Review Article

Endoscopic Ultrasound-Guided Vascular Interventions: From Diagnosis to Treatment

Jiannis Anastasiou, Tyler M. Berzin[1]

Department of Gastroenterology, King Fahd Hospital of the University, Imam Abdulrahman Bin Faisal University, Khobar, Saudi Arabia, [1]Division of Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA

Abstract

The development of endoscopic ultrasound was driven by the need to develop less invasive alternatives to surgical and radiologic interventions for a wide variety of gastrointestinal conditions. During the past decade, there has been a very rapid growth in the clinical role and capabilities of endoscopic ultrasound-guided therapeutic interventions. Endoscopic ultrasound offers both real-time imaging and access to structures within and adjacent to the gastrointestinal tract. The proximity of the gastrointestinal system to vascular structures throughout the abdomen and the mediastinum allows for endoscopic ultrasound-guided vascular access and therapy. The recent development of endoscopic ultrasound-guided vascular interventions has relied both on finding new applications for standard endoscopic accessories and on commandeering tools originally developed for use in interventional radiology. This article provides a review of the literature regarding the current state of endoscopic ultrasound for the management of variceal and nonvariceal bleeding, portal vein angiography and pressure measurements, intrahepatic portosystemic shunts, endoscopic ultrasound-guided fine-needle aspiration for portal vein sampling, drug administration and embolization as well as endoscopic ultrasound-guided cardiac access and treatment.

Keywords: Endoscopic ultrasound, therapeutic EUS, vascular interventions

Address for correspondence: Dr. Tyler M. Berzin, Division of Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, 110 Francis Street, Boston, MA 02215, USA.
E-mail: tberzin@bidmc.harvard.edu

INTRODUCTION

Since its advent in the 1980s, the endoscopic ultrasound (EUS) technology has evolved dramatically, starting first as a supplementary diagnostic modality available only in large medical centers, and now representing a core diagnostic and therapeutic tool that is much more widely available.[1-3] While the initial focus in the use of EUS had been for diagnosis and management of various gastrointestinal (GI) conditions, ranging from tumor staging and biopsy to evaluation of submucosal lesions, it has also become clear that EUS can provide important clinical and anatomic information with regard to the appearance, size and location of vascular structure. EUS can also allow precise interventions to target certain vascular sites that are inaccessible, or less accessible, using conventional access techniques. By implementing techniques and tools acquired from interventional radiology (IR) and minimally invasive surgery, EUS combines real-time imaging with the possibility of anatomically specific guided vascular treatment.[4]

When considering potential opportunities for the development of new EUS-guided vascular approaches,

Access this article online	
Quick Response Code:	Website: www.sjmms.net
	DOI: 10.4103/sjmms.sjmms_131_17

How to cite this article: Anastasiou J, Berzin TM. Endoscopic ultrasound-guided vascular interventions: From diagnosis to treatment. Saudi J Med Med Sci 2018;6:61-7.

it is important to first take stock of some of the core IR techniques that have been in use for many decades, including selective angiographic embolization for refractory GI bleeding and transjugular intrahepatic portosystemic shunt (TIPS) for refractory gastroesophageal variceal bleeding.[5] The development of EUS-guided vascular access to manage these conditions is feasible owing to the proximity of the GI tract to vascular structures in the mediastinum and the abdomen. Large vessels such as the aorta, celiac axis, portal vein (PV), hepatic vein (HV), mesenteric vessels and aberrant vascular shunts as well as smaller vessels such as the gastroduodenal artery and splenic vessels can be accessed and visualized by EUS. EUS-guided therapies provide a promising, minimally invasive route for accessing vascular structures. Therapeutic agents and devices such as sclerosants, cyanoacrylate (CYA), thrombin and coils can all be delivered using a standard EUS fine-needle aspiration (FNA) into the targeted vessel.

VARICEAL BLEEDING

Endoscopic sclerotherapy and endoscopic band ligation are considered the standard of care for the treatment of esophageal varices.[6,7] Endoscopic band ligation is the preferred method for primary and secondary treatment of esophageal varices.[8] The reported recurrence rates of 15%–65% are attributed to failure to treat the perforating veins and collateral vessels feeding the esophageal varices.[7-12] Therefore, alternative, more effective approaches must be considered and evaluated for variceal bleeding.

EUS-guided sclerotherapy has been proven to be effective in a small pilot study by Lahoti *et al.*[13] The perforating vessels were targeted by EUS-guided needle puncture and injected with sodium morrhuate. The eradication of varices was achieved after a mean of 2.2 sessions. A 15-month follow-up showed no rebleeding or adverse events. EUS-guided sclerotherapy was compared with endoscopic sclerotherapy and no difference was noted in the mean number of sessions needed for eradication and the recurrence rates were not significantly different. However, recurrence was correlated with the identification of collateral vessels ($P = 0.003$), which was higher in the endoscopic group.[13]

EUS-guided therapy of esophageal varices, as promising as it may appear, needs further evaluation by larger, randomized controlled trials to prove its efficacy and cost-effectiveness compared with band ligation and other standard techniques and to identify whether it can best serve as a first- or second-line therapy. The use of CYA glue injection, in place of sclerosant, may also be an alternative approach to consider for EUS-guided treatment.[14]

GASTRIC VARICES

Gastric varices may be present in up to 20% of patients with portal hypertension. Bleeding from gastric varices can be severe and 35%–90% of the patients rebleed after the initial spontaneous hemostasis.[15] CYA glue injection has become the standard treatment for both acute bleeding and secondary prophylaxis. Hemostasis is achieved in 80%–90% of cases, although rebleeding is a risk.[16]

The primary role for EUS in this condition is diagnostic. Gastric varices are located in the deep submucosal layer and may appear similar to the prominent mucosal gastric folds. Boustiere *et al.*[17] demonstrated that EUS increased the detection of fundal varices sixfold, and thus EUS is a useful tool if gastric varices are suspected, but cannot be confirmed (or targeted) endoscopically.

Endoscopic ultrasound-guided glue injection

EUS-guided glue treatment for gastric varices has an array of potential advantages compared with standard endoscopic glue injection. EUS not only permits accurate delivery of glue into the target varix but also enables the confirmation of complete flow obliteration of the varix using color Doppler. EUS also allows for identification and glue injection into perforating vessels, theoretically, minimizing the risk of embolization.[18] A limitation of this method is that it may be difficult and time-consuming to determine the exact feeding vessel. Injection of contrast has been proposed, prior to glue injection, to ensure that the correct afferent vessel was selected.[19]

Endoscopic ultrasound-guided coil embolization

An alternative method for treating gastric varices is EUS-guided coil embolization. By placing microcoils into the varices, obliteration is achieved. Synthetic fibers cover the coils, thereby promoting clot formation. The varix is identified and punctured by a standard EUS needle, after which the coils are advanced through the needle and into the varix, using the stylet as a "pusher." This technique was initially described as a case series and has been increasingly used both as a monotherapy and in combination with CYA.[20,21]

Endoscopic ultrasound-guided glue and coil combination therapy

Binmoeller *et al.*[20] reported the combined use of EUS-guided coil deployment with glue injection. The rationale was that the use of coils would facilitate the CYA injection by providing CYA a scaffold to form.[19] Binmoeller *et al.*'s study evaluated the treatment of patients with active recent bleeding due to large gastric varices and who were poor candidates for TIPS placement. In total,

30 patients were included, and they underwent combined treatment with EUS-guided coiling and CYA injection through a transesophageal route, thereby obviating a direct puncture of the gastric varix mucosa. A single coil was applied in the majority of patients (93%). Two patients developed esophageal bleeding at the needle injection site, which was treated with band ligation. The rebleeding rate was 16.6% after a 6.6-month follow-up.[20]

The advantage of EUS-guided combined glue injection is the ability to perform treatment through the transesophageal route, thereby avoiding bleeding at the site of the gastric varix puncture. In the presence of active bleeding, this EUS transesophageal route could also be beneficial over a standard endoscopic approach from the stomach because the latter approach may be compromised by the presence of blood in the gastric lumen, obscuring the precise location of gastric variceal hemorrhage. Nevertheless, comparative prospective studies are needed to investigate the efficacy and cost-effectiveness of the combined treatment.

Ectopic variceal therapy

EUS-guided treatment has been applied in case reports regarding variceal bleeding at other anatomical locations.[22] The use of EUS-guided coil to stop massive variceal bleeding has been described.[23] Rectal varices are not uncommon, but they have a lower potential of bleeding than the esophageal and gastric varices. The use of both EUS-guided CYA injection and combined EUS-guided coil/CYA treatment for rectal varices has been reported.[24] EUS has also been applied to treat parastomal varices,[25] and although the data are insufficient to support EUS-guided treatment as first line in such cases, it has evolved as a promising modality for rescue treatment.

Nonvariceal gastrointestinal bleeding

EUS-guided treatment may be applied as an alternative modality to patients with refractory GI bleeding who have not responded to standard endoscopic treatment with epinephrine, hemoclips and electrosurgical coagulation. The data on EUS-guided techniques for nonvariceal GI bleeding have largely been confined to case reports. The treatment of bleeding from Dieulafoy lesions, GI stromal tumors, duodenal ulcers and hemosuccus pancreaticus has been reported in patients for whom conventional endoscopic and IR treatments had failed.[26] The methodology in most cases involved identification of feeder vessels and injection of sclerosing agents, with the confirmation of cessation of vascular flow by Doppler.

Pseudoaneurysms are a rare and potentially lethal complication of pancreatitis or abdominal surgery. Rupture of a pseudoaneurysm and the subsequent bleeding are typically treated by angiography or surgery and are associated with high morbidity and mortality.[27,28] EUS-guided treatment for pancreatic pseudoaneurysm bleeding has been reported.[29] Law *et al.*[30] reported 17 cases of refractory pseudoaneurysm bleeding treated with a combination of glue, coils, alcohol and epinephrine injection using fine-needle EUS access with a linear echoendoscope.

Although such reports hold promise for an exciting future, the data available are not sufficient to support EUS-guided use over the standard therapies. Therefore, presently, EUS should be considered primarily in expert centers when other modalities are not technically feasible or have failed.

PORTAL VEIN: POTENTIAL APPLICATIONS

Portal vein access and pressure measurement

PV access can provide valuable information regarding patients with portal hypertension and other hepatobiliary diseases.[31] EUS allows for transgastric or transduodenal access into PV, contrast injection and/or pressure monitoring, using a standard FNA needle. Initial approaches to EUS-guided PV interventions were developed in a porcine model. PV access and pressure measurement were first achieved using a 22G needle.[32] Subsequently, PV angiography in a porcine model was reported using a 25G needle.[33] Giday *et al.*[34] demonstrated that using carbon dioxide for portal venography obviated the need for injecting any contrast media. The same group performed EUS-guided transhepatic PV catheterization with a modified endoscopic retrograde cholangiography catheter.[35] The authors used a transhepatic puncture approach of the PV to reduce the risk of bleeding. Necropsy examination did not show any signs of bleeding or any vascular damage.

In the first human pilot study of EUS-guided portal pressure gradient measurement, 28 patients with a history of chronic liver disease or suspected cirrhosis underwent EUS-guided PV puncture with a 25G FNA needle attached to a newly developed compact manometer (Cook Medical, Bloomington, Ind) [Figures 1 and 2].[36] The patients also underwent standard upper endoscopy to investigate if the findings were consistent with portal hypertension. Measurements were recorded in the intrahepatic PV close to its bifurcation and in the HV approximately 2 cm from its takeoff from the intrahepatic inferior vena cava. Correlation of the measured portal pressure gradients with clinical parameters of portal hypertension (varices and

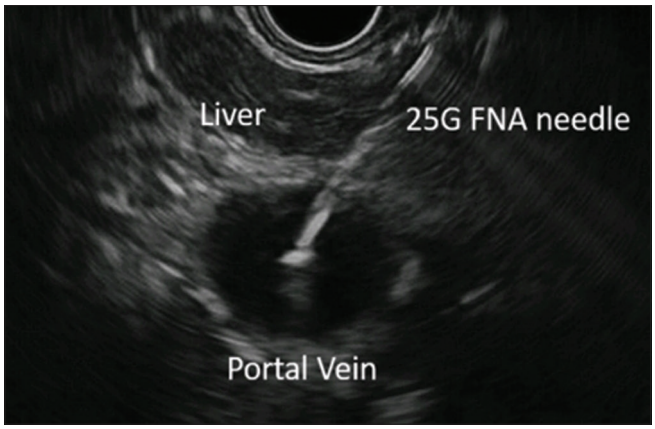

Figure 1: Linear endoscopic ultrasound view of portal vein (Images obtained by permission of *Gastrointestinal Endoscopy*)

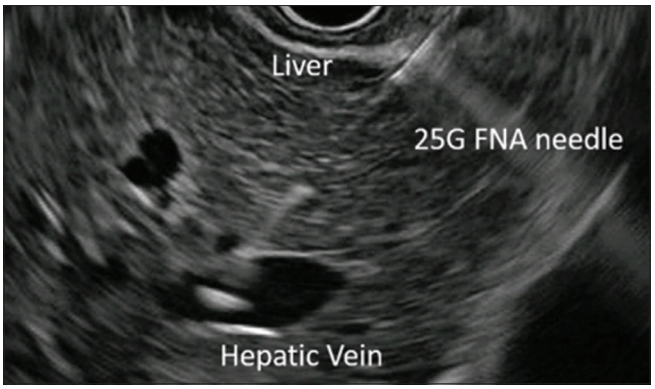

Figure 2: Linear endoscopic ultrasound view of hepatic vein (Images obtained by permission of *Gastrointestinal Endoscopy*)

portal hypertensive gastropathy) was noted and no adverse events were reported.

Intrahepatic portosystemic shunt

Rescue therapy for refractory gastroesophageal bleeding is the placement of TIPS, which currently requires transjugular access. The first insertion of an intrahepatic portosystemic shunt (IPSS) by EUS was performed in a porcine model in 2009.[37] The authors were able to identify a sonographic plane that achieved simultaneous visualization of the intrahepatic branches and of HV and PV. Under EUS guidance, the HV was punctured with a 19G needle that traversed the hepatic parenchyma. A self-expandable uncovered metal biliary stent was placed between the HV and PV, forming an IPSS. No adverse events were reported at 2 weeks postprocedure or at necropsy of the animals. Binmoeller *et al.*[38] used a similar method to create an IPSS using a lumen-apposing stent, also in a porcine model. No evidence of vascular or tissue injury was noted in necropsy. To date, this approach has not yet been reported in humans, but further development of this technique is anticipated.

Endoscopic ultrasound-guided fine-needle aspiration of portal vein thrombosis for staging of hepatocellular carcinoma

Curative resection or liver transplantation is contraindicated in case of hepatocellular carcinoma invading the PV.[39,40] Endosonography may be useful in differentiating a benign thrombus from a tumor thrombus by providing cytopathologic confirmation using FNA. Transabdominal ultrasound sampling is limited by the potential of sample contamination with normal hepatocytes or tumor tissues, as the needle passes through the liver, and there is also a risk of serious biliary or vascular injury, depending on the path of the needle.[41] EUS-guided FNA is an alternative approach that may offer a more direct access, particularly to the extrahepatic PV, which can be accessed directly, as the needle is not required to pass through the hepatic parenchyma. In several case reports, malignant PV thrombi were diagnosed using an EUS–FNA transduodenal approach without adverse events.[41-44] The diagnosis of hepatocellular carcinoma has also been reported by EUS–FNA of malignant PV thrombi in patients with no evidence of liver mass depicted on cross-sectional imaging.[41,42]

Endoscopic ultrasound-guided portal vein sampling of circulating tumor cells in pancreatobiliary malignancies

Circulating tumor cells (CTCs) migrate from the primary tumor through the vasculature to distant sites while maintaining similar characteristics to those of the tumor of origin.[45] A recent study showed that CTCs were found in PV blood samples (obtained by portal venous puncture at the time of surgical resection) in 58% of patients undergoing pancreaticoduodenectomy for resectable pancreatic or periampullary cancer [Figure 3].[46]

A high CTC count in PV samples has been found to a useful predictor for the future development of liver metastases. EUS sampling of CTCs before and during cancer treatment may, in the future, provide a window into treatment progress and changes in tumor biology in response to therapy. It is also conceivable that CTCs could have a potential use for developing cell lines, human tumor xenografts and organoids to test treatments and evaluate drug resistance mechanisms.[47]

Endoscopic ultrasound-guided portal injection chemotherapy using drug-eluting microbeads

Treatment options for patients with diffuse hepatic metastases are limited to systemic palliative chemotherapy. Transarterial microbead administration into the hepatic artery can lead to ischemic biliary strictures because the bile duct receives its blood supply from the hepatic artery. EUS-guided PV injection of chemotherapy (EPIC)

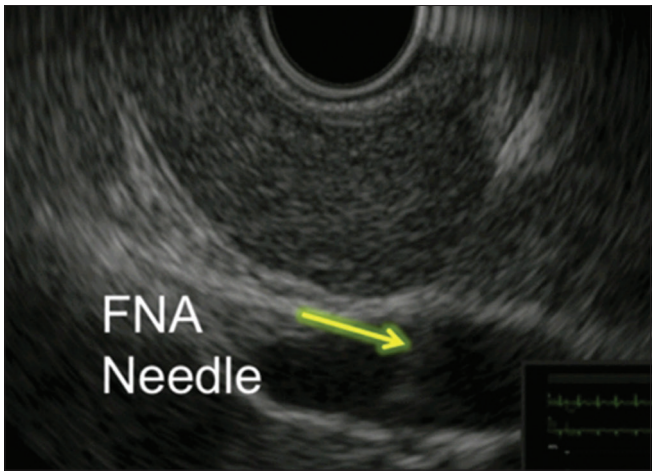

Figure 3: Transhepatic access of the portal vein with a 19G needle to aspirate blood for circulating tumor cell analysis

may be a better approach to target the liver parenchyma while sparing the bile duct. EPIC was first reported in a porcine study demonstrating EUS–PV injection of drug-eluting microbeads or nanoparticles.[48] The study showed that EPIC is feasible and results in higher hepatic concentrations of the chemotherapeutic agent (irinotecan) and lower systemic levels of the agent, compared with systemic administration. This approach may prove to be advantageous in a wide variety of clinical conditions for which prolonged, targeted hepatic drug exposure is desired.

Selective portal vein embolization

Selective PV embolization of either the right or left PV branch to achieve compensatory hypertrophy of the contralateral hepatic lobe before resection for hepatic malignancy has been reported.[49] An animal model study demonstrated that EUS-guided microcoil embolization of the right PV can result in hypertrophy of the right hepatic lobe. In a proof-of-concept study, the authors injected an ethylene–vinyl alcohol copolymer into the main PV of a Yorkshire pig and achieved an immediate increase in PV pressure from a baseline of 3–15 mmHg. In addition, a solid thrombus was identified in the main PV during necropsy, extending to the left PV on Day 7.[49]

ACCESS TO THE HEART

The heart and pulmonary trunk are in proximity to the esophagus, and thus directly accessible to EUS. This anatomic relationship is routinely used in cardiology for transesophageal echocardiography.[50,51] A successful EUS-guided puncture of the heart in a survival porcine study was followed by three clinical cases.[52] In the animal group, the authors performed EUS-guided access to the left atrium, left ventricle, coronary arteries and aortic valve. No adverse events were reported. At necropsy, the puncture sites were identified, but were unremarkable in appearance. Subsequently, the authors proceeded with EUS-cardiac access in humans. Pericardial fluid aspiration was performed in two patients, and an FNA of a 5-cm left atrial mass in the third patient. No adverse events were reported. EUS-guided FNA of a right atrial mass and a pericardial tumor has also been reported.[53,54]

CONCLUSION

The GI system can provide unique access approaches to vascular structures in the abdomen, pelvis and mediastinum. The evolution of EUS technology has led to the development of many new EUS-guided vascular interventions, although the clinical experience in humans is currently extremely limited. There is a great deal of opportunity for endoscopists to take on the expanding roles in the management of a wide variety of GI and liver conditions, and access to the vasculature represents an important new territory. The development of new approaches and dedicated equipment for EUS-guided vascular intervention is enthusiastically awaited.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Strohm WD, Phillip J, Hagenmüller F, Classen M. Ultrasonic tomography by means of an ultrasonic fiberendoscope. Endoscopy 1980;12:241-4.
2. DiMagno EP, Buxton JL, Regan PT, Hattery RR, Wilson DA, Suarez JR, *et al.* Ultrasonic endoscope. Lancet 1980;1:629-31.
3. Dimagno EP, Regan PT, Clain JE, James EM, Buxton JL. Human endoscopic ultrasonography. Gastroenterology 1982;83:824-9.
4. Sharma V, Rana SS, Bhasin DK. Endoscopic ultrasound guided interventional procedures. World J Gastrointest Endosc 2015;7:628-42.
5. Boyer TD, Haskal ZJ; American Association for the Study of Liver Diseases. The role of transjugular intrahepatic portosystemic shunt in the management of portal hypertension. Hepatology 2005;41:386-400.
6. de Franchis R, Baveno VI Faculty. Expanding consensus in portal hypertension: Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. J Hepatol 2015;63:743-52.
7. Hou MC, Lin HC, Lee FY, Chang FY, Lee SD. Recurrence of esophageal varices following endoscopic treatment and its impact on rebleeding: Comparison of sclerotherapy and ligation. J Hepatol 2000;32:202-8.
8. Krige JE, Bornman PC, Goldberg PA, Terblanche J. Variceal rebleeding and recurrence after endoscopic injection sclerotherapy: A prospective evaluation in 204 patients. Arch Surg 2000;135:1315-22.

9. Irisawa A, Saito A, Obara K, Shibukawa G, Takagi T, Shishido H, *et al.* Endoscopic recurrence of esophageal varices is associated with the specific EUS abnormalities: Severe periesophageal collateral veins and large perforating veins. Gastrointest Endosc 2001;53:77-84.
10. Irisawa A, Obara K, Bhutani MS, Saito A, Shishido H, Shibukawa G, *et al.* Role of para-esophageal collateral veins in patients with portal hypertension based on the results of endoscopic ultrasonography and liver scintigraphy analysis. J Gastroenterol Hepatol 2003;18:309-14.
11. Lahoti S, Catalano MF, Alcocer E, Hogan WJ, Geenen JE. Obliteration of esophageal varices using EUS-guided sclerotherapy with color Doppler. Gastrointest Endosc 2000;51:331-3.
12. Sarin SK, Lahoti D, Saxena SP, Murthy NS, Makwana UK. Prevalence, classification and natural history of gastric varices: A long-term follow-up study in 568 portal hypertension patients. Hepatology 1992;16:1343-9.
13. Wani ZA, Bhat RA, Bhadoria AS, Maiwall R, Choudhury A. Gastric varices: Classification, endoscopic and ultrasonographic management. J Res Med Sci 2015;20:1200-7.
14. Al-Hillawi L, Wong T, Tritto G, Berry PA. Pitfalls in histoacryl glue injection therapy for oesophageal, gastric and ectopic varices: A review. World J Gastrointest Surg 2016;8:729-34.
15. Boustière C, Dumas O, Jouffre C, Letard JC, Patouillard B, Etaix JP, *et al.* Endoscopic ultrasonography classification of gastric varices in patients with cirrhosis. Comparison with endoscopic findings. J Hepatol 1993;19:268-72.
16. Romero-Castro R, Pellicer-Bautista FJ, Jimenez-Saenz M, Marcos-Sanchez F, Caunedo-Alvarez A, Ortiz-Moyano C, *et al.* EUS-guided injection of cyanoacrylate in perforating feeding veins in gastric varices: Results in 5 cases. Gastrointest Endosc 2007;66:402-7.
17. Weilert F, Binmoeller KF. New endoscopic technologies and procedural advances for endoscopic hemostasis. Clin Gastroenterol Hepatol 2016;14:1234-44.
18. 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;67:572-4.
19. Romero-Castro R, Pellicer-Bautista F, Giovannini M, Marcos-Sánchez F, Caparros-Escudero C, Jiménez-Sáenz M, *et al.* Endoscopic ultrasound (EUS)-guided coil embolization therapy in gastric varices. Endoscopy 2010;42 Suppl 2:E35-6.
20. 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;74:1019-25.
21. Sharma M, Somasundaram A. Massive lower GI bleed from an endoscopically inevident rectal varices: Diagnosis and management by EUS (with videos). Gastrointest Endosc 2010;72:1106-8.
22. Weilert F, Shah JN, Marson FP, Binmoeller KF. EUS-guided coil and glue for bleeding rectal varix. Gastrointest Endosc 2012;76:915-6.
23. Tsynman DN, DeCross AJ, Maliakkal B, Ciufo N, Ullah A, Kaul V, *et al.* Novel use of EUS to successfully treat bleeding parastomal varices with N-butyl-2-cyanoacrylate. Gastrointest Endosc 2014;79:1007-8.
24. Levy MJ, Wong Kee Song LM, Farnell MB, Misra S, Sarr MG, Gostout CJ, *et al.* Endoscopic ultrasound (EUS)-guided angiotherapy of refractory gastrointestinal bleeding. Am J Gastroenterol 2008;103:352-9.
25. Kalva SP, Yeddula K, Wicky S, Fernandez del Castillo C, Warshaw AL. Angiographic intervention in patients with a suspected visceral artery pseudoaneurysm complicating pancreatitis and pancreatic surgery. Arch Surg 2011;146:647-52.
26. Fankhauser GT, Stone WM, Naidu SG, Oderich GS, Ricotta JJ, Bjarnason H, *et al.* The minimally invasive management of visceral artery aneurysms and pseudoaneurysms. J Vasc Surg 2011;53:966-70.
27. Eisen GM, Baron TH, Dominitz JA, Faigel DO, Goldstein JL, Johanson JF, *et al.* The role of endoscopic therapy in the management of variceal hemorrhage. Gastrointest Endosc 2002;56:618-20.
28. Van Stiegmann G, Cambre T, Sun JH. A new endoscopic elastic band ligating device. Gastrointest Endosc 1986;32:230-3.
29. Gamanagatti S, Thingujam U, Garg P, Nongthombam S, Dash NR. Endoscopic ultrasound guided thrombin injection of angiographically occult pancreatitis associated visceral artery pseudoaneurysms: Case series. World J Gastrointest Endosc 2015;7:1107-13.
30. Law R, Fujii-Lau L, Wong Kee Song LM, Gostout CJ, Kamath PS, Abu Dayyeh BK, *et al.* Efficacy of endoscopic ultrasound-guided hemostatic interventions for resistant nonvariceal bleeding. Clin Gastroenterol Hepatol 2015;13:808-120.
31. Abraldes JG, Tarantino I, Turnes J, Garcia-Pagan JC, Rodés J, Bosch J, *et al.* Hemodynamic response to pharmacological treatment of portal hypertension and long-term prognosis of cirrhosis. Hepatology 2003;37:902-8.
32. Lai L, Poneros J, Santilli J, Brugge W. EUS-guided portal vein catheterization and pressure measurement in an animal model: A pilot study of feasibility. Gastrointest Endosc 2004;59:280-3.
33. Magno P, Ko CW, Buscaglia JM, Giday SA, Jagannath SB, Clarke JO, *et al.* EUS-guided angiography: A novel approach to diagnostic and therapeutic interventions in the vascular system. Gastrointest Endosc 2007;66:587-91.
34. Giday SA, Ko CW, Clarke JO, Shin EJ, Magno P, Jagannath SB, *et al.* EUS-guided portal vein carbon dioxide angiography: A pilot study in a porcine model. Gastrointest Endosc 2007;66:814-9.
35. Giday SA, Clarke JO, Buscaglia JM, Shin EJ, Ko CW, Magno P, *et al.* EUS-guided portal vein catheterization: A promising novel approach for portal angiography and portal vein pressure measurements. Gastrointest Endosc 2008;67:338-42.
36. Huang JY, Samarasena JB, Tsujino T, Lee J, Hu KQ, McLaren CE, *et al.* EUS-guided portal pressure gradient measurement with a simple novel device: A human pilot study. Gastrointest Endosc 2017;85:996-1001.
37. Buscaglia JM, Dray X, Shin EJ, Magno P, Chmura KM, Surti VC, *et al.* A new alternative for a transjugular intrahepatic portosystemic shunt: EUS-guided creation of an intrahepatic portosystemic shunt (with video). Gastrointest Endosc 2009;69:941-7.
38. Binmoeller KF, Sendino O, Kane SD. Endoscopic ultrasound-guided intravascular therapy. J Hepatobiliary Pancreat Sci 2015;22:44-50.
39. Dodd GD 3rd, Carr BI. Percutaneous biopsy of portal vein thrombus: A new staging technique for hepatocellular carcinoma. AJR Am J Roentgenol 1993;161:229-33.
40. Dusenbery D, Dodd GD 3rd, Carr BI. Percutaneous fine-needle aspiration of portal vein thrombi as a staging technique for hepatocellular carcinoma. Cytologic findings of 46 patients. Cancer 1995;75:2057-62.
41. Michael H, Lenza C, Gupta M, Katz DS. Endoscopic ultrasound -guided fine-needle aspiration of a portal vein thrombus to aid in the diagnosis and staging of hepatocellular carcinoma. Gastroenterol Hepatol (N Y) 2011;7:124-9.
42. Lai R, Stephens V, Bardales R. Diagnosis and staging of hepatocellular carcinoma by EUS-FNA of a portal vein thrombus. Gastrointest Endosc 2004;59:574-7.
43. Storch I, Gomez C, Contreras F, Schiff E, Ribeiro A. Hepatocellular carcinoma (HCC) with portal vein invasion, masquerading as pancreatic mass, diagnosed by endoscopic ultrasound-guided fine needle aspiration (EUS-FNA). Dig Dis Sci 2007;52:789-91.
44. Kayar Y, Turkdogan KA, Baysal B, Unver N, Danalioglu A, Senturk H, *et al.* EUS-guided FNA of a portal vein thrombus in hepatocellular carcinoma. Pan Afr Med J 2015;21:86.
45. Nagrath S, Jack RM, Sahai V, Simeone DM. Opportunities and challenges for pancreatic circulating tumor cells. Gastroenterology 2016;151:412-26.
46. Tien YW, Kuo HC, Ho BI, Chang MC, Chang YT, Cheng MF, *et al.* A high circulating tumor cell count in portal vein predicts liver metastasis from periampullary or pancreatic cancer: A High portal venous CTC count predicts liver metastases. Medicine (Baltimore) 2016;95:e3407.

47. Chapman CG, Waxman I. Portal-vein blood samples as a new diagnostic entity for pancreatic cancer. Expert Rev Gastroenterol Hepatol 2016;10:665-7.
48. Faigel D, Lake D, Landreth T, Kelman C, Marler R. Endoscopic ultrasonography-guided portal injection chemotherapy for hepatic metastases. Endosc Ultrasound 2014;3:S1.
49. Vazquez-Sequeiros E, Olcina JR. Endoscopic ultrasound guided vascular access and therapy: A promising indication. World J Gastrointest Endosc 2010;2:198-202.
50. Kühl HP, Hanrath P. The impact of transesophageal echocardiography on daily clinical practice. Eur J Echocardiogr 2004;5:455-68.
51. García-Orta R, Moreno E, Vidal M, Ruiz-López F, Oyonarte JM, Lara J, *et al.* Three-dimensional versus two-dimensional transesophageal echocardiography in mitral valve repair. J Am Soc Echocardiogr 2007;20:4-12.
52. Fritscher-Ravens A, Ganbari A, Mosse CA, Swain P, Koehler P, Patel K, *et al.* Transesophageal endoscopic ultrasound-guided access to the heart. Endoscopy 2007;39:385-9.
53. Romero-Castro R, Rios-Martin JJ, Gallego-Garcia de Vinuesa P, Castro-Fernandez AJ, Marques-Asin FJ, Caparros-Escudero C, *et al.* Pericardial tumor diagnosed by EUS-guided FNA (with video). Gastrointest Endosc 2009;69:562-3.
54. Gornals JB, de la Hera M, de Albert M, Claver E, Catala I. EUS cardiac puncture-guided right atrial tumor. Gastrointest Endosc 2015;82:165.