

Endoscopic Ultrasound in the Diagnosis and Treatment of Upper Digestive Bleeding: a Useful Tool

Andrada Seicean

3rd Medical Clinic, University
of Medicine and Pharmacy
Iuliu Hatieganu, and
Regional Institute of
Gastroenterology and
Hepatology Prof. Dr. Octavian
Fodor
Cluj-Napoca, Romania

Address for correspondence:

Andrada Seicean, MD PhD
3rd Medical Clinic
University of Medicine and
Pharmacy Iuliu Hatieganu
Croitorilor Str. 19-21
400162 Cluj-Napoca
Romania

andradaseicean@yahoo.com

Received: 30.06.2013

Accepted: 02.09.2013

ABSTRACT

The use of endoscopic ultrasound (EUS) in identifying the causes of upper digestive bleeding is less individualised. EUS can find the small vessel responsible for intermittent active bleeding in case of Dieulafoy ulcer or for discriminating it from vascular abnormalities. The EUS diagnosis of portal hypertension has to describe esophageal and gastric varices, perforant and paraesophageal veins, dilatations of the azygos, portal, superior mesenteric vein and splenic vein. Few studies have involved EUS in the prediction of variceal bleeding and variceal bleeding recurrence, and in the guided therapy of gastric varices or submucosal gastric neoplasms. The EUS aspect of hemobilia is that of an enlarged inhomogeneous common bile duct, without a Doppler signal, and the origin of the bleeding can be identified as a biliary tumor, bile duct stone or vascular abnormality. The EUS image of the pseudoaneurysm responsible for hemosuccus pancreaticus is that of a cystic lesion with Doppler signal; sometimes, a pseudoaneurysm can be found to communicate with a blood vessel and EUS-guided therapies have been reported.

Despite the limitations of the current devices and accessories, EUS has established its place among the endoscopic and radiologic tools. However, rational patient selection is mandatory.

Key words: endosonography – EUS – gastrointestinal hemorrhage – esophageal varices – gastric varices – portal hypertension – hemobilia – hemosuccus pancreaticus – gastrointestinal neoplasms – Dieulafoy ulcer.

INTRODUCTION

Acute gastrointestinal bleeding is a potentially life-threatening abdominal emergency that remains a common cause of hospitalization. Although 90% of the cases have a source that can be identified by upper and lower digestive tract endoscopy, there are other situations, called obscure gastrointestinal bleeding, in which the origin was missed or no active bleeding was found on the initial examination. Other endoscopic techniques, such as small bowel endoscopy, endoscopic ultrasound (EUS) or angiography can subsequently be used, but data concerning EUS are less individualised.

We review the situations in which EUS can be useful in the

diagnosis or treatment of upper digestive bleeding. Several sections are presented concerning the Dieulafoy ulcer, portal hypertension, submucosal tumors, hemobilia and hemosuccus pancreaticus.

DIEULAFOY ULCER

This occurs when a submucosal arteriole of 1-2 mm in diameter penetrates the surface of the mucosa, sometimes causing severe bleeding. Finding the lesion can often be difficult because the small vessel cannot be always visible due to intermittent active bleeding. When the conventional methods of treatment fail, EUS can help in finding the vessel [1] and directing the therapy [2]. Rarely, the Dieulafoy ulcer can be mistaken for other vascular abnormalities, such as a splenic artery pseudoaneurysm. EUS can help in discriminating the real cause [3]. However, EUS practical usefulness in the Dieulafoy ulcer detection is limited.

PORTAL HYPERTENSION AND BLEEDING

Diagnosis of portal hypertension

EUS can visualise varices as anechoic vascular structures in the submucosa of the esophagus or stomach (Fig. 1A), and can sometimes identify ectopic varices situated in the

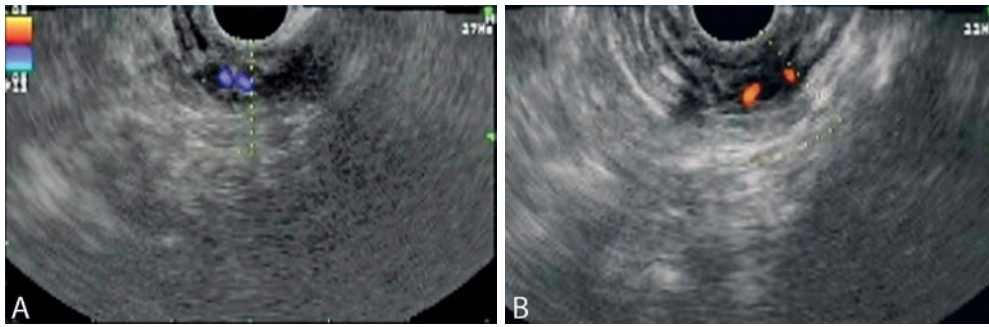


Fig. 1 A. Esophageal varices seen as hypoechoic structures with a Doppler or power Doppler signal situated in the submucosal layer; B. Perforating vessels visible as structures with a power Doppler signal crossing the muscle layer. Esophageal varices seen between muscularis mucosae and muscle layer.

duodenum, in a gastro-duodenal anastomosis or in the biliary tree. Paraesophageal vessels are seen in the adventitia, outside the muscle layer, and they establish the connection with the superior vena cava via the azygos vein. Perforating vessels establish the connection between the esophageal varices and the paraesophageal veins (Fig. 1B). The portal gastropathy is visualised as a thickened submucosal and mucosal layer, with multiple small (2–3mm), round, anechoic structures, with Doppler signal in the submucosal layer. Dilatations of the azygos, portal, superior mesenteric vein and splenic vein have to be looked for at every occasion. Gastric varices appear as hypoechoic tortuous tubular structures in the submucosal layer (Fig. 2).

The radial and convex linear echoendoscopes are similar in the evaluation of perforating veins and paraesophageal veins, but the radial assessment provides better results in detecting palisade veins and pulsatile waves [4].

Despite the lower performance of EUS compared to endoscopy in the diagnosis of esophageal varices, the accuracy is nowadays similar with the use of newer echoendoscopes. However, being an expensive and time-consuming technique, EUS is not the preferred method [5]. Miniproboscopes, without balloon compression of the varices, have demonstrated better accuracy in variceal detection; they can also be used to identify the hematocystic spots on the surface of esophageal varices, appearing like saccular projections suggestive for focal weakness of the esophageal wall [6].

Gastric varices are sometimes mistaken for large gastric folds or submucosal tumors and EUS helps in differentiating them. Using EUS as a gold standard for evaluation of the

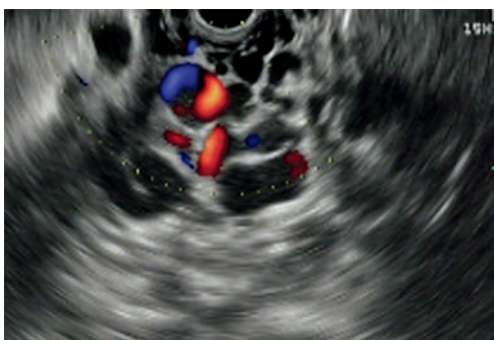


Fig. 2. Gastric varices seen as hypoechoic structures situated in the submucosal layer, with a Doppler signal.

presence of gastric varices, the sensitivity and specificity value for conventional endoscopy are only 44% and 94%, respectively [7]. An EUS study on the origin of gastric varices showed that the feeding vein for the junctional type of gastric varices was mainly the left gastric vein, whereas the gastric varices of fundic type were fed by the short gastric vein [8].

Apart from differential diagnosis of gastric varices, the clinical use of EUS for portal hypertension diagnosis is very limited.

Esophageal varices

Estimation of bleeding risk

It was shown that a cumulative cross-sectional surface area of the varices of 0.45 cm² predicted the bleeding with a sensitivity of 83% and a specificity of 75%. There was a 76-fold increase per year in the risk of future variceal bleeding for each cm² increase in the variceal cross-sectional area. However, no correlation was found between the endoscopic grading of esophageal varices and future bleeding [7].

The direct portal vein pressure measurement by variceal puncture under EUS guidance, postulated as a predictor of bleeding, was safely performed in pigs [9], but in humans it is considered unethical. As a result, the indirect measurement of intravariceal pressure has been developed.

An experimental study showed that each varix had a different intravariceal pressure, which correlated well with the intravariceal radius, but not with the wall thickness [10].

Prediction of variceal bleeding recurrence

Large paraesophageal and paragastric varices after ligation (5 mm or greater), high velocity of anterior branches and a left gastric vein may be risk factors for variceal hemorrhage [11]. The rebleeding rate after EUS sclerotherapy was similar with that after conventional endoscopic sclerotherapy, although variceal recurrence occurred later and less frequently in the EUS-guided group [12].

Gastric varices

The EUS study of gastric varices showed that blood flow velocity is higher in bleeding varices as compared to non-bleeding varices, and the variceal wall is thinner in bleeding varices [13].

Several studies were performed using preferably cyanoacrylate injection in the perforating veins, the rate of total obliteration was successful in all five cases, with a mean number

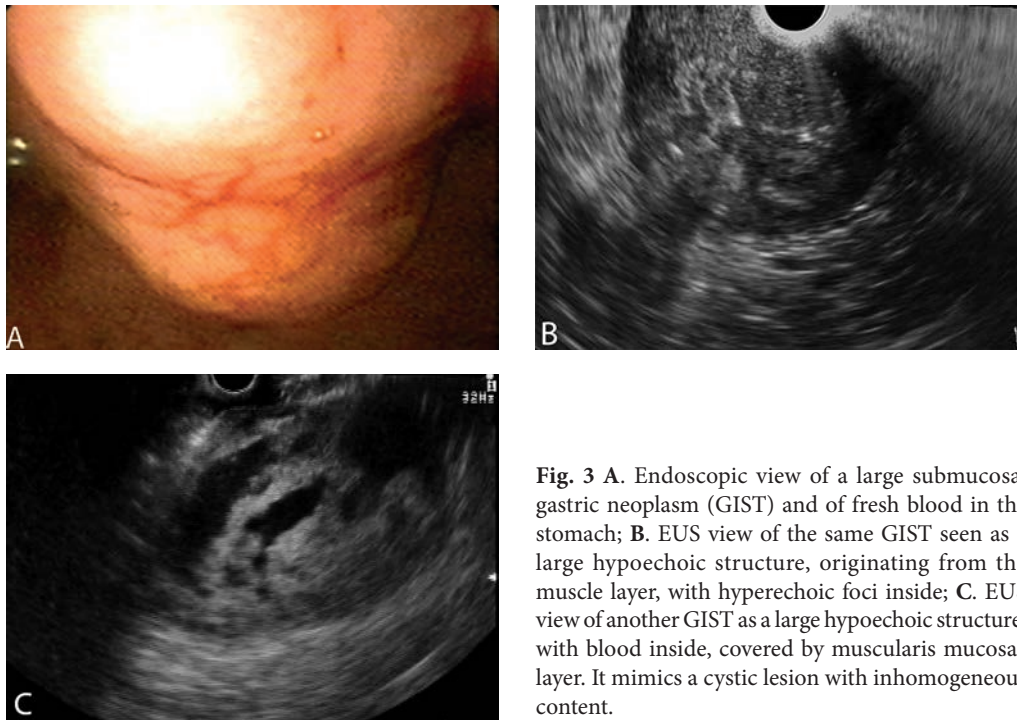


Fig. 3 A. Endoscopic view of a large submucosal gastric neoplasm (GIST) and of fresh blood in the stomach; B. EUS view of the same GIST seen as a large hypoechoic structure, originating from the muscle layer, with hyperechoic foci inside; C. EUS view of another GIST as a large hypoechoic structure, with blood inside, covered by muscularis mucosae layer. It mimics a cystic lesion with inhomogeneous content.

of sessions of 1.6 [14]. Repeated injections of cyanoacrylate gave better results in terms of late recurrent bleeding than on demand injection in response to recurrent bleeding (18.5% vs 44.7%) [15]. However, coil embolization delivered by EUS seems to be very promising. Under EUS and fluoroscopy guidance, stainless steel, synthetic-fiber coils of 0.035 inch diameter were deployed through a 19-gauge needle into the perforating feeding vein, with the aim of forming a mesh to block the flow of blood [16]. The combination of cyanoacrylate injection and coil embolization showed good results in a larger study [17]. A severe complication due to cyanoacrylate diffusion into the hepatic artery has been reported [18].

Balloon-occluded retrograde transvenous obliteration for the management of gastric varices was performed in 39 cirrhotic patients and esophageal varices recurrence was evaluated. The presence of esophageal varices, a higher Child-Pugh class and a higher resistance index assessed by EUS before the procedure were significant risk factors for the worsening of esophageal varices after obliteration [19]. An assessment of gastric vessels before devascularisation surgery for isolated gastric varices seemed highly effective [20].

Duodenal and ectopic varices

EUS can identify duodenal varices as the cause of obscure bleeding after liver transplantation [21]. Direct EUS-guided injection with thrombin or cyanoacrylate were used as a therapeutic procedure. Microcoil injection in anastomotic varices after total pancreatectomy with good short-term outcome was reported [22].

SUBMUCOSAL NEOPLASMS

EUS guided fine needle aspiration (EUS-FNA) represents a useful method for the diagnosis of submucosal neoplasms, although recent studies have shown its low accuracy [23].

Sometimes they are associated with extraluminal bleeding with spontaneous hemoperitoneum or they mimic a pancreatic cyst; in these cases, EUS can establish the diagnosis [24] (Fig. 3). Cyanoacrylate injection of an actively bleeding GIST of the proximal stomach was reported to have a good outcome [2], but this technique is reserved for patients who cannot have surgery.

WIRSUNGORRHAGIA

Wirsungorrhagia occurs intermittently and can be caused by a pancreatic benign or malignant neoplasm, chronic pancreatitis with lithiasis or pseudoaneurysms, or a ruptured arterial aneurysm [25]. EUS plays an important role when the cause of the digestive bleeding is not established.

The pseudoaneurysm may originate from the left gastric artery, splenic artery, right hepatic artery, gastroduodenal artery and pancreaticoduodenal artery [26] (Fig. 4). The EUS image of the pseudoaneurysm is that of a cystic lesion with a Doppler signal; sometimes, a pseudoaneurysm can be found to communicate with a blood vessel. The treatment alternatives are transcatheter arterial embolization, injection with N-butyl-2-cyanoacrylate [27] or surgery, but 99% of alcohol EUS-guided injections in pancreatic pseudoaneurysms have been reported to have a successful outcome [2].

HEMOBILIA

Hemobilia is caused usually by medical invasive procedures (percutaneous biopsies, transhepatic cholangiographies or self expanding metal biliary stents placed during ERCP) or by abdominal trauma. Other causes could be gallbladder and bile duct stones, biliary varices, benign and malignant tumors involving the biliary tree, liver surgery (including transplantation), congenital or acquired vascular aneurysms. The main symptom is jaundice, and sometimes blood clots

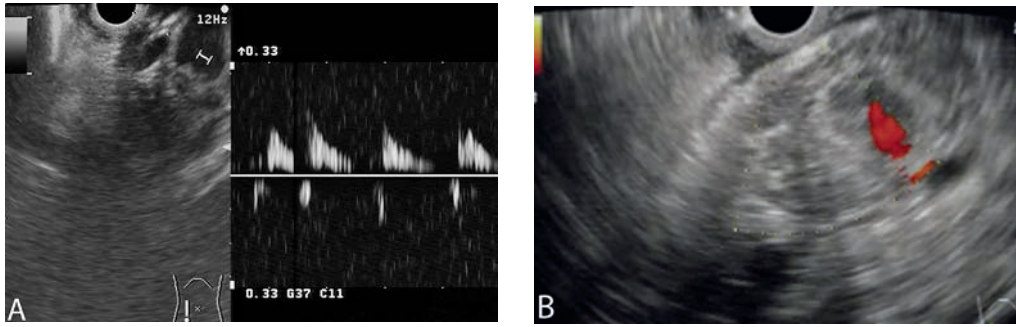


Fig. 4 **A.** EUS view of a pseudoaneurysm in the pancreas, as an inhomogeneous hypoechoic structure with anechoic region inside, which presents a Doppler arterial signal. The splenic artery is situated nearby as an anechoic round structure; **B.** EUS view of a pseudoaneurysm in the pancreatic body, appearing as a moderately hypoechoic structure with inhomogeneous solid content from previous bleeding. In the central part of the structure there is an anechoic region with power Doppler flow.

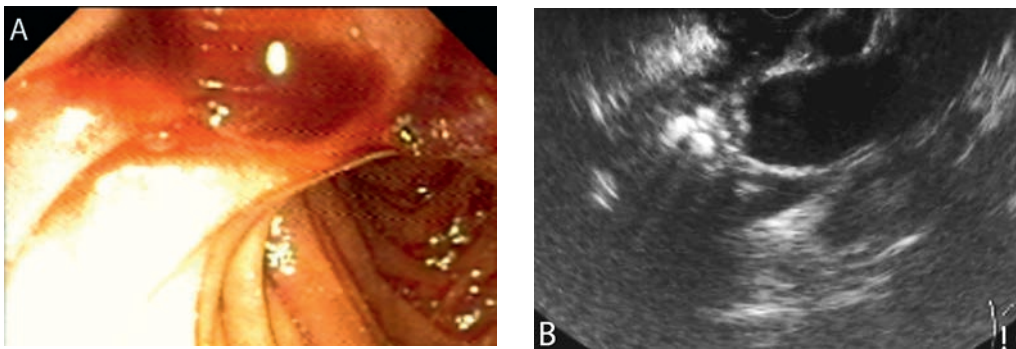


Fig. 5 **A.** Hemobilia – endoscopic view. Presence of fresh blood at the papillary level; **B.** Hemobilia - EUS view. A large common bile duct with inhomogeneous moderately hypoechoic content without a Doppler signal. The origin was a gallbladder tumour.

drain externally or are cleared endoscopically. During CT or MRI a filling defect becomes apparent in the biliary tree and, on endoscopy, blood and/or a clot surround the duodenal papilla. Cases of hepatic artery pseudoaneurysms with hemobilia identified by EUS have been rarely reported [28]. Hemobilia can be seen in EUS as an enlarged inhomogeneous common bile duct, without a Doppler signal, and the origin of the bleeding can be identified as a biliary tumor, biliary stone or vascular anomaly [29] (Fig. 5).

POST-THERAPEUTIC BLEEDING

Doppler US miniprobes were used in eight patients for assessing the bleeding sites after submucosal dissection for early gastric cancer and coagulation was applied until the Doppler signal disappeared. No delayed bleeding was seen in one month follow-up [30]. Also, EUS assessment of submucosal vessels might predict the bleeding during submucosal dissection for early gastric cancer [31].

CONCLUSION

EUS can be of great help in diagnosing the cause of obscure gastrointestinal bleeding and the rational selection of the patients is mandatory. Although there are still limitations of the actual devices and accessories, the EUS has to be considered among the endoscopic and radiologic tools.

Conflicts of interest: None.

REFERENCES

- Schilling D, Jüngling B, Adamek HE, Benz C, Riemann JF. The endoscopic diagnosis and therapy as well as the long-term course of Dieulafoy ulcer hemorrhage. *Dtsch Med Wochenschr* 1999;124:419-423.
- Levy MJ, Wong Kee Song LM, Farnell MB, Misra S, Sarr MG, Gostout CJ. Endoscopic ultrasound (EUS)-guided angiotherapy of refractory gastrointestinal bleeding. *Am J Gastroenterol* 2008;103:352-359.
- Pinto-Marques P, Gíria J, Brito M, Camacho R, Loureiro R. Unusual cause for upper GI bleeding: a splenic artery aneurysm mimicking a Dieulafoy lesion. Role for systematic EUS assessment? *Gastrointest Endosc* 2010;71:845-846.
- Sato T, Yamazaki K, Toyota J, et al. Usefulness of electronic radial endoscopic color Doppler ultrasonography in esophageal varices: comparison with convex type. *J Gastroenterol* 2006;41:28-33.
- Burtin P, Cales P, Oberti F, et al. Endoscopic ultrasonographic signs of portal hypertension in cirrhosis. *Gastrointest Endosc* 1996;44:257-261.
- Miller LS, Schiano TD, Adrain A, et al. Comparison of high-resolution endoluminal sonography to video endoscopy in the detection and evaluation of esophageal varices. *Hepatology* 1996;24:552-555.
- Faigel DO, Rosen HR, Sasaki A, Flora K, Benner K. EUS in cirrhotic patients with and without prior variceal hemorrhage in comparison with noncirrhotic control subjects. *Gastrointest Endosc* 2000;52:455-462.

7. Lee YT, Chan FK, Ching JY, et al. Diagnosis of gastroesophageal varices and portal collateral venous abnormalities by endosonography in cirrhotic patients. *Endoscopy* 2002;34:391-398.
8. Iwase H, Suga S, Morise K, Kuroiwa A, Yamaguchi T, Horiuchi Y. Color Doppler endoscopic ultrasonography for the evaluation of gastric varices and endoscopic obliteration with cyanoacrylate glue. *Gastrointest Endosc* 1995;41:150-154.
9. Giday SA, Clarke JO, Buscaglia JM, et al. EUS-guided portal vein catheterization: a promising novel approach for portal angiography and portal vein pressure measurements. *Gastrointest Endosc* 2008;67:338-342.
10. Pontes JM, Leitão MC, Portela F, Nunes A, Freitas D. Endosonographic Doppler-guided manometry of esophageal varices: experimental validation and clinical feasibility. *Endoscopy* 2002;34:966-972.
11. Leung VK, Sung JJ, Ahuja AT, et al. Large paraesophageal varices on endosonography predict recurrence of esophageal varices and rebleeding. *Gastroenterology* 1997;112:1811-1816.
12. de Paulo GA, Ardengh JC, Nakao FS, Ferrari AP. Treatment of esophageal varices: a randomized controlled trial comparing endoscopic sclerotherapy and EUS-guided sclerotherapy of esophageal collateral veins. *Gastrointest Endosc* 2006;63:396-402.
13. Sato T, Yamazaki K, Toyota J, Karino Y, Ohmura T, Akaike J. Observation of gastric variceal flow characteristics by endoscopic ultrasonography using color Doppler. *Am J Gastroenterol* 2008;103:575-580.
14. Romero-Castro R, Pellicer-Bautista FJ, Jimenez-Saenz M, et al. EUS-guided injection of cyanoacrylate in perforating feeding veins in gastric varices: results in 5 cases. *Gastrointest Endosc* 2007;66:402-407.
15. Lee YT, Chan FK, Ng EK, et al. EUS-guided injection of cyanoacrylate for bleeding gastric varices. *Gastrointest Endosc* 2000;52:168-174.
16. Romero-Castro R, Pellicer-Bautista F, Giovannini M, et al. Endoscopic ultrasound (EUS)-guided coil embolization therapy in gastric varices. *Endoscopy* 2010;42 Suppl 2:E35-E36.
17. Binmoeller KF, Weilert F, Shah JN, Kim J. EUS-guided transesophageal treatment of gastric fundal varices with combined coiling and cyanoacrylate glue injection (with videos). *Gastrointest Endosc* 2011;74:1019-1025.
18. Gonzalez JM, Giacino C, Pioche M, et al. Endoscopic ultrasound-guided vascular therapy: is it safe and effective? *Endoscopy* 2012;44:539-542.
19. Elsamman MK, Fujiwara Y, Kameda N, et al. Predictive factors of worsening of esophageal varices after balloon-occluded retrograde transvenous obliteration in patients with gastric varices. *Am J Gastroenterol* 2009;104:2214-2221.
20. Hsieh JS, Wang WM, Perng DS, Huang CJ, Wang JY, Huang TJ. Modified devascularization surgery for isolated gastric varices assessed by endoscopic ultrasonography. *Surg Endosc* 2004;18:666-671.
21. Curcio G, Pisa MD, Miraglia R, et al. Case of obscure-overt gastrointestinal bleeding after pediatric liver transplantation explained by endoscopic ultrasound. *World J Gastrointest Endosc* 2012;4:571-574.
22. Levy MJ, Wong Kee Song LM, Kendrick ML, Misra S, Gostout CJ. EUS-guided coil embolization for refractory ectopic variceal bleeding (with videos). *Gastrointest Endosc* 2008;67:572-574.
23. Reddymasu SC, Oropeza-Vail M, Pakseresht K, et al. Are endoscopic ultrasonography imaging characteristics reliable for the diagnosis of small upper gastrointestinal subepithelial lesions? *J Clin Gastroenterol* 2012;46:42-45.
24. Harindhanavudhi T, Tanawuttiwat T, Pyle J, Silva R. Extra-gastrointestinal stromal tumor presenting as hemorrhagic pancreatic cyst diagnosed by EUS-FNA. *JOP* 2009;10:189-191.
25. Gonzalez JM, Giacino C, Pioche M, et al. Endoscopic ultrasound-guided vascular therapy: is it safe and effective? *Endoscopy* 2012;44:539-542.
26. Seicean A, Badea R, Stan-Iuga R, Iancu C, Seicean R. Double splenic artery pseudoaneurysm associating splenic infarction in chronic pancreatitis. *J Gastrointest Liver Dis* 2012;21:313-315.
27. Sayilir A, Onal IK, Beyazit Y, et al. A rare cause of upper gastrointestinal bleeding: hemosuccus pancreaticus: angiographic and endoscopic combined treatment. *Surg Laparosc Endosc Percutan Tech* 2011;21:e286-e287.
28. Cattan P, Cuillerier E, Cellier C, et al. Hemobilia caused by a pseudoaneurysm of the hepatic artery diagnosed by EUS. *Gastrointest Endosc* 1999;49:252-255.
29. Trakarnsanga A, Sriprayoon T, Akaraviputh T, Tongdee T. Massive hemobilia from a ruptured hepatic artery aneurysm detected by endoscopic ultrasound (EUS) and successfully treated. *Endoscopy* 2010;42 Suppl 2:E340-E341.
30. Uedo N, Takeuchi Y, Ishihara R, et al. Endoscopic Doppler US for the prevention of ulcer bleeding after endoscopic submucosal dissection for early gastric cancer: a preliminary study (with video). *Gastrointest Endosc* 2010;72:444-448.
31. Kikuchi D, Iizuka T, Hoteya S, et al. Usefulness of endoscopic ultrasound for the prediction of intraoperative bleeding of endoscopic submucosal dissection for gastric neoplasms. *J Gastroenterol Hepatol* 2011;26:68-72.