Gastrointestinal bleeding

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There were a number of interesting abstracts presented at the 2012 Digestive Disease Week (DDW; 19-22 May, San Diego, California, USA) that covered gastrointestinal bleeding and endoscopy. The following abstracts are those that were found to have particular high clinical importance and the potential for direct impact on the endoscopic care of patients.

PEPTIC ULCER BLEEDING

Emerging endoscopic hemostasis therapies for acute nonvariceal upper gastrointestinal hemorrhage (NVUGIH) that do not involve using injection, thermal methods, or mechanical techniques have been developed and are now being evaluated in clinical studies. Sung et al.[1] from the Hong Kong group recently reported pilot data on the use of Hemospray (Cook Medical, Winston-Salem, North Carolina, USA) in acute peptic ulcer bleeding. At DDW 2012, Morris et al.[2] reported the initial prospective, multicenter European study (the SEAL Study) evaluating the use of Hemospray as monotherapy or in combination with another endoscopic hemostasis modality in NVUGIH. Over a 3-month period (June to September 2011) at nine separate European centers, 71 patients (49 males; median age 70 years) were treated using Hemospray as monotherapy (n = 39), adjuvant endotherapy (n = 8), or as rescue therapy following failed primary hemostasis using an alternative technique (n = 24). In the monotherapy group, there was a 97% primary hemostasis rate, 16% rebleeding rate, and 8% associated mortality. In the adjuvant group, there was 75% primary hemostasis, 17% rebleeding, and no associated mortality. In the rescue therapy group, there was 67% primary hemostasis, 38% rebleeding, and 8% mortality. Overall, five deaths were reported (7.0%), none of which was directly due to gastrointestinal bleeding, and eight technical complications (11.3%) with the use of Hemospray. These are provocative data, but large-scale prospective randomized trial data are now needed to more rigorously evaluate this interesting and new hemostasis modality.

The role of scheduled second-look endoscopy in NVUGIH remains controversial.[3,4] Park et al.[5] reported on a prospective randomized trial comparing scheduled second-look endoscopy (n = 113) performed at 24–36 hours after index endoscopy versus clinical observation (n = 110) with upper endoscopy performed only if there was evidence of rebleeding in patients. All patients had peptic ulcer hemorrhage and high risk stigmata (Forrest Ia-IIb) and all received endotherapy at the time of index endoscopy. Baseline patient characteristics in both groups were reported to be equal, and there was no observed difference between groups in rebleeding, transfusions, surgery, radiological intervention, duration of hospitalization or mortality. Multivariate analysis showed that a Rockall Score ≥6 and unsatisfactory endotherapy reported by the endoscopist at index endoscopy were independent risk factors for ulcer rebleeding. The authors recommended a scheduled second-look endoscopy only in those patients with a Rockall Score ≥6 or in cases where endotherapy at the time of index endoscopy was thought to be suboptimal. This was an interim analysis, and therefore the noninferiority reported may be due to low patient numbers recruited at this time and a statistical beta error; thus, data from the fully completed trial are awaited.

Finally, Sung et al.[6] reported on a prospective, double-blind, double-dummy, randomized trial comparing the efficacy and safety of intravenous (IV) and oral esomeprazole in patients with peptic ulcer bleeding (Forrest I or IIab). After receiving endoscopic hemostasis, patients were randomly assigned to receive either IV esomeprazole 80 mg bolus followed by 8 mg/hour continuous infusion for 72 hours plus oral placebo (n = 95) or oral esomeprazole 40 mg twice daily for 72 hours plus IV placebo infusion (n = 105). The authors reported no statistically significant difference in rates of recurrent bleeding at 3, 7, or 56 days postendoscopic hemostasis. Not explicitly mentioned by the authors was the important issue of whether there was adequate power to detect a statistical difference between IV and oral esomeprazole post-hemostasis, and thus we anxiously await further information on this important study.

GASTRIC VARICEAL BLEEDING

The endoscopic use of "glue" for hemostasis of acute gastric variceal hemorrhage is commonly practiced in many

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parts of the world.[7] Chantarojanasiri et al.[8] reported on clinical outcomes and complications associated with histoacryl injection for gastric variceal hemorrhage. The investigators from Thailand retrospectively reviewed their data on 88 procedures for patients (mean age 55 years; 73% male) with acute gastric variceal hemorrhage who were treated with histoacryl from April 2008 to October 2011. Primary hemostasis using histoacryl was 96.6% and rebleeding over the ensuing 5 days was 10.1%. Early complications (14.6%) were mainly from nonfatal systemic embolization (41.6%). Factors associated with early complications were poor underlying liver status, emergency endoscopy, concurrent hepatocellular carcinoma, and higher requirements for blood transfusions. Overall mortality for this cohort was 21.3%, reported to be due primarily to infectious causes.

Data on the use of glue are even more limited in the United States due to this hemostasis modality not being approved for use in gastric variceal bleeding by the US Food and Drug Administration. Abu Rajab et al.[9] reported on a single United States tertiary care center experience using cyanoacrylate glue for gastric variceal hemorrhage. In total, 46 patients with gastric varices (32 male; mean age 60.6 years) were included, 44 of whom had acute gastric variceal bleeding. Active gastric variceal bleeding at the time of endoscopy was found in seven patients (15%), with primary hemostasis being achieved in 100%. Early rebleeding occurred in one patient (2%), which was controlled with repeat cyanoacrylate glue injection. Adverse events included ischemic stroke in two patients (4%) and portal vein emboli in one (2%). In 30/33 (91%) patients with long term follow-up (median 14 months), there was no recurrent gastric variceal bleeding. Three patients (9%) had rebleeding that was successfully retreated with glue injection. The authors concluded that cyanoacrylate glue injection for gastric variceal bleeding was effective and had few complications.

POST-ESD BLEEDING

There were a number of abstracts presented on the topic of upper gastrointestinal bleeding associated with endoscopic submucosal dissection (ESD). Uedo et al.[10] reported on the feasibility of using Doppler ultrasound for predicting post-ESD bleeding in 80 patients with early gastric cancer. Upon completion of ESD, a Doppler ultrasound probe was placed in contact with the ulcer base to search for a positive Doppler signal. Soft coagulation was performed for areas or vessels with Doppler-positive signals. Areas without a Doppler signal were left untreated. The incidence of delayed bleeding was evaluated. Delayed bleeding occurred in six patients (7.5%). Delayed bleeding occurred in 4/252 (1.6%) Doppler-positive vessels or areas, despite being prophylactically treated with soft coagulation. In one patient, the source of bleeding was not identified. Delayed bleeding arose from only 1/744 (0.13%) Doppler-negative vessels or areas. Thus, it appears that the post-ESD use of Doppler ultrasound may have a role in the prevention of post-ESD bleeding episodes.

Two retrospective Japanese studies appeared to demonstrate the synergistic effect of anti-platelet agents and anti-coagulants (defined together as anti-thrombotic drugs, ATDs) on the risk of post-ESD ulcer bleeding in patients with early gastric cancer.[11,12] These two studies assessed the association between the use of ATDs and the rate of secondary post-ESD ulcer hemorrhage in patients with early gastric cancer. Kawai et al.[11] reported on 552 patients, of whom 131 (23.7%) were taking ATDs and Takeuchi et al.[12] reported on 833 patients, 90 of whom (10.8%) were taking ATDs. In the study by Kawai et al., anti-coagulants or anti-platelet drugs alone did not increase the rate of secondary hemorrhage (4/104, 3.8%; $P < 0.60$) or blood transfusion (1/104, 1.0%; $P = 0.99$), but the combination of anti-coagulants and anti-platelet drugs increased the rate of secondary hemorrhage (25.9%; $P < 0.01$) and blood transfusions (14.8%; $P < 0.01$). Takeuchi et al. also showed that in patients taking both anti-platelet agents and anti-coagulants, post-ESD hemorrhage occurred in 24% (5/21) compared with 6% (4/69) in those not taking both types of ATDs ($P < 0.016$). Moreover, Takeuchi et al. reported that the use of post-ESD proton pump inhibitors or mucosal protective agents significantly reduced the incidence of post-ESD hemorrhage ($P = 0.039$).

POST-POLYPECTOMY BLEEDING

On the topic of lower gastrointestinal bleeding, there were several abstracts that related to post-polypectomy bleeding. Kishino and Oyama[13] compared the incidence of post-polypectomy bleeding and thromboembolic events for patients who had their anti-thrombotic agents withheld for a period before and after polypectomy (aspirin alone withheld from 5 days before until 3 days after; dual anti-platelet therapy 7 days before and 5 days after; and warfarin 4 days before and 3 days after). A control group of patients who did not normally take anti-thrombotic agents was also included. For those taking warfarin, the international normalized ratio was checked on the day of colonoscopy and if ≥1.5 the colonoscopy procedure was cancelled. The immediate post-polypectomy bleeding rate was 11/282 (3.9%) in the drugs-withheld group and 76/1648 (4.6%) in the control group ($P = 0.45$). The delayed post-polypectomy bleeding rate was 4/282 (1.4%) in the drugs-withheld group and 18/1648 (1.1%) in the control group ($P = 0.52$). There were no thromboembolic events in either group. Logistic regression analysis showed that withholding anti-thrombotic agents did not appear to influence post-polypectomy bleeding rates (odds ratio 1.29; 95% confidence interval 0.38-4.41).

In a retrospective, matched case–control study of patients who underwent elective colonoscopy at a single VA hospital between July 2008 and December 2009, Iqbal et al.[14] compared the rates of delayed post-polypectomy