Gastrointestinal bleeding

Ian M. Gralnek, MD

Haifa, Israel

A number of interesting abstracts on gastrointestinal bleeding and endoscopy were presented at Digestive Disease Week (DDW) this year (3–6 May 2014, Chicago, Illinois). The following abstracts are those that have particular high clinical importance and the potential for direct impact on the endoscopic care of patients with gastrointestinal bleeding.

BLEEDING PEPTIC ULCERS

Proton pump inhibitor therapy

Current international guidelines recommend the use of proton pump inhibitors (PPIs), administered as a bolus (80 mg) followed by a continuous infusion (8 mg/hour for 72 hours), following endotherapy for bleeding peptic ulcers.[1-3] In a systematic review and meta-analysis, Sachar et al[4] reported on intermittent PPI use vs. the bolus+infusion regimen for patients with high risk peptic ulcers (active bleeding, nonbleeding visible vessel, adherent clot). The primary outcome of the study was ulcer rebleeding within 7 days, and the noninferiority margin was defined as a 3% absolute risk difference. Secondary outcomes included rebleeding at 3 days, rebleeding at 30 days, mortality, need for surgery or interventional radiology, length of hospital stay, and blood transfusions. A total of 12 studies met the inclusion criteria. For the primary outcome of ulcer rebleeding at 7 days (n = 1308), the upper limit of the one-sided 95% confidence interval (CI) for the absolute risk difference was 0% (i.e. below the 3% noninferiority margin value). Moreover, for all other study outcomes, relative risks were <1 and mean differences were <0. These results indicate that there is no apparent increased risk with intermittent PPI therapy. The authors concluded that intermittent PPI therapy was as effective as the current standard of care regimen of bolus PPI followed by continuous infusion for patients with ulcer bleeding and high-risk stigmata, and that a revision of current guidelines regarding recommendations on post-hemostasis PPI therapy may therefore be necessary.

Transarterial angiographic embolization

Three abstracts at DDW focused on the role of transarterial angiographic embolization (TAE) therapy in patients with peptic ulcer bleeding.[5-7] As we know, ulcer rebleeding following endoscopic hemostasis is associated with significantly increased morbidity and mortality. In the first abstract, Lau et al[5] evaluated whether "pre-emptive" TAE of high-risk ulcers reduces rebleeding rates and improves patient outcomes. The study included patients with gastric or duodenal ulcers who had undergone successful endoscopic hemostasis yet had at least one of the following clinical characteristics at the time of esophagogastroduodenoscopy (EGD): Forrest Ia bleeding (spurting type bleeding), large ulcer size $\geq$1.5 cm, systolic blood pressure $<$90 mmHg, or hemoglobin $\leq$9 g/dL. Patients were randomly assigned (within 12 hours of EGD) to undergo pre-emptive TAE plus high-dose intravenous PPI (n = 109) or to receive high-dose intravenous PPI only (n = 113). The primary end point was ulcer rebleeding within 30 days of randomization.

Baseline patient demographics were similar between groups. On intention-to-treat analysis, ulcer rebleeding occurred in 8/109 patients (7.3%) in the TAE group and in 12/113 patients (10.6%) in the PPI only group (P = 0.39; odds ratio [OR] 0.67, 95%CI 0.26–1.70). On per-protocol analysis, ulcer rebleeding occurred in 4/91 patients (4.4%) in the TAE group and 12/110 patients (10.9%) in the PPI only group (P = 0.89; OR 2.66, 95% CI 0.8–8.5). There were no observed significant differences between groups in terms of mortality, length of hospital stay, or blood transfusion requirements. There was significantly less ulcer rebleeding in the subgroup of patients with large ulcers ($\geq$1.5 cm) who received pre-emptive TAE (2/40 [5.0%] vs. 10/43 [23.3%]; P = 0.027). Thus, in this specific high-risk subgroup, there may be a role for early pre-emptive TAE therapy. Additional data are warranted.

Abbreviations: DDW, Digestive Disease Week; EGD, esophagogastroduodenoscopy; NGT, nasogastric tube; OTSC, over-the-scope clip; PPI, proton pump inhibitor; TAE, transarterial angiographic embolization.

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In another study by the same group, the authors reported on a study of patients with massive gastroduodenal ulcer bleeding in whom endoscopic hemostasis was unsuccessful.[6] Over more than 6 years, 31 patients were randomized to undergo TAE (n = 17) or surgery (n = 14) as rescue therapy. On intention-to-treat analysis, there were no deaths in either group at 30 days postrandomization. Treatment failures were higher in the TAE group (9/17 [52.9%] vs. 3/14 [21.4%]; $P = 0.052$; OR 4.7, 95%CI 0.9–23.7) as were the median number of blood transfusions (2 units [range 0–18] vs. 0 units [range 0–9]; $P = 0.058$). Compared with surgery, patients receiving TAE spent significantly fewer days in the intensive care unit (0 days vs. 2 days; $P = 0.037$), although overall length of hospital stay was similar between the groups (9 days [range 3–36] vs. 12 days [range 3–27]; $P = 0.91$).

Finally, in a retrospective cohort study (from 2008 to 2012), Wu et al[7] evaluated the role of adjunctive prophylactic TAE following endoscopic hemostasis in selected patients with peptic ulcer bleeding who were at "extreme" risk of ulcer rebleeding. Using univariate and multiple regression analysis, the authors attempted to identify independent predictors of the need for prophylactic TAE. The authors identified 245 patients who had peptic ulcer bleeding requiring endoscopic hemostasis. All patients received intravenous PPI therapy, and the overall ulcer rebleeding rate was 33/245 (13.5%). A total of 10 patients received prophylactic TAE following endoscopic hemostasis. On multiple logistic regression analysis, initial hypotension (systolic blood pressure < 100 mmHg) and prolonged endoscopy time required to achieve primary hemostasis (≥60 minutes) were significant independent factors contributing to ulcer rebleeding. In those patients with prolonged endoscopy time, the ulcer rebleeding rate was 2/8 (25.0%) in those who received the TAE therapy and 18/26 (69.2%) in those who did not receive the prophylactic therapy ($P = 0.042$). The authors concluded that prolonged endoscopy time to achieve primary hemostasis may be a predictor of ulcer rebleeding and could be used to select patients who would benefit from prophylactic TAE therapy.

NONVARICEAL UPPER GASTROINTESTINAL BLEEDING

Chan et al[8] evaluated the role of antisecretory agents in nonvariceal upper gastrointestinal bleeding, and presented data at DDW on an interim analysis of a double-blind, randomized trial comparing a PPI (rabeprazole) with a histamine-2 receptor antagonists (famotidine) for the prevention of recurrent ulcer bleeding in low-dose (80 mg/day) aspirin users. Following ulcer healing, aspirin users were randomly assigned to receive either rabeprazole 20 mg/day or famotidine 40 mg/day for up to 12 months. The primary end point was recurrent upper gastrointestinal bleeding as determined by an independent adjudication committee. In an intention-to-treat analysis of 163 patients (84 rabeprazole, 79 famotidine), 15 patients had suspected recurrent bleeding (9 rabeprazole, 6 famotidine). The committee confirmed recurrent upper gastrointestinal bleeding in one patient (1.2%) from the rabeprazole group and in three patients (3.8%) from the famotidine group ($P = 0.29$). Eight rabeprazole patients (9.5%) and three famotidine patients (3.8%) had lower gastrointestinal bleeding ($P = 0.17$). The authors concluded from this interim analysis that, in aspirin users with a history of nonvariceal upper gastrointestinal bleeding, there is no significant difference in recurrent upper gastrointestinal bleeding between patients receiving rabeprazole and those receiving famotidine. It should, however, be noted that this was only an interim analysis of an ongoing study and the lack of statistical significance between groups may be due to inadequate power to detect a true difference (beta error). We therefore eagerly await the final study results.

NASOGASTRIC TUBE PLACEMENT TO PREDICT NEED FOR ENDOSCOPIC THERAPY

Although nasogastric tube (NGT) placement with aspiration and lavage is often used in the emergency department as part of the initial evaluation of patients with suspected upper gastrointestinal bleeding, its clinical utility remains unproven. Rockey et al[9] reported on the results of a single-center, single-blind, randomized, noninferiority study comparing NGT placement with aspiration and lavage vs. no NGT placement in patients presenting with suspected acute upper gastrointestinal bleeding (hematemesis and/or melena). Physicians completed a validated questionnaire (pre- and post-NGT placement) to predict the need for endoscopic intervention at the time of EGD. The primary outcome was the ability of NGT aspiration to predict the need for endoscopic therapy at EGD performed within the subsequent 24 hours. A total of 280 patients were randomized (140 NGT, 140 no NGT). The groups were evenly matched for demographic and clinical variables. NGT placement and aspiration led to a change in the physicians' prediction of whether or not patients were likely to need endoscopic therapy in 41/140 patients (29%). There was an absolute change of more than 20% in physicians' prediction in only 21/140 patients (15%). Endoscopic therapy was delivered in 34% and 31% in the NGT and no NGT arms, respectively ($P = 0.70$). The authors concluded that the routine placement of NGT with aspiration and lavage in patients with suspected upper gastrointestinal bleeding did not assist in predicting the need for subsequent endoscopic therapy. Furthermore, NGT placement led to patient discomfort, nasal bleeding,