# Feasibility of Endoscopic Ultrasound-guided Portal Vein Embolization with Enteryx

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## Abstract

***Background* : Portal vein embolization (PVE) has been used as a preoperative strategy to induce hepatic lobar atrophy and contralateral lobe hypertrophy. We determined the feasibility of endoscopic ultrasound (EUS)-guided Enteryx (EVAL/ethylene-vinyl alcohol copolymer) embolization of the portal vein (EUS-PVE) in an animal model as a potential, minimally invasive, endoscopic technique.**

***Methods* : EUS-guided embolization of the portal vein (EUS-PVE) using Enteryx was performed in a Yorkshire breed swine. Portal pressure measurements were obtained before and after vascular embolization. The animal was carefully monitored for seven days for evidence of abdominal pain, shock, or bleeding. An upper abdominal contrast-CT scan was performed to verify the location of the embolus.**

***Results* : The PV pressure increased from 3 mmHg at baseline to a mean of 15 mmHg after EUS-PVE. The CT-scan on day 4 demonstrated Enteryx in the main portal vein with extension into the left branch. At sacrifice on day 7, a solid thrombus was visible grossly and histologically inside the main portal vein and the left branch of the portal vein.**

***Conclusions* : Selective embolization of the portal vein by EUS guidance appears to be feasible and a potential, minimally invasive, preoperative treatment option for patients undergoing extensive hepatectomy**(Acta gastroenterol. belg., **2005**, 68, **412-415**).

**Key words** : EUS, Enteryx, portal vein embolisation.

## Introduction

Portal vein embolization (PVE) before hepatectomy is designed to induce an atrophy of the embolized lobe to be resected, with a compensatory hypertrophy of the contralateral lobe to be preserved.[1] The interruption of blood flow towards a hepatic segment can be induced by the surgical ligation of a portal vein branch or by the percutaneous intraportal injection of an embolizing agent under transabdominal ultrasound guidance. The procedure is well tolerated and the risk of hepatic failure is low in patients without liver insufficiency.[2-10] Compensatory hypertrophy of the non-embolized segments is maximal during the first two weeks and persists for up to six weeks.[11] The magnitude of hypertrophy is correlated with the volume of embolized parenchyma, and is reduced in diabetic or jaundiced patients with active chronic liver disease. Liver resection is timed to occur six weeks after embolization.

Previous studies have demonstrated ultrasound-guided portal vein embolization using polyvinyl alcohol.[12] This technique was successful in the induction of portal hypertension for several weeks, which slowly resolved as patency of the portal vein was spontaneously reconstituted.

Recently, we demonstrated the feasibility of Endoscopic Ultrasound (EUS)-guided portal vein catheterization in 21 pigs.[13] In addition to portal vein pressure measurements, portal hypertension was induced by EUS-guided injection of polyvinyl alcohol particles into the portal vein in 14 animals, which lead to an increased of portal venous pressure of 10.2 mm Hg.

Enteryx (EVAL/ethylene-vinyl alcohol copolymer) or Onyx is used for the embolization of pseudoaneurysms of femoral artery branches[14] and for the treatment of cerebral and pelvic arteriovenous malformations.[15-17] There are no previous reports demonstrating the use of Enteryx in the portal vein.

In this study we determined the feasibility of Endoscopic-Ultrasound (EUS)-guided Enteryx embolization of the portal vein (EUS-PVE) in an animal model as a potential minimally invasive technique of preoperative portal vein embolization before hepatectomy.

## Materials and Methods

This experimental protocol was approved by the subcommittee for research animal care of the Massachusetts General Hospital, in compliance with the Federal Regulation for the Use of Laboratory Animals. The committee granted approval for a pilot study involving one animal. A female Yorkshire breed swine with the age of 126 days and the weight of 151 pounds was pre-anesthetized by intravenous administration of Telazol/Xylazine 4.4 mg/kg IM + 2.2 mg/kg IM (Parke-Davis, Morris Plains, N.J.) and received endotracheal intubation with isoflurane anesthesia (1.5-3.0%) with oxygen (3.0 L/min.). The animal was monitored by pulse oxymetry in a surgical animal laboratory.

A linear-array echoendoscope (FG 32 UA, Pentax Medical Company, Montvale, NJ) was inserted into the

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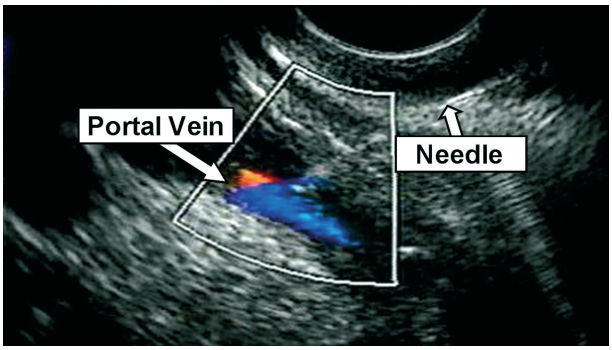


Fig. 1. — EUS-Doppler image of the portal vein catheterization. The portal vein lumen and the EUS needle are illustrated by white arrows.

esophagus via the mouth and passed to the proximal duodenum. The portal vein (PV) was identified by EUS and a 22-gauge needle (EchoTip Ultra, Model Echo-3-22 ; Wilson-Cook Medical Inc., Winston-Salem, N.C.) was introduced into the portal vein from the duodenum. After withdrawing the stylet, with the needle tip in the PV lumen as visualized by EUS (figure 1), the proximal end of the needle was connected to a pressure transducer. With the needle in a proper position, the PV pressure was displayed on a monitor. Three pressure measurements were made to determine a baseline PV pressure. Immediately after this measurement, 4 ml of Enteryx [Ethylene-vinyl alcohol (EVOH) mixed with dimethyl sulfoxide (DMSO), EVOH : DMSO = 1:4] were injected via the EUS needle into the PV lumen. A portal pressure measurement was obtained again with the EUS needle after the injection to determine the increase of PV

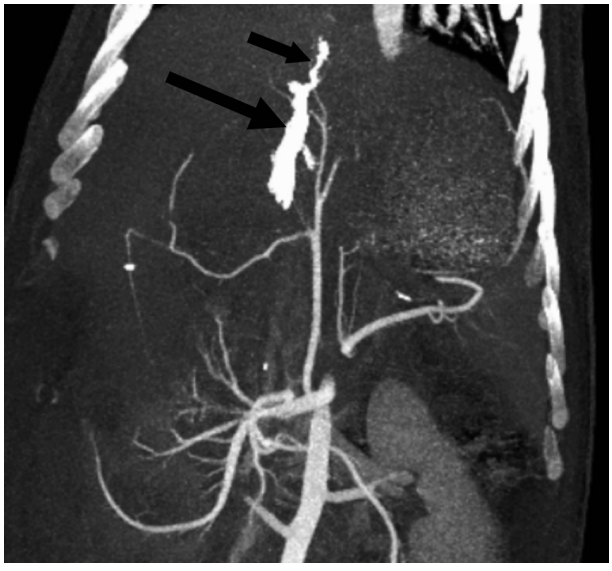

Fig. 2. — Contrast enhanced coronal 3D multiplanar reformatted CT image showing Enteryx in the main portal vein (illustrated by large black arrow) with extension into the left branch (illustrated by small black arrow).

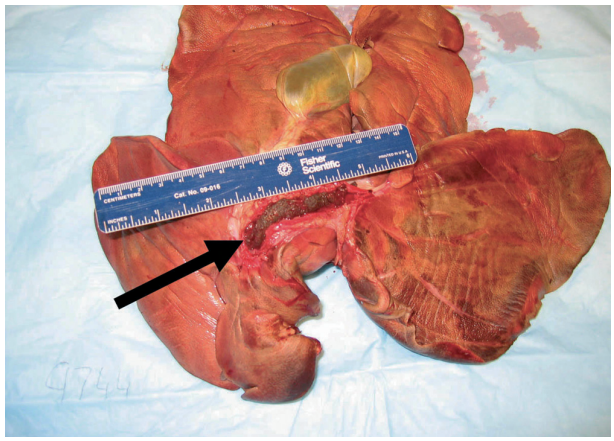

Fig. 3. — Gross image of the liver of the study pig with a 70 mm × 10 mm solid thrombus visible in the portal vein representing Enteryx (illustrated by black arrow).

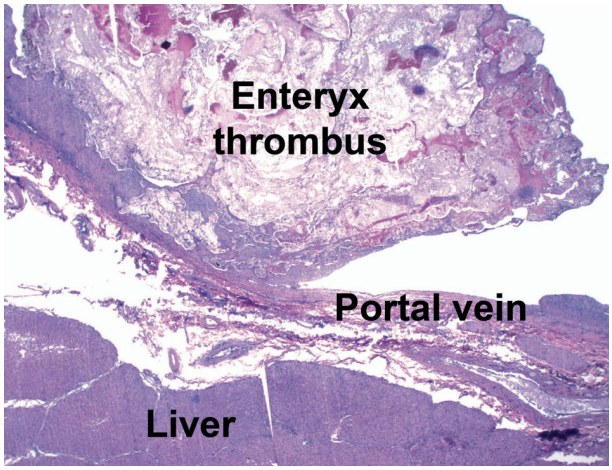


Fig. 4. — Histology slide showing the Enteryx thrombus in the portal vein. Magnification : × 12.5. Staining technique : Haematoxylin and Eosin (HE).

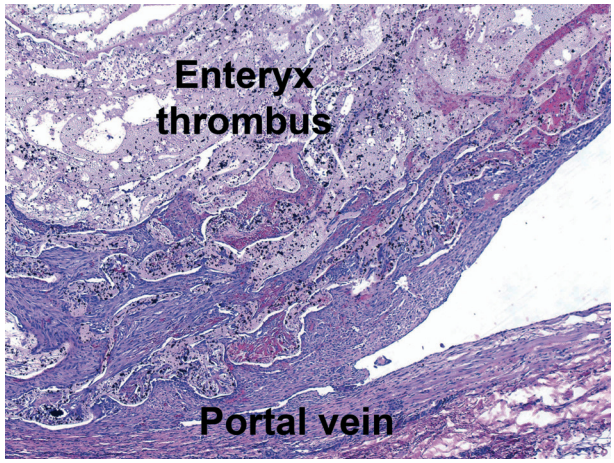


Fig. 5. — Histology slide showing an enlarged section of the Enteryx thrombus in the portal vein. Magnification : × 50. Staining technique : Haematoxylin and Eosin (HE).

pressure due to the vascular embolization. After the procedure, the animal was carefully monitored for seven days for evidence of abdominal pain, shock, or bleeding.

During the observational period, the animal had access to regular solid food. In addition to clinical observation, blood levels of lipase, amylase, AST, ALT, creatinine and BUN were determined on day 4 after the procedure to detect any clinical signs of acute pancreatitis, hepatic or renal failure. To be able to draw the blood samples, the animal was sedated again by Telazol/ Xylazine 4.4mg/kg IM + 2.2mg/kg IM. At the same time, the animal received an upper abdominal CT scan to determine the location of the Enteryx radio-opaque embolus.

On day 7, following sacrifice under anesthesia induction and pentobarbital overdose, the liver was examined for necrosis and removed for histological studies.

The purpose of this experiment was to determine the feasibility (time and ease of procedure) and safety (evidence of bleeding, peritonitis as evidenced by changes in vital signs and/or jaundice, pancreatic, hepatic and renal failure as documented by necropsy) of endoscopic ultrasound-guided portal vein embolization (EUS-PVE) with Enteryx.

## Results

Baseline PV pressure measurement was 3 mmHg (mean) and increased to a mean of 15 mmHg after EUS-PVE. The total procedure time was 150 minutes with a PV injection time of 16 minutes. The upper abdominal CT-scan on day 4 demonstrated Enteryx in the main portal vein with extension into the left branch (figure 2). The blood values of lipase, amylase, AST, ALT, creatinine and BUN were within normal limits on day 4. At sacrifice on day 7, a solid thrombus with a size of 70 mm $\times$ 10 mm was visible grossly inside the main portal vein and the left branch of the portal vein (figure 3). By histology, an organized thrombus could be localized inside of the lumen of the portal vein (figures 4 and 5).

## Discussion

Preoperative embolization of portal vein branches performed before extensive hepatectomy has been shown to be safe and well tolerated.[2-10, 18] The interruption of the portal flow in the liver segments planned to be removed during surgery induced atrophy and compensatory hypertrophy of the remaining segments.[6, 19, 20,21]

Preoperative portal vein embolization is usually indicated when the predicted remnant liver volume accounts for less than 25-40% of the total liver volume.[11] This approach has shown promise as a relatively safe and effective strategy in patients prior to hepatic resection, timed to occur two to six weeks after embolization.[11]

In the current study, we have presented for the first time, an EUS-guided embolization of the portal vein using Enteryx. The procedure was well tolerated by the animal without any complications in a one-week observational period. Presumably, this technique offers the advantage of a variation of the grade of endovascular embolization by using Enteryx in an increasing amount leading to a controllable grade of obstruction of the vascular lumen. Although the procedure was demonstrated in only one animal, the technique was relatively simple using standard endoscopic techniques.

EUS-PVE offers the advantage of minimally invasiveness with the option of a controlled repetitive applicability. In a clinical setting, we expect that a selective EUS-guided injection of the embolizing agent into the left or the right branch of the portal vein would provide a selective induction of atrophy in the affected hepatic segments. The complication rate of this procedure is anticipated to be comparable to other EUS-guided fine needle injections or aspirations of organs adjacent to the duodenum .

In conclusion, selective embolization of the portal vein by endoscopic ultrasound-guidance appears to be feasible and a potential minimally invasive preoperative treatment option for patients undergoing extensive hepatectomy. Future evaluation in patients is required to determine the clinical applicability of this new technique.

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