NEW METHODS & MATERIALS

EUS-guided portal vein catheterization and pressure measurement in an animal model: a pilot study of feasibility

Lawrence Lai, MB, John Poneros, MD, John Santilli, MD, William Brugge, MD

Background: **The extrahepatic portal vein is inaccessible to direct catheterization.**

Methods: **Because EUS can readily image the portal vein, the feasibility of EUS-guided portal vein catheterization by using a 22-gauge needle was studied in 7 normal pigs and 14 pigs in which portal hypertension was induced (7/14 anticoagulated).**

Results: **Catheterization was not possible by EUS or transhepatic methods in, respectively, 3 and 5 animals. One anticoagulated animal had a small amount of periduodenal bleeding as a result of EUS catheterization. The mean normal portal vein pressure (1 standard deviation) as determined by EUS and transhepatic methods was, respectively, 20.3 (4) mm Hg and 20.4 (2) mm Hg. Injection of polyvinyl alcohol particles increased the portal vein pressure by 10.2 (11.59) mm Hg. There was a close correlation under all conditions between the mean portal vein pressures obtained by EUS and transhepatic catheterization (r = 0.91).**

Conclusions: **EUS-guided portal vein catheterization appears to be feasible in an animal model and provides accurate pressure measurements.**

Obstruction of the portal venous system is common in patients with advanced pancreaticobiliary malignancies, cirrhosis, and portal vein (PV) thrombosis.[1] The resultant varices are prone to spontaneous bleeding when PV pressure increases above the critical value of 12 mm Hg.[2] There is no safe clinical method available for direct catheterization of the portal venous system.[3,4] However, studies of indirect methods when using EUS have demonstrated a good correlation between Doppler-based flow measurements and blood flow in the azygous and portal veins.[5,6] The ability to catheterize the PV would allow endoscopists to measure extrahepatic PV pressures. Because the PV lies directly adjacent to the duodenum, catheterization under EUS guidance should be possible.[7,8] Although FNA of vascular structures associated with the liver has not been reported, EUS-guided FNA of the liver is relatively safe.[9]

The primary purpose of these experiments was to determine the feasibility of EUS-guided PV catheterization in animals in a normal state, after induction of portal hypertension and during an induced coagulopathic state. An attempt also was made to determine whether EUS-guided pressure measurements correlated with transhepatic pressure measurements under a variety of conditions.

MATERIALS AND METHODS

Animal model

Twenty-one farm swine (40-50 kg) were pre-anesthetized by intravenous administration of Telazol (Parke-Davis, Morris Plains, N.J.) followed by anesthesia with isoflurane (1.5%-3.0%) and oxygen. For all experiments, the animals were monitored (pulse, blood pressure, oxygenation) in a cardiac animal laboratory by means of an arterial line. The 21 animals were arbitrarily divided into 3 groups of 7 (groups A, B, and C), and the experiments were completed over a 3-month period. All animals underwent EUS and attempted PV catheterization. Group A and B pigs underwent transhepatic PV catheterization by using a 22-gauge Chiba needle guided by transabdominal US immediately after EUS.[4] A mean hepatic vein pressure measurement also was obtained during the transhepatic PV catheterization.[10] Group C pigs underwent EUS-guided PV catheterization but not transhepatic PV catheterization.

The experimental protocols were approved by the subcommittee for research animal care of our hospital and were in compliance with the Federal Regulation for the Use of Laboratory Animals.

EUS procedure

A linear-array echoendoscope (FG-32UA; Pentax Precision Instrument Corp., Orangeburg, N.Y.) was inserted into the proximal duodenum, and the PV was identified.[11] Under EUS guidance, a 22-gauge, (5.5F) fine needle of the type used for EUS-FNA (EchoTip; Wilson-Cook Medical Inc., Winston-Salem, N.C.) was inserted into the PV lumen. After withdrawing the stylet, a small volume of contrast medium (Renograffin 60; Bracodiagnostic, Inc., Princeton, N.J.) was injected under fluoroscopic monitoring to confirm the location in the PV lumen. With the needle tip in the PV lumen, as visualized endosonographically, the proximal end of the needle was connected to a fluid-filled manometer and pressure recorder (Fig. 1). With the needle in a proper position, the PV pressures were observed to fluctuate with respiration while maintaining a stable, reproducible pressure. A mean of 3 pressure measurements was made in all pigs, and a tracing of 1-minute duration was recorded. Group C pigs were given an intravenous infusion of

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Current affiliations: Caritas Medical Center Hong Kong, Brigham and Women's Hospital, Vascular Radiology and GI Unit, Massachusetts General Hospital.

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Reprint requests: William R. Brugge, MD, Massachusetts General Hospital, GI Endoscopy Unit, Blake 452c, Boston, MA 02114.

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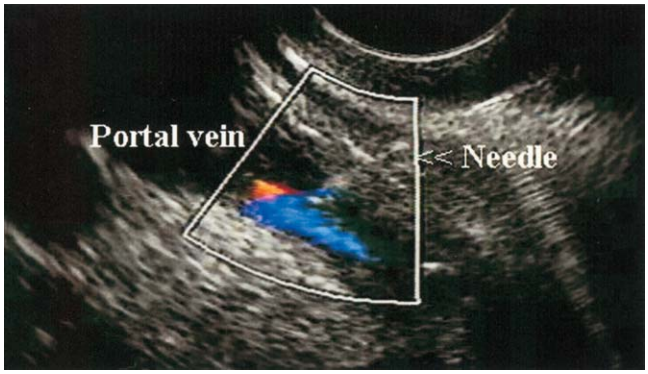

Figure 1. EUS image showing transduodenal placement of 22-gauge needle in portal vein.

heparin. The mean activated partial thromboplastin time level before EUS catheterization was 220 seconds. Group C animals did not undergo transhepatic catheterization.

Induction of portal hypertension

After the PV pressure measurements were obtained in Groups B and C pigs, polyvinyl alcohol particles (PVA particles 2-300 μm; Cook, Bloomington, Ind.) were injected via the EUS needle into the PV.[12] Before injection, the PVA particles were mixed with contrast medium at a ratio of 1:9. Injection of the PVA particles/contrast mixture continued until there was stasis of contrast flow in the PV, as determined fluoroscopically. Portal pressure measurements were obtained again with the EUS needle after PVA particle injection.

After completion of the PVA infusion and pressure measurements, 50 μg of octreotide (Sandostatin; Norvartis, New York, N.Y.) were injected intravenously in two animals, and PV pressure was measured again after 5 minutes.[13]

Safety

All animals were carefully monitored for 4 hours after the procedure. During a 4-day period, the animals were monitored twice daily for evidence of abdominal pain, shock, or bleeding. All 21 pigs were euthanized under anesthesia 4 days after the procedure, and the abdomen, the PV, and the liver were examined by detailed necropsy for evidence of peritonitis, infection, abscess, and blood.

RESULTS

Baseline PV catheterization was possible in all 21 animals under EUS guidance; transhepatic catheterization was possible in 9 of 14 animals. High-quality PV pressure tracings were obtained in 18 of 21 animals with EUS and in 9 of 14 animals by transhepatic catheterization. Matched EUS and transhepatic PV pressure measurements were obtained in 13 of 21 animals.

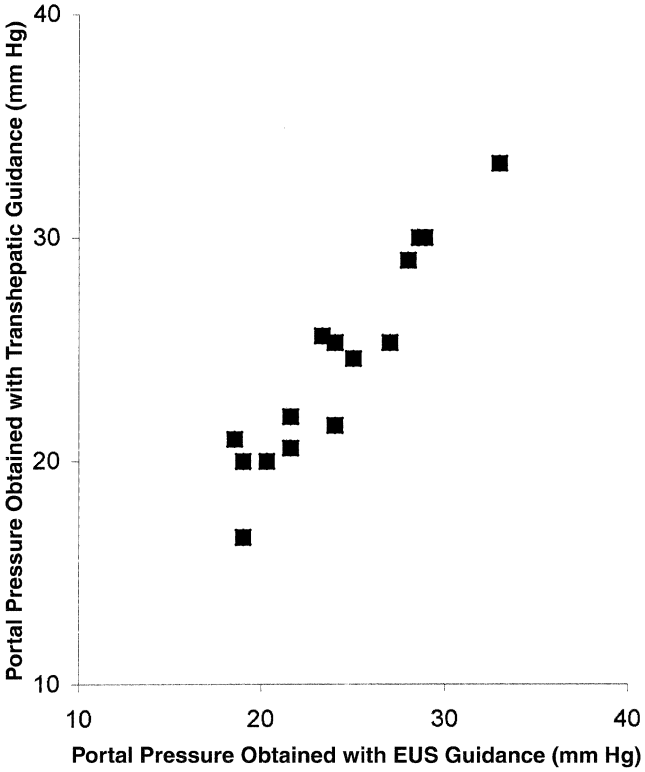

Figure 2. Comparison of portal pressure measurements derived by EUS portal vein catheterization vs. transhepatic catheterization (n = 13) under a variety of conditions.

Pressure measurements

The mean PV pressure (1 standard deviation [SD]) as determined by EUS-guided catheterization (n = 18) was 20.3 (4) mm Hg. The mean PV pressure (1 SD) as determined by transhepatic catheterization (n = 9) was 20.4 (2) mm Hg. In pigs with baseline PV measurements obtained by both transhepatic and EUS-guided PV catheterization (n = 6), the average difference (1 SD) was 2.2 (2.04) mm Hg.

In the 4 pigs that had PV measurements by EUS and transhepatic catheterization after the administration of PVA particles, the mean difference between the two approaches was 0.2 (1.5) mm Hg. The mean increase in PV pressure as determined by EUS catheterization in group C pigs after the administration of PVA was 10.2 (11.6) mm Hg. After administration of octreotide, mean PV pressure decreased from 30.5 to 26.0 mm Hg in two animals. The average difference in PV pressure by both methods after PVA and octreotide administration (n = 2) was 0.5 (0.7) mm Hg. The mean PV pressures obtained by EUS and transhepatic catheterization under all conditions (n = 13) correlated closely (r = 0.91; Fig. 2). In the matched PV pressure measurements, mean PV pressure (20.8 mm Hg) by EUS was slightly greater

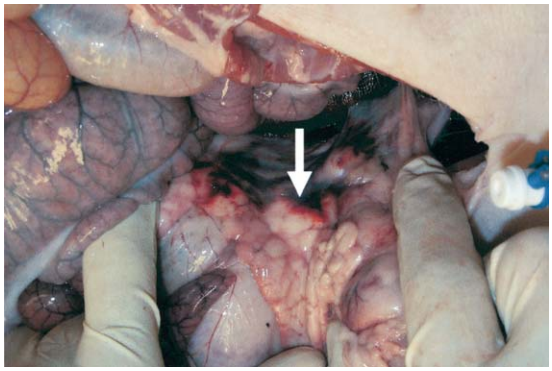

Figure 3. Postmortem view of duodenum 4 days after EUS-guided catheterization of portal vein showing subserosal hematoma *(arrow)*.

than the mean PV pressure (20.0 mm Hg) measured transhepatically.

Safety

EUS-guided PV catheterization succeeded in all 21 animals. However, in the first 3 pigs, catheterization was technically difficult and high-quality PV pressure measurements could not be obtained. These initial failures were a result of tissue occlusion in the needle tip; this problem was not encountered in subsequent animals and catheterizations were completed in a few minutes. Transhepatic PV catheterization failed in 5 of 14 pigs because the needle could not be placed into or access maintained within the PV lumen. The PV was accessed within 15 minutes in the last 18 EUS-guided catheterizations. However, transhepatic PV catheterization required 20 to 60 minutes. One of the 14 pigs undergoing transhepatic catheterization died of intra-abdominal bleeding after a prolonged attempt at transhepatic catheterization. Necropsy demonstrated a large hematoma inside and surrounding the liver. At necropsy, there were small subserosal hematomas at the EUS puncture site in all pigs (Fig. 3). In one anticoagulated pig, there was a small (approximately 25 mL) collection of blood between the PV and duodenum. There were no signs of inflammation or abscess within the peritoneal cavity, around the PV, or in the liver.

DISCUSSION

This investigation demonstrates, for the first time, that EUS with a linear-array echoendoscope might be used to guide catheterization of the PV. The endoscopists who performed the procedures were experienced in EUS and had little difficulty in visualizing the extrahepatic PV. The PV catheterization site chosen was remote from the pancreas and as close as possible to the duodenal wall to minimize the risk of bleeding. In the first 3 experiments, technical difficulties were encountered in obtaining high-quality pressure measurements during EUS. With experience, however, catheterization became simple and required less than 15 minutes. It is our anticipation that EUS-guided PV catheterization in humans will require a degree of expertise in linear-array EUS that is common to endoscopists who perform EUS-FNA of the pancreas.

Pressure measurements obtained by EUS guidance correlated well with measurements made by transhepatic catheterization of the extrahepatic PV. This finding was expected because the catheterization sites were fairly close, and the methods for pressure monitoring were identical. Both procedures used a relatively small needle (22-gauge), which might dampen the pressure waves. However, our pressure recording studies indicated that the lumen of the needle was large enough to provide reproducible and reliable pressure measurements. A tight correlation was observed in the baseline state, as well as after induction of portal hypertension, suggesting that this technique could be applicable in patients with portal hypertension. The induction of portal hypertension in animals through the use of PVA particles is valid only for transient measurements, because a permanent portal hypertensive state cannot be achieved through repeated injections of PVA into the PV.[14] More detailed studies will be needed to establish reproducibility and accuracy over a wide range of pressures and with the possible use of smaller gauge needles.

Although EUS-guided PV catheterization technically is similar to EUS-FNA, it is likely that the complication rate will be higher. Bleeding at the catheterization site and between the duodenum and the PV is likely to be the most common complication. The risk of bleeding will be greatly increased in the setting of portal hypertension and/or coagulopathy. This is highlighted by the one animal that expired as a result of bleeding after transhepatic catheterization. There was little evidence of significant bleeding as a result of EUS catheterization, as determined by monitoring of the animals after the procedure and necropsy 4 days after the procedure. Technical factors will play an important role in determining safety; a single catheterization over 10 minutes with minimal needle movement will assure a high degree of safety, whereas, high PV pressure and severe coagulopathy will increase the risk of bleeding.

Other potential risks of EUS-guided catheterization of the PV include bacteremia, induction of thrombi in the PV, and phlebitis. Prophylactic administration of antibiotics will likely reduce the risk of bacteremia and PV infection. However, antibiotics

were not used in the present study, and no evidence of infection in the PV was found at 4 days after the procedure. Studies of EUS-FNA that use blood cultures have not demonstrated high levels of bacteremia.[15] An attempt was made in the current study to determine the risk of bacteremia by obtaining blood cultures before and after catheterization. However, most of the baseline blood cultures demonstrated gross contamination, making interpretation of the post-catheterization cultures extremely difficult. However, measures will have to be taken to minimize the transport of GI secretions into the PV. Patients with severe liver disease will be at particular risk for bacteremia inasmuch as they may be unable to clear bacteria introduced by PV catheterization from the bloodstream.

The results of this pilot study in an animal model will form the basis of a pilot study of the safety of EUS-guided PV catheterization in patients with portal hypertension. Only after careful investigation and demonstration of the safety of the procedure in patients will studies of clinical applicability be possible. However, the potential for the use of this technique in the management of patients with suspected portal hypertension is promising.

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