results: 799 patients were enrolled in the study. Endoscopic ultrasound was performed in 52%, ERCP in 42%, and small-bowel enteroscopy in 5%. Sixty percent of patients were American Society of Anesthesiologists (ASA) 3, and 0.5% had a Mallampati score of 4. Eighty-seven percent of patients had deep sedation as evidenced by no response to intubation. AMs were performed on 14% of patients (n=115), for a total of 154 maneuvers (97 chin lifts, 29 mask airways, and 28 nasal airways). No patient required bag-mask ventilation or endotracheal intubation. Five cases (0.6%) were terminated because of sedation issues (4 for hypotension requiring a single dose of a vasopressor). AM patients were more likely to be male ($P < 0.006$), have an increased body mass index (BMI) ($P < 0.0001$), and have an ASA score of ≥ 3 and a Mallampati score > 4 (not significant). When using a combination of agents, the total propofol dose used was significantly lower, and the patient's ability to breathe and maintain a higher O₂ saturation after the procedure was better.

Conclusions: Propofol can be used safely for advanced endoscopic procedures using trained individuals such as CRNAs. Independent risk factors for the use of airway modifications included male sex, ASA score of ≥ 3 , and increased BMI.

Reviewer's Comments: These data are not unexpected, as CRNAs are trained to perform deeper, longer sedations during advanced endoscopic procedures. Whether these data can be translated to having nurse-administered or GI-directed propofol sedation in these types of patients is questionable. Many of these patients had high ASA scores and were obese—not the typical patient that trained nurses or physicians using propofol may be seeing. (Reviewer-Roy K.H. Wong, MD).

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Keywords: Propofol, ERCP, EUS, Single-Balloon, Spiral Overtube-Assisted SB Enteroscopy, Complications, Incidence

Print Tag: Refer to original journal article

Is Rosiglitazone Effective in NASH?

Long-Term Efficacy of Rosiglitazone in Nonalcoholic Steatohepatitis: Results of the Fatty Liver Improvement by Rosiglitazone Therapy (FLIRT 2) Extension Trial.

Ratziu V, Charlotte F, et al:

Hepatology 2010; 51 (February): 445-453

Rosiglitazone provides improvements in insulin resistance (IR) and steatosis in the initial year without additional benefits with longer therapy, despite a maintained effect on IR and liver enzymes.

Background: Nonalcoholic steatohepatitis (NASH) is associated with insulin resistance (IR) and features of the metabolic syndrome and can progress to cirrhosis and its complications. Although there are no proven therapies for NASH, glitazones are attractive candidates because of their insulin-sensitizing mechanisms of action. Although several studies have been published, they were limited in duration. Consequently, the possible delayed effect of improving IR is unknown.

Objective: To determine if prolonged therapy with rosiglitazone (RSG) is associated with further histologic improvement and, in particular, if fibrosis regression can be obtained.

Design: Open-label study.

Participants: Those who participated in the randomized, placebo-controlled Fatty Liver Improvement by Rosiglitazone Therapy (FLIRT) trial.

Methods: Of the 63 patients in the FLIRT trial randomized to 12 months of RSG (8 mg/day; n=32) or placebo (PLB; n=31), 25 randomized to RSG and 28 to placebo were included in this open-label extension trial. The RSG patients received 4 mg/day for 1 month then 8 mg/day for 2 additional years up to month 40. Of these, 44 patients completed the extension study, and 40 patients (22 PLB-RSG and 18 RSG-RSG) underwent a third biopsy. IR was assessed by the homeostasis model assessment (HOMA) and histology for steatosis and NASH activity score (NAS).

Results: During the 2-year extension, serum insulin decreased by 26%, HOMA-IR by 30%, and ALT by 24%. However, there were no significant changes in NAS, cytologic ballooning, or fibrosis stage. In the PLB-RSG group, steatosis improved (median, 15%) to the same extent as during the initial 1 year FLIRT trial (median, 20%) in those who received RSG. In extension, 2 additional years of RSG provided no further improvements in steatosis, cytologic ballooning, intralobular inflammation, NAS, or fibrosis (RSG-RSG group). The median weight gain was 2 kg (interquartile range, 4 to 25), and 36% gained >3 kg.

Conclusions: RSG provides improvements in IR and steatosis in the initial year without additional benefits with longer therapy, despite a maintained effect on IR and liver enzymes.

Reviewer's Comments: These data suggest that the benefit of glitazones occur in the first year of therapy, and there is no delayed effect of prolonged enhancement of IR on improving liver histology. Therefore, targets other than improving IR will be needed in the treatment of NASH. That, coupled with the risk of weight gain, should lessen enthusiasm for routine use of glitazones in the treatment of NASH. With the results of the recent Piaglitazone vs Vitamin E vs Placebo for Treatment of Nondiabetic Patients With Nonalcoholic Steatohepatitis trial presented at the American Association for the Study of Liver Disease showing that vitamin E was as effective as a glitazone, vitamin E may be a safer option until other treatments for NASH become available. (Reviewer-Richard K. Sterling, MD).

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Keywords: NASH, Rosiglitazone

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Ascites -- Combined vs Sequential Diuretic Treatment

Combined Versus Sequential Diuretic Treatment of Ascites in Non-Azotaemic Patients With Cirrhosis: Results of an Open Randomised Clinical Trial.

Angeli P, Fasolato S, et al:

Gut 2010; 59 (January): 98-104

Less hyperkalemia occurs when both furosemide and an aldosterone antagonist are used to treat ascites than when an aldosterone antagonist is employed initially.

Background: A randomized trial published in 2003 suggested that, when treating ascites, it is better to begin with an aldosterone antagonist (spironolactone) and add furosemide only if the patient does not respond ("sequential therapy"). If both agents are used together at the outset (combination therapy), it may be that an earlier response can be achieved.

Objective: To compare sequential and combination therapy for the treatment of ascites.

Design: Randomized, controlled trial.

Participants: Patients presenting with ascites due to cirrhosis who were not azotemic.

Methods: After discontinuing diuretics for 5 days, the patients were randomized into 1 of 2 arms. The sequential group received 200 mg/day of potassium canrenoate, an aldosterone antagonist. At 4-day intervals, if there was no response (body weight loss of at least 700 g over 3 days), doses were increased (400 mg/day), and serially increasing doses of furosemide (50, 100, and then 150 mg/day) were provided. The combination group received 200 mg potassium canrenoate/50 mg furosemide daily; if there was no response, these daily doses were then increased to 400/100 mg and then to 400/150 mg. Because of concern regarding excessive diuresis and hypovolemia, body weight losses in excess of 500 g daily, or 1000 g daily if there was concomitant edema, were also viewed as therapeutic failures. The patients were monitored for alterations in renal function and serum electrolytes. The primary outcome was the occurrence of a diuretic response. A sample size calculation indicated that 49 patients would be needed in each arm.

Results: 50 patients were entered into each group, and none were lost to follow-up. Responses occurred in 44 of 48 patients in the sequential/combo groups (not significant). Two patients in each arm developed excessive diuresis. Adverse events, largely hyperkalemia, occurred in 14 and 8 patients (claimed to be significant) in the 2 groups. Thus, responses occurred in 28 of 38 individuals ($P < 0.05$).

Conclusions: Combination therapy is preferable to sequential therapy for treating ascites due to cirrhosis.

Reviewer's Comments: This was a reasonably well-conducted trial, although it was not blinded, which could have led to the introduction of bias. When I performed a chi-squared analysis of the adverse events, I was not able to duplicate a significant difference, although I was able to show such a difference for the numbers of responders. The severity of the hyperkalemia was not noted; if it was minimal, this may not have had any clinical significance. Curiously, even though the cirrhosis was almost entirely due to viral or alcohol causes, two-thirds of the patient population was female; the investigators did not comment on this. Finally, the aldosterone antagonist that was used (canrenoate) is not the same thing as spironolactone, and it may or may not truly be comparable. (Reviewer-Ronald L. Koretz, MD).

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Keywords: Canrenoate Furosemide, Ascites, Cirrhosis

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Hepatitis C With Advanced Fibrosis and Cirrhosis

Efficacy and Safety of Peginterferon Alfa-2a (40KD) Plus Ribavirin in Hepatitis C Patients With Advanced Fibrosis and Cirrhosis.

Bruno S, Shiffman ML, et al:

Hepatology 2010; 51 (February): 388-397

Compared to those without advanced fibrosis, those with bridging fibrosis and cirrhosis have lower SVR rates, and time to response is the strongest predictor of SVR.

Background: Response-guided therapy is now used to maximize sustained virologic response (SVR). The patients with the most to gain from SVR response are those with advanced fibrosis (AF). However, these patients are often under-represented in most large trials.

Objective: To determine the efficacy and safety of peginterferon alfa-2a (PEG)/ribavirin (RVN) in patients with AF.

Design: Retrospective review.

Participants: Data from 341 genotype (GT) 1/4 patients (99 with bridging fibrosis [BF] or cirrhosis [Cx]) treated for 48 weeks and 1547 GT 2/3 patients treated for 16 weeks (n=729; 191 with BF/Cx) or 24 weeks (n=818; 189 with BF/Cx) who were enrolled in 3 randomized trials.

Methods: All patients were treated with PEG 180 µg/week and RVN (1000 to 1200 mg/day for GT 1/4 and 800 mg/day in GT 2/3). The primary end point was SVR. Secondary end points were rapid virologic response (RVR) and early virologic response (EVR).

Results: Response rates decreased progressively as fibrosis increased. In GT 1/4, RVR (23%, 11%, and 5%), complete EVR (cEVR) (46%, 39%, and 28%), and SVR (60%, 51%, and 33%) occurred in those without AF, BF, and Cx, respectively. Similarly, in those with GT 2/3 treated for 24 weeks, RVR (68%, 57%, 47%) and SVR (76%, 61%, and 57%) also decreased as fibrosis increased. Although SVR was similar in those without AF and BF with GT 1/4 who had RVR (89% to 95%), those with Cx who had RVR had only a 50% SVR. Conversely, the SVR rate was similar among all fibrosis groups (68% to 72%) in those who were able to achieve EVR. In those with GT 2/3 treated for 24 weeks, SVR decreased as fibrosis increased (87% to 79%) in those with RVR and was 65% to 47% in those with cEVR. Relapse rates were higher in those with AF mirroring lower response rates. Independent predictors of SVR were RVR or EVR and cumulative RVN exposure >60% in those with GT 1/4. When those with GT 2/3 and AF were considered, predictors of SVR were RVR, female gender, lower HCV RNA, higher ALT, cumulative RVN dose >60%, and 24 weeks of treatment. Overall safety and tolerability were not affected by fibrosis.

Conclusions: Compared to those without AF, those with BF and Cx have lower SVR rates, and time to response (RVR>cEVR) was the strongest predictor of SVR.

Reviewer's Comments: These data nicely show that RVR, the holy grail in achieving SVR, is lower as fibrosis increases, suggesting that earlier treatment, before AF develops, maximizes SVR with current therapy. Only time will tell how this will change with the addition of STAT-C agents. (Reviewer-Richard K. Sterling, MD).

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Keywords: HCV, Advanced Fibrosis, Cirrhosis, Treatment

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PPIs Better Than H2RAs for Symptoms With Low-Dose Aspirin

Famotidine Is Inferior to Pantoprazole in Preventing Recurrence of Aspirin-Related Peptic Ulcers or Erosions.

Ng F-H, Wong S-Y, et al:

Gastroenterology 2010; 138 (January): 82-88

Patients who have symptoms associated with the use of low-dose aspirin have less dyspepsia if they receive PPIs than if they receive high-dose H2RAs.

Background: Low-dose aspirin can cause gastroduodenal mucosal disease with associated dyspepsia and/or bleeding. While it is known that histamine-2 receptor antagonist (H2RA) and proton pump inhibitor (PPI) therapy can protect the mucosa, little is known regarding their comparative efficacy in preventing such symptoms.

Objective: To compare the efficacy of pantoprazole to high-dose famotidine when used as secondary prophylaxis.

Design: Randomized (allegedly), double-blind trial.

Participants: Patients included had gastrointestinal bleeding or dyspepsia while consuming low-dose aspirin (80 to 320 mg/day) and, on endoscopy, had frank ulcers or >5 erosions in the stomach or duodenum and required continuous low-dose aspirin afterward.

Methods: Patients were treated for their underlying gastro-duodenal diseases with 8 (or 16 if the initial therapy was not successful) weeks of PPI therapy (as well as *Helicobacter pylori* eradication if they were *H. pylori* positive). They were then randomized (computer-generated sequence with concealed allocation) to receiving 80 mg aspirin and either pantoprazole (20 mg/day) or famotidine (20 mg twice a day) for 1 year. The 2 drugs were repackaged in an identical manner (with placebo pantoprazole as the second daily dose). Patients were assessed at 3 monthly intervals as well as at any time when more than minimal dyspepsia occurred or when bleeding was suspected. The primary end point was recurrent dyspepsia or a complication of mucosal disease (bleeding, perforation, etc). A sample size calculation indicated that 79 patients would be needed in each arm.

Results: 160 patients (78 PPI/82 H2RA) were randomized, and none were lost to follow-up; 13 of 17 PPI/H2RA patients were excluded from the analysis because of noncompliance (mostly refusing to undergo repeat endoscopy when dyspepsia occurred), premature termination of therapy for suspected adverse effects, protocol violation (cessation of aspirin therapy or introduction of non-protocol medications), or suspected small intestinal bleeding. Eight famotidine recipients developed dyspepsia, and 5 others allegedly had bleeding (although 3 of those presented only with anemia) compared to none in the pantoprazole group.

Conclusions: High-dose famotidine was inferior to pantoprazole as secondary prophylaxis.

Reviewer's Comments: Subtle biases may have exaggerated the reported effect. Since all of the patients took PPIs for 8 to 16 weeks before entry, early dyspepsia may have been a PPI withdrawal effect. (The 9 dyspeptic famotidine recipients who refused endoscopy all developed symptoms within 8 weeks.) It is unclear how well the trial was blinded; the repackaging was not described in any detail. Clearly, the bias of the investigators was that PPIs would be superior; their power calculation was so based. While the 2 frank bleeding episodes in the famotidine group were discussed in detail, the fact that 2 patients in the PPI group had major neurologic events that led to exclusion was noted only in a table. (Reviewer-Ronald L. Koretz, MD).

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Keywords: Proton Pump Inhibitors, H₂Receptor Antagonists, Low-Dose Aspirin, Dyspepsia, GI Bleeding

Print Tag: Refer to original journal article

Maintenance Therapy for GERD -- What Works Best?

Efficacy of Three Different Dosages of Esomeprazole in the Long-Term Management of Reflux Disease: A Prospective, Randomized Study, Using the Wireless Bravo pH System.

Vasiliadis KV, Viazis N, et al:

Am J Gastroenterol 2010; 105 (February): 308-313

Acid reflux is well controlled with the use of esomeprazole 40 mg once daily.

Objective: Using different proton pump inhibitor (PPI) regimens, the authors tried to determine the lowest PPI dose that consistently normalizes intraesophageal pH in patients with endoscopy-negative reflux disease (ENRD) or with LA class A or B esophagitis.

Methods: Patients included in the study were those diagnosed with ENRD and abnormal 24-hour pH study, with typical GERD symptoms but no use of antisecretory agents, or esophagitis patients with LA grade A or B. Patients were randomized to 1 of 3 regimens: group A, esomeprazole 40 mg orally twice a day; group B, esomeprazole 40 mg orally once a day; or group C, esomeprazole 40 mg orally every other day. Patients with esophagitis received esomeprazole 40 mg orally twice a day for 1 month and had a repeat endoscopy to confirm healing before being randomized. All patients underwent 48-hour pH Bravo studies after taking protocol medications for 1 month.

Results: Of the 75 patients entered into the study, 73% were male. Body mass index, *Helicobacter pylori* status, and the presence of hiatal hernia were similar in all groups; 9% (n=7) had LA grade A or B esophagitis, with 2 patients having incomplete studies, leaving 73 patients in the analysis. There were no statistically significant differences between the 3 groups on day 1 in terms of pH time <4 or De Meester score ($P=0.262$). On the second day of the study, there was a significant difference between the every-other-day dosing versus the other 2 regimens of once-a-day and twice-a-day dosing ($P<0.001$ for pH and $P<0.001$ for De Meester score). The percentage of time the pH was <4 for twice a day, once a day, and every other day doses was 0.7, 1.5, and 7, respectively. The De Meester scores for once-a-day, twice-a-day, and every-other-day dose were 3.9, 6.4, and 29.4, respectively. The reported rates of symptoms of heartburn were as follows: twice a day, 8% (n=2); once a day, 12.5% (n=3); and every other day, 28% (n=7), with 2 patients having a positive symptom index in group C ($P<0.145$).

Conclusions: On the day off of esomeprazole (every other day dosing schedule), significantly more acid reflux was noted compared to the daily dosing schedule. However, there was no added benefit with a twice a day versus once a day dose of esomeprazole 40 mg.

Reviewer's Comments: We may be overdosing our patients with PPIs in treating GERD. A single dose is sufficient for typical GERD. Some studies indicate that one can treat patients with PPI or antisecretory medications for a month and stop their medications and note no recurrence or <3 recurrences of heartburn over a year. Patients in this study may have more severe GERD as 70% had hiatal hernia. (Reviewer-Roy K.H. Wong, MD).

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Keywords: Esomeprazole, Reflux, Efficacy, Long-Term Management

Print Tag: Refer to original journal article

Flexible Sigmoidoscopy Provides Higher Diagnostic Yield

Screening for Colorectal Cancer: Randomised Trial Comparing Guaiac-Based and Immunochemical Faecal Occult Blood Testing and Flexible Sigmoidoscopy.

Hol L, van Leerdam ME, et al:

Gut 2010; 59 (January): 62-68

Using an immunochemical test results in a higher participation rate and diagnostic yield than guaiac testing; sigmoidoscopy is less well accepted but results in the highest detection rate for advanced neoplasia.

Background: Colon cancer screening requires individuals to participate. It is unknown if stool occult-blood testing is more or less acceptable than flexible sigmoidoscopy. One prior randomized trial suggested that immunochemical tests for blood were a better strategy than guaiac testing of stool.

Objective: To compare the acceptability and detection rate for advanced neoplasia that resulted from offers to do stool hemoccult testing by the standard guaiac approach, by the use of an immunochemical test, or by flexible sigmoidoscopy.

Design: Randomized controlled trial.

Participants: Residents of Rijnmond, The Netherlands, between the ages of 50 and 74 years.

Methods: 15,011 individuals were randomly identified and assigned to 1 of 3 arms, stool occult blood testing by guaiac, or by immunochemical testing, or by flexible sigmoidoscopy. All were mailed information regarding colon cancer screening in general. Those assigned to each group subsequently received specific information about the test to which they had been randomized and were asked to participate. The primary outcome of interest was the percentage in each group who participated. The secondary outcome was the percentage in each group who had an advanced neoplasm (>1 cm, serrated villous histology, high-grade dysplasia, or frank cancer). Individuals with histories of inflammatory bowel disease, prior colonoscopies or flexible sigmoidoscopies (or barium enemas), other major health problems, or who had died or moved away were excluded after the fact.

Interventions: Those assigned to guaiac testing submitted 3 consecutive stool specimens, whereas the immunochemical test was performed on a single specimen. Flexible sigmoidoscopy was scheduled when the patient opted to do so. Any person with a positive screening test underwent colonoscopy.

Results: Approximately 5000 individuals were randomized to each arm; significantly more people were excluded from the sigmoidoscopy arm (300) than from the guaiac or immunochemical testing arms (206 and 164, respectively). The participation rates were 49.5% (guaiac), 61.5% (immunochemical), and 32.4% (sigmoidoscopy); these differences were all significant. The detection rates for advanced neoplasia, considering both those who did and did not participate, were 0.6%, 1.5%, and 2.4%, respectively.

Conclusions: Immunochemical testing is preferable to guaiac testing, but flexible sigmoidoscopy resulted in the highest detection rate.

Reviewer's Comments: Excluding patients after the fact did introduce potential bias, since more such exclusion factors were identified in the sigmoidoscopy group. However, if one believes that the excluded patients would have been more likely to have advanced neoplasia, this bias would act in favor of occult blood testing with regard to the detection rates. The issue that this trial did not address was whether or not the better participation and/or detection rates translated into an improvement in morbidity or mortality. (Reviewer-Ronald L. Koretz, MD).

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Keywords: Colorectal Ca, Flexible Sigmoidoscopy, Fecal Occult Blood Testing

Print Tag: Refer to original journal article

Advanced Age, Low PLT Counts Associated With Increased Risk of HCC

Risk of Hepatocellular Carcinoma in Patients With Chronic Hepatitis B Virus Infection.

Ito K, Arai M, et al:

Scand J Gastroenterol 2010; 45 (February): 243-249

Patients who have HBV are at increased risk for the development of HCC if they are >40 years of age, have low platelet counts and have high levels of serum HBV DNA.

Objective: To determine the risk factors for the development of hepatocellular carcinoma (HCC) in patients with chronic hepatitis B virus infection (HBV).

Methods: Between February 1985 and March 2008, a total of 620 patients who tested positive for hepatitis B surface antigen were referred to Chiba University Hospital and were included in this study. This group was analyzed with regard to age, gender, status of hepatitis B e antigen (HbeAg), alanine aminotransferase level (ALT), HBV DNA level, and number of platelets (PLTs) in order to determine if the presence or level of any of these factors was associated with an increased risk of the development of HCC.

Results: During a follow-up period of 5.4 ± 5.1 years, a total of 30 patients developed HCC. By means of multivariate analysis, it was determined that patients whose age was >40 years (compared to patients aged <40 years; OR, 4.28; 95% CI, 1.68 to 10.9) and PLT <206,000 μ l (compared to patients with higher PLT levels; OR, 8.50; 95% CI, 1.98 to 36.3) were predictors for the development of HCC. It was also noted that in patients >40 years of age, the HBV DNA level (compared with <5.0 log copies/mL; OR, 4.2, 95% CI, 1.13 to 15.8) and PLT level (compared with patients with >196,000 μ l PLTs; OR, 15.6, 95% CI, 2.06 to 118.3) were also predictive factors for the development of HCC.

Conclusions: The conclusions reached by the authors of this study were that advanced age (which they defined as >40 years) and low PLT counts were risk factors for the development of HCC in patients with HBV. They also found that in patients >40 years of age, viral load was a risk factor for the development of HCC.

Reviewer's Comments: This interesting study found that the HBeAg status of patients with HBV is not a risk factor for the development of HCC. The findings suggest that although screening for HCC in patients with HBV who are <40 years of age should not be abandoned, the greatest attention and aggressive screening should be focused on those >40 years of age. (Reviewer-Michael M. Phillips, MD).

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Keywords: Chronic HBV Infection, Hepatocellular Carcinoma, Risk Factors

Print Tag: Refer to original journal article

Increased Physical Exercise May Improve Colorectal Cancer Survival

Physical Activity and Male Colorectal Cancer Survival.

Meyerhardt JA, Giovannucci EL, et al:

Arch Intern Med 2009; 169 (December 14/28): 2102-2108

In analysis of data from a large prospective observational cohort, men with a history of nonmetastatic colorectal cancer had improved survival associated with greater physical activity.

Background: Increased physical activity is associated with reduced risk for colorectal cancer development. Less information is available describing the relationship between physical activity and outcome after colorectal cancer is diagnosed. Data from 2 observational cohorts suggests that pre- and post-diagnosis physical activity is associated with reduced colorectal cancer recurrence and improved mortality.

Objective: To study the association between physical activity and colorectal cancer mortality.

Design: Data analysis from a large, prospective, observational cohort.

Participants: Subjects in the male Health Professionals Follow-Up Study who had been diagnosed with nonmetastatic colorectal cancer.

Methods: Physical activity assessment was by analysis of returned bi-annual questionnaires. Self-reported physical activity was converted to metabolic equivalent tasks (MET score). The activity assessment occurred between 6 months and 4 years after diagnosis to minimize risk of treatment-associated decreased physical activity. Cox proportional hazard models were used to calculate hazard ratios (HR). The primary outcome measure was death from colorectal cancer; death from any cause was a secondary end point.

Results: From 1986 to 2004, 1041 out of the total original cohort of >50,000 men were diagnosed with colorectal cancer. Of these, 661 were eligible for analysis, diagnosed with stage I, II, or III disease. There were 258 deaths, of which 88 were due to colorectal cancer. Men in the highest quintile of physical activity (>27 MET hours/week) had a 53% reduced risk of colorectal cancer mortality compared with men in the lowest quintile (≤ 3 MET hours/week) (HR, 0.47; 95% CI, 0.24 to 0.92; $P = 0.002$ for trend). The adjusted decreased risk for overall mortality was similarly significantly reduced (HR, 0.59; 95% CI, 0.41 to 0.86; $P < 0.001$ for trend). Statistical modeling suggested that survival benefit started at 6 to 12 MET hours/week and achieved a maximum benefit at 35 MET hours/week.

Conclusions: Physical activity in men after a diagnosis of nonmetastatic colorectal cancer is associated with significantly reduced colorectal cancer as well as all-cause mortality.

Reviewer's Comments: These data confirm findings from 2 other observational cohorts. As is true with all observational studies, extensive attempts were made to reduce confounding factors, but the results can only be taken as associations, not causality. Apparently, there is a randomized trial that will be undertaken to test the hypothesis that supervised physical activity and behavioral support in high-risk stage II and III nonmetastatic colorectal cancer will improve disease-free survival. (Reviewer-Timothy O. Lipman, MD).

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Keywords: Colon Cancer, Survival, Males, Physical Exercise

Print Tag: Refer to original journal article

Super Obese Have Higher Risk of Death After Bariatric Surgery

Predictors of Long-Term Mortality After Bariatric Surgery Performed in Veterans Affairs Medical Centers.

Arterburn D, Livingston EH, et al:

Arch Surg 2009; 144 (October): 914-920

In a retrospective analysis evaluating risk factors for death after bariatric surgery, the super obese (BMI ≥ 50) and those with comorbid disease have decreased 30-day and 1-year survival.

Background: There is accumulating evidence that bariatric surgery improves body weight, obesity-associated comorbidities, quality of life, and long-term survival. The risk of death after bariatric surgery is considered to be low, with 30-day and 1-year mortality quoted as 0.28% and <1%, respectively. These prior estimates have primarily included younger female patients and may not apply to an older male population.

Objective: To examine predictors of mortality in veterans undergoing bariatric surgery.

Design: Retrospective analysis of data from the Veterans Administration (VA) National Surgical Quality Improvement Program (NSQIP).

Participants: Veterans who underwent bariatric surgery over a 6-year period at 12 VA-approved bariatric surgery programs were included.

Methods: The primary end point was mortality. Multiple variables, including estimate of morbidity using the diagnostic cost group (DCG) risk adjustment measure, were analyzed via Cox proportional hazard regression models.

Results: Of 911 patients who had undergone bariatric surgery, 856 surgical patients had sufficient data for analysis. Seventy-three percent were men and 83.9% were white; their mean age was 54 years, and the mean body mass index (BMI) was 48.7. Median follow-up was 984 days. Among the group, 25% underwent laparoscopic surgery and the vast majority underwent Roux-en-Y bypass. Thirty-six percent of the patients were super obese (BMI ≥ 50). At baseline, these patients were more likely to be hypertensive, have heart failure, chronic obstructive pulmonary disease, an open wound or infection, and higher American Society of Anesthesiologists (ASA) class. Multivariable-adjusted Cox model found that a BMI ≥ 50 or a DCG score ≥ 2 carried a significantly higher risk of death (hazard ratio [HR], 1.77; $P = 0.04$ and HR, 3.4; $P < 0.001$, respectively). A preoperative ASA classification of 4 trended towards increased risk of death compared with ASA 2. The super obese had 30-day, 90-day, and 1-year mortality rates of 2.0%, 3.6%, and 5.2%, respectively, which are higher than previous literature reports indicate.

Conclusions: Super obese veteran patients with chronic comorbidity have higher 30-day, 90-day, and 1-year risk of death compared with prior literature reports.

Reviewer's Comments: This late 2009 journal article remains clinically relevant and important because it documents increased bariatric surgical mortality in a high-risk group as compared with healthier peers. This risk of death, which actually increased to 25% in 3.5 years of follow-up, needs to be weighed against the risk of death in this same population who may not undergo bariatric surgery. As indicated in the invited critique of the article, these results suggest that there may be a group of patients (male, older, super obese, and with high morbidity scores) for whom bariatric surgery does not offer a survival advantage. More prospective data are needed to help with making intelligent decisions regarding bariatric surgery in high-risk individuals. (Reviewer-Timothy O. Lipman, MD).

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Keywords: Obesity, Bariatric Surgery, Mortality

Print Tag: Refer to original journal article

Fecal Calprotectin Is Marker of Endoscopic Activity in CD

Fecal Calprotectin Correlates More Closely With the Simple Endoscopic Score for Crohn's Disease (SES-CD) Than CRP, Blood Leukocytes, and the CDAI.

Schoepfer AM, Beglinger C, et al:

Am J Gastroenterol 2010; 105 (January): 162-169

Correlation of FCAL concentration with CD endoscopic scores is higher than CRP, WBC, or CDAI.

Background: Fecal calprotectin (FCAL) represents 60% of cytosolic proteins in granulocytes. Fecal concentrations correlate with neutrophil migration to bowel mucosa. Studies support its use as a marker of Crohn's disease (CD) activity.

Objectives: To compare results of the Simple Endoscopic Score for Crohn's disease (SES-CD) with FCAL, C-reactive protein (CRP), blood leukocytes (WBC), and the Crohn's disease activity index (CDAI). **Patients:** 118 CD patients, all of whom had ileocolonoscopy (with 22 having 2 examinations) were included; 43 healthy control volunteers gave fecal and blood specimens but did not undergo ileocolonoscopy.

Design: Prospective, blinded, comparison study.

Methods: Endoscopic CD activity was quantified utilizing the SES-CD in patients undergoing ileocolonoscopy (inactive, 0 to 3; mild, 4 to 10; moderate, 11 to 19; and high, ≥ 20). FCAL was measured by quantitative enzyme-linked immunosorbent assay (PhiCal, Medical Instrument Corp, Solothurn, Switzerland). WBC and CRP were determined by routine lab analysis 3 days before endoscopy.

Results: The SES-CD correlated closest with FCAL ($r=0.75$). Mean FCAL levels were 18.5 $\mu\text{g/g}$ in controls and 104 $\mu\text{g/g}$ in inactive CD patients, 231 $\mu\text{g/g}$ in mild CD patients, 395 $\mu\text{g/g}$ in moderate CD patients, and 718 $\mu\text{g/g}$ in high CD patients. Correlation of SES-CD and CRP was $r=0.53$, with CRP values of 3.2 mg/L in the control group and values of 12, 8, 23 and 40 mg/L for inactive, mild, moderate, and high endoscopic disease activity, respectively. Correlation of SES-CD with WBC and CDAI was poor, with mean CDAI >150 (218) only in patients with high (≥ 20) SES-CD scores. Calprotectin was the only marker that could discriminate inactive from mild endoscopic activity (103 vs 231; $P<0.001$). The overall accuracy for detection of endoscopically active disease was 87% for FCAL (cutoff 70 $\mu\text{g/g}$), 66% for elevated CRP (>5 mg/L), 54% for leukocytosis, and 40% for CDAI >150 .

Conclusions: FCAL correlates more closely with endoscopic activity in Crohn's disease than does CRP, leukocytosis, or CDAI. It was the only marker that discriminated between inactive and mild endoscopic disease activity.

Reviewer's Comments: A noninvasive test that correlates with CD endoscopic activity might be helpful in diagnosing CD, in determining whether a disease flare is occurring, and could potentially predict an impending flare that might be prevented by early therapeutic intervention. I am not yet convinced that FCAL will serve these purposes. I am not impressed by the claim that FCAL values above a cutoff of 70 $\mu\text{g/g}$ had an 87% accuracy of predicting active endoscopic disease since the mean FCAL in inactive endoscopic activity is 104 (range, 10 to 725 $\mu\text{g/g}$). Differences in mean scores between inactive versus mild or moderate disease do not apply to the individual patient when the FCAL ranges for each category have a wide spread (range for mild, 12 to 1009 $\mu\text{g/g}$; range for moderate, 68 to 912 $\mu\text{g/g}$). These limitations must be kept in mind by those who use this test. (Reviewer-Allen L. Ginsberg, MD).

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Keywords: Calprotectin, Crohn's Disease

Print Tag: Refer to original journal article

Antiviral Therapy Reduces Risk of HCC in Some Cirrhotic Patients

Antiviral Therapy Reduces Risk of Hepatocellular Carcinoma in Patients With Hepatitis C Virus-Related Cirrhosis.

Singal AK, Singh A, et al:

Clin Gastroenterol Hepatol 2010; 8 (February): 192-199

The risk of HCC is reduced among patients who achieved SVR, and maintenance IFN does not reduce the risk of HCC in those who do not respond.

Background: Those with cirrhosis, especially those with hepatitis C virus (HCV), are at increased of developing hepatocellular carcinoma (HCC). One theoretical benefit of sustained virologic response (SVR) in those with HCV is reduced mortality including HCC. However, the long-term effects of SVR on developing HCC are unclear.

Objectives: To assess HCC risk reduction in patients with HCV who received antiviral therapy.

Design: Systematic review and meta-analysis. **Materials:** Studies that compared untreated patients with those given interferon (IFN) alone or in combination with ribavirin (RVN), those that compared SVR to no SVR, and those that examined maintenance IFN.

Methods: After a systematic review of 84 studies, 32 were included: 20 comparing treatment to no treatment (n=4700); 14 comparing those with and without SVR (n=3310); and 4 studies looked at maintenance treatment with IFN (n=1152). The quality of studies was assessed for heterogeneity, and the risk ratio (RR) and 95% confidence interval (CI) were calculated using a random effects model.

Results: Of the 32 studies comparing treatment to no treatment, 9 were randomized controlled trials (RCT), 15 were retrospective, and 8 were prospective. Pooled data showed reduced risk in treatment versus no treatment (RR, 0.43; 95% CI, 0.33 to 0.56). Those with SVR had reduced risk of HCC (RR, 0.35; 95% CI, 0.26 to 0.46), with the maximum benefit in those who received combination IFN/RVN (RR, 0.25; 95% CI, 0.14 to 0.46) due to the increased SVR rates associated with combination therapy. There was no risk reduction with maintenance IFN (RR, 0.58; 95% CI, 0.33 to 1.03).

Conclusions: The risk of HCC is reduced among patients who achieve SVR, and maintenance IFN does not reduce the risk of HCC in those who do not respond.

Reviewer's Comments: HCV-related cirrhosis remains the most common indication for liver transplantation (LT) and is a common cause of HCC. This analysis of published studies shows that HCV therapy, especially in those with SVR, reduces the risk of developing HCC. Unfortunately, those without response, including those on maintenance IFN, do not have this benefit. Hopefully, the increased SVR rates with the addition of STAT-C agents will further reduce the need for LT and risk of HCC. (Reviewer-Richard K. Sterling, MD).

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Keywords: Cirrhosis, Antiviral Therapy, Hepatocellular Carcinoma

Print Tag: Refer to original journal article

Extending Tx Reduces Relapse

Peginterferon Alfa-2a/Ribavirin for 48 or 72 Weeks in Hepatitis C Genotypes 1 and 4 Patients With Slow Virologic Response.

Ferenci P, Laferl H, et al:

Gastroenterology 2010; 138 (February): 503-512

Extending therapy to 72 weeks reduces relapse in those with EVR, but not overall SVR, because of higher drop outs and those with LVR have low SVR despite longer duration of therapy.

Background: The faster the hepatitis C virus (HCV) RNA becomes undetectable, the higher the sustained virologic response (SVR). Response-guided therapy uses a more tailored approach depending on when the HCV RNA clears. However, shortening therapy in those with rapid virologic response (RVR) and prolonging treatment in those with those with an early virologic response (EVR) or late virologic response (LVR), defined as first undetectable at week 24, to maximize SVR remains controversial.

Objectives: To evaluate individualization of treatment duration based on the rapidity of VR.

Design: Randomized, multicenter study.

Participants: Treatment naïve adults from 13 sites in Austria with genotype (GT) 1 and 4 and evidence of chronic HCV were included.

Methods: All patients received peginterferon (PEG) alfa-2a 180 µg/week and ribavirin 1000 to 1200 mg/d. HCV RNA was assessed at weeks 4, 12, 24, 48, and week 72 for those on prolonged treatment. Those without RVR (negative at week 4) and at least a 2-log decline (partial EVR) or negative HCV RNA (complete EVR) at week 12 were randomized to 48 (group A; n=139) or 72 (group B; n=150) weeks of therapy. Those without EVR but negative at week 24 (LVR) continued to week 72 (group C; n=78). Those treated beyond 48 weeks (groups B and C) received reduced PEG 135 µg/wk after week 48. All were followed for 24 weeks off therapy for SVR. Stepwise dose reductions were allowed.

Results: Of 550 patients, 150 (27%) had RVR and were treated for 24 weeks, 289 had EVR and were randomized to group A or B, and 78 did not have EVR and were in group C. At the end of therapy, a similar percentage of those in group A and B had negative HCV RNA (77% vs 73%). The relapse rate was higher in group A than B (33% vs 18%; $P=0.01$), while the dropout rate was higher in group B than in group A (32% vs 19%). Consequently, the SVR was similar (51% in group A vs 59% in group B). The SVR rate in group C was only 5%.

Conclusions: Extending therapy to 72 weeks reduces relapse in those with EVR, but not overall SVR, because of higher dropout rates, and those with LVR have low SVR despite a longer duration of therapy.

Reviewer's Comments: Several studies have looked at the utility of extending therapy to improve SVR in those without RVR. The present study shows that extending therapy to 72 weeks in those with EVR can reduce relapse. A limitation is the higher dropout rate in those who continue therapy resulting in similar SVRs between 48 and 72 weeks of therapy. Given the increased RVR seen when newer STAT-C agents are combined with PEG and ribavirin extended therapy will not be needed in the near future. (Reviewer-Richard K. Sterling, MD).

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Keywords: Hepatitis C, Extended Treatment, Slow Response

Print Tag: Refer to original journal article

Highest Diagnostic Yield for DBE Within First Month of Bleeding

Long-Term Outcome of Patients With Obscure Gastrointestinal Bleeding Investigated by Double-Balloon Endoscopy.

Shinozaki S, Yamamoto H, et al:

Clin Gastroenterol Hepatol 2010; 8 (February): 151-158

DBE should be performed within the first month of bleeding to obtain the highest diagnostic yield.

Objectives: To determine the diagnostic yield and long-term outcome of double-balloon enteroscopy (DBE).

Participants/Methods: This retrospective study included 200 patients who underwent DBE for occult GI bleeding (OGIB). Patients were divided into 3 groups: (1) overt bleeding – within 24 hours of DBE; (2) previous overt bleeding – >24 hours before DBE; (3) persistent occult bleeding – iron deficiency anemia with positive fecal occult blood tests (+FOBT). Control of OGIB was defined as Hgb level >10 and no transfusions or iron replacement for 6 months prior to the final examination. In some cases, another DBE was performed if bleeding continued. Endoscopies performed included: antegrade, 24%; retrograde, 25%; and combined, 52% (last 102 cases; 76% success rate). The majority of failures were related to intestinal adhesions; no major complications were noted. Before DBE was done, other studies done included CE in 10%, RBC scan in 44%, and abdominal CT in 52%. Lesions were categorized as ulcers/erosions, vascular lesions, and tumors/polyps. Vascular and bleeding lesions were treated with argon plasma coagulation (APC) or clips.

Results: Median patient age was 60 years old, and the mean follow-up period was 29 months for 151 patients. Approximately 78% (155/200) had lesions identified (definite diagnosis, 62%; suspicious, 16%). The highest diagnostic yield was noted in overt bleeding (83%) versus previous overt bleeding (58%; $P < 0.008$) and occult (60%; $P < 0.045$). DBE within the first month of bleeding resulted in significantly more diagnoses (87% vs 57%; $P < 0.002$). The diagnosis in small intestinal overt bleeding was ulcer/erosions 55% (58 of 106 patients), vascular 30% (32 of 106), and tumors/polyps 15% (16 of 106). A reverse trend was noted for occult bleeding: tumors/polyps 45% (9 of 20); vascular 30%; and ulcer/erosion 25%. The overall control of OGIB was 64%. Esophagogastroduodenoscopy or colonoscopy could have identified 19% of lesions. Of the 100 patients with small bowel bleeding, control was less likely with vascular lesions (40%) versus ulcer/erosions (65%; $P < 0.031$) or tumors/polyps (84%; $P < 0.002$). Following DBE, the number of transfusions decreased from 29 to 1, requirement for iron replacement dropped from 26 to 4, and Hgb from 6.9 to 12.5 (all $P < 0.001$). Patients with a definite diagnosis for the bleeding did significantly better than patients with an indefinite diagnosis. Significant predictors of re-bleeding vascular lesions include many transfusions before DBE, multiple vascular lesions, and suspicious lesions. Vascular lesions are prone to re-bleed at shorter intervals.

Conclusions: The highest diagnostic yield for DBE is early within the first month of the bleeding. Vascular lesions of the small bowel tend to re-bleed and should be followed closely.

Reviewer's Comments: Although clinically beneficial, doing DBE early within the first month or first episode of bleeding of all occult may not be cost-effective or practical, especially if doing a combined DBE procedure on all patients. (Reviewer-Roy K.H. Wong, MD).

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Keywords: Obscure, GI Bleeding, Double-Balloon, Endoscopy, Outcome

Print Tag: Refer to original journal article

Marked Deposition of Extracellular EDN Noted in EoE Biopsies

Marked Deposition of Eosinophil-Derived Neurotoxin in Adult Patients With Eosinophilic Esophagitis.

Kephart GM, Alexander JA, et al:

Am J Gastroenterol 2010; 105 (February): 298-307

EDN deposition is noted in esophageal biopsy specimens of EoE patients, but not in controls, which may make it a useful marker for diagnosis of EoE.

Objectives: To determine the extent of eosinophil-derived neurotoxin (EDN) deposition in the esophagus of patients with eosinophilic esophagitis (EoE) as compared with normal histology controls.

Participants/Methods: The study group consisted of 10 patients (mean age, 41 years, range 28 to 49 years; 9 males) with EoE defined as having dysphagia and ≥ 20 eosinophils/high-power field (HPF) from mid-esophageal biopsies. Twenty-four hour pH studies were not performed on these patients. For controls, 8 patients with histologically normal mid-esophageal specimens were chosen. The mean age of these patients was 39 year (age range, 10 to 70 years; 4 males; 3 patients <17 years old) with 4 patients having dysphagia, 5 with heartburn or regurgitation. EoE patients could not have had any treatment related to EoE in the previous 3 months, no erosive esophagitis, or esophageal dilation at the time of index endoscopy. Serial sections of mid-esophageal biopsies were examined by immunofluorescence to detect EDN. Two investigators unaware of the diagnosis scored the biopsies according to the degree of eosinophilic infiltrate and EDN deposition.

Results: No EDN was noted in the histologically normal control biopsies. Three distinct patterns of EDN staining were observed in EoE specimens: EDN mainly within eosinophils; EDN in both eosinophils and extracellular locations; and EDN mainly as extracellular deposition. Different parts of the same biopsy may have heavy EDN infiltration, while an adjacent section may show small amounts of EDN. The degree of EDN deposition does not correlate to the degree of eosinophilic infiltration. EDN deposition can be diffuse or concentrated in the luminal surface of the biopsy specimen.

Conclusions: Marked deposition of extracellular EDN is noted in biopsies of patients with EoE. The EDN can be diffuse in the lamina propria, sporadic, or located mainly on the luminal side of specimen. There is no correlation between the degree of eosinophil infiltrate and the extent of EDN deposition.

Reviewer's Comments: It is difficult to say what physiologic effects EDN have on the esophagus. We do know that eosinophils degranulate and probably release EDN when exposed in vitro to IL-5, IL-3 and eotaxin-3. An IL-5 antibody, mepolizumab decreases eosinophil counts and eosinophil cell activation suggesting that blocking IL-5 may be therapeutic for EoE. What this study does show is that even with fewer eosinophils, degranulated material (EDN) is present in the esophagus, which could lead to further pathology. EDN may also be a marker to identify activity even with <20 eosinophils/HPF. (Reviewer-Roy K.H. Wong, MD).

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Keywords: Eosinophil-Derived Neurotoxin, Eosinophilic Esophagitis, Infiltration

Print Tag: Refer to original journal article

GJ Bypass Superior Palliation for Malignant GOO

Surgical Gastrojejunostomy or Endoscopic Stent Placement for the Palliation of Malignant Gastric Outlet Obstruction (SUSTENT) Study): A Multicenter Randomized Trial.

Jeurnink SM, Steyerberg EW, et al:

Gastrointest Endosc 2010; 71 (March): 490-499

Gastrojejunostomy bypass is superior to endoscopic stenting for the treatment of malignant gastric outlet obstruction in patients living >2 months.

Background: New developments in endoscopic stenting have raised questions as to as to the best palliative method for patients with malignant gastric outlet obstruction (GOO).

Objective: To compare outcomes of gastrojejunostomy (GJ) with endoscopic stenting for the treatment of malignant GOO.

Design: Multicenter, randomized trial.

Participants: 77 patients with malignant GOO.

Methods: Patients were randomized using a computer-generated system to receive surgical GJ by open or laparoscopic approach or stent placement with an Enteral Wallflex stent of 22 mm in width and a length of 60, 90, or 120 mm. Outcomes of medical effects, quality of life, and costs were analyzed by intent to treat.

Interventions: Surgical GJ via open laparoscopic approach or endoscopic stenting.

Results: 18 patients underwent GJ, and 21 had stent placement. Initial food tolerance was better with stent placement compared to GJ (5 vs 8 days; $P < 0.01$). Better long-term outcomes were noted in GJ patients who had fewer GOO symptom days compared to stent patients on scoring (72 vs 50 days; $P = 0.05$). More complications, including recurrent obstruction and need for reintervention, were noted in stent patients ($P < 0.01$). If stent obstruction was not considered a major complication, the complication rates were similar. Quality-of-life measures and median survival were similar in both groups. Mean total costs were higher in the GJ patients compared to those having stent placement (\$16,535 vs \$11,720).

Conclusions: Although initial symptom improvement was slower in the GJ patients and costs slightly higher, better long-term results were noted compared to patients who had stent placement. GJ is the treatment of choice in patients expected to live >2 months.

Reviewer's Comments: This small study does suggest that patients without end-stage malignant GOO do better with surgical bypass compared to stenting. The problems I see with this conclusion, beyond the small sample size we have already noted, includes the fact that 50% of eligible patients declined to participate in the study with most opting for stent placement. I am not sure that the magnitude of the difference in outcomes between these 2 procedures is that great although statistical significance was noted. Many patients are fearful of surgery in the setting of advanced gastric cancer. (Reviewer-J. Mark Lawson, MD).

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Keywords: Gastrojejunal Bypass, Endoscopic Stenting, Malignant Gastric Outlet Obstruction

Print Tag: Refer to original journal article