Endovascular Management of Portal Vein Obstruction in Hepatobiliary Cancer Patients.

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Abstract

Background:
Obstruction of the splenoportal or mesoportal venous system occurs in approximately 15-25% of patients with hepatobiliary malignancies. These patients are prone to develop obstruction of the portal and mesenteric veins both because of local factors (tumor compression, stenosis after surgery) and systemic factors (hypercoagulability). Diagnosis requires a high index of clinical suspicion because symptoms may be non-specific and directly attributed to the existing malignancy. Cross-sectional imaging methods (contrast-enhanced CT scan and MRI) are key to diagnosis. The best treatment strategy has not been established. The purpose of this article is to describe a single center experience in the endovascular management of portal and mesenteric venous obstruction with metallic stent placement on patients with hepatobiliary neoplasms.

Results:
IRB approved, HIPAA compliant study. Retrospective review of medical and imaging records of 21 consecutive patients with hepatobiliary malignancy who underwent endovascular portal vein recanalization and stent placement between January 2012 and March 2020. Clinical diagnoses were pancreatic cancer (n=19), colon cancer metastatic to the liver (n=1) and cholangiocarcinoma (n=1). The presenting symptoms were: ascites (n=5), abdominal pain, portal vein thrombosis, abnormal liver function tests and ascites (n=4), abdominal pain and ascites (n=4), abdominal pain and diarrhea (n=3), gastrointestinal bleed (n=3) and abdominal pain (n=2). Study results are presented in means and percentages. Stent patency and patient survival are presented with Kaplan-Meier method.

The technical success rate was 100%. Self-expandable and balloon-expandable stents were placed. A transhepatic approach was used in 20 cases (95.2%); trans-splenic access in one. Primary stent patency was 95.2%, 84%, and 68% at 1, 3 and 6 months respectively. All stent occlusions were caused by tumor progression. A total of 80% of patients reported symptomatic improvement. Patient survival at 10 months was 40%. The early death rate was 4.76%. Portal vein perforation with massive bleeding was seen in one patient and managed with self-expandable stent-graft placement. There were no bleeding complications from the percutaneous tracts.

Conclusion
Endovascular recanalization with stent placement is safe with high technical and clinical success. Stent patency is acceptable and determined by disease progression.

Background
Obstruction of the splenoportal or mesoportal venous system occurs in approximately 15–25% of patients with hepatobiliary malignancies (1, 2). These patients are prone to develop obstruction of the
portal and mesenteric veins both because of local factors (tumor compression, stenosis after surgery) and systemic factors (hypercoagulability) (3). Obstruction may be acute or chronic (3); acute obstruction presents with thrombus formation, abdominal pain, ascites and abnormal liver function tests, and it is usually secondary to surgery (liver resection or pancreatico-duodenectomy with venous reconstruction) (2). Chronic obstruction presents with diffuse, non-specific abdominal pain, abdominal distention, ascites, variceal bleeding or lower gastrointestinal bleed. Chronic obstruction is usually secondary to extrinsic compression or encasement by unresectable, locally invasive tumors (4).

Diagnosis requires a high index of clinical suspicion because symptoms may be non-specific and directly attributed to the existing malignancy (2); Cross-sectional imaging methods (contrast-enhanced CT scan and MRI) are key to diagnosis, but high suspicion by imaging professionals is also important because description of imaging findings may be focused on the neoplastic process and vascular findings may be missed or under-reported (2, 5). The best treatment strategy has not been established; reported therapeutic options include anticoagulation, infusion of thrombolytics into the portal vein via a percutaneous or transjugular approaches and percutaneous recanalization with stent placement (6–8). Percutaneous recanalization followed by stent placement using a transhepatic or a trans-splenic approach has been described as safe and effective (1, 6, 7, 9–12).

The purpose of this article is to describe a single center experience in the endovascular management of portal and mesenteric venous obstruction with metallic stent placement on patients with hepatobiliary neoplasms.

**Methods**

This is an IRB approved, HIPAA compliant retrospective study. The medical and imaging records of 21 consecutive patients who underwent endovascular portal vein recanalization and stent placement between January 2012 and March 2020 were reviewed. Patients included 14 women and 7 men with a mean age of 66 (48–83) years. Portal vein obstruction was identified by contrast enhanced CT in all cases. Cases were presented at the multidisciplinary Tumor Board Conference to determine if patients were suitable candidates for intervention and decision to proceed was by group consensus. The clinical diagnoses were pancreatic cancer (n = 19), colon cancer metastatic to the liver (n = 1) and cholangiocarcinoma (n = 1). The etiology of venous obstruction included extrinsic compression by unresectable tumor (n = 9), portal vein stenosis after Whipple with venous reconstruction (n = 7), Yerdel class IV acute portal vein thrombosis after Whipple with venous reconstruction (n = 2), extrinsic compression and erosion of the portal vein by abdominal fluid collection after Whipple (n = 1) and Yerdel class IV acute portal vein thrombosis after partial liver resection (n = 2). Clinical presentation included: ascites (n = 5), abdominal pain, portal vein thrombosis, abnormal liver function tests and ascites (n = 4), abdominal pain and ascites (n = 4), abdominal pain and diarrhea (n = 3), gastrointestinal bleed (n = 3) an abdominal pain (n = 2). All patients signed written informed consent for the procedure.
Procedural Technique

The procedures were performed in a state of the art interventional radiology suite by two board certified interventional radiologists with more than 10 years of experience. Conscious sedation with midazolam and fentanyl was used in 18 patients and general anesthesia in 3. Broad spectrum prophylactic antibiotics with coverage for Gram negative bacteria were administered to all patients.

Access into the portal venous system was obtained using a transhepatic approach in 20 patients and a trans-splenic approach in one. Access was ultrasound guided, using a fine needle access system (Merit S-MAK, Merit Medical, South Jordan, UT). Entry into the portal venous system was confirmed by injection of non-ionic contrast through the needle. Then, a 0.018” guidewire was advanced followed by tract dilation and placement of a 5 Fr dilator. A direct portogram was then performed to confirm obstruction of the portal venous system; a 0.035” Benston guidewire (Cook, Bloomington, IN), was advanced followed by placement of a vascular access sheath (Pinnacle, Terumo, Japan). Figure # 1 illustrates portal vein access technique.

The obstruction of the portal vein was crossed using a combination of a Bernstein catheter (Angiodyamics, Latham, NY) and a stiff type glidewire (Terumo, Japan). Once the obstruction was crossed, a direct portogram using a measuring catheter (Cook Medical, Bloomington, IN) was performed in preparation for stent placement.

Four patients had Yerdel class IV acute thrombosis of the portal vein and required additional intervention including mechanical thrombectomy with Angiojet Zelante device (Boston Scientific, Natick, MS) (n = 2), thromboaspiration with the Indigo Cat-8 system (Penumbra, Alameda California) (n = 1) and power-pulse infusion of 4 mg of alteplase followed by mechanical thrombectomy with the Angiojet Zelante device (Boston Scientific, Natick, MS) (n = 1).

Stent Selection And Placement Technique

Stent choice was based on operator’s judgment and venographic findings. The stent length was selected based on the portogram with measuring catheter and the diameter was determined by measurements obtained from the CT scans. Bare self-expandable nitinol stents were used in 17 patients (Zilver, Cook, Bloomington IN and Protege EV-3, Minneapolis, MN), a balloon-expandable stent was used in 1 (Express, Boston Scientific, Natick MS), a balloon expandable stent-graft in 1 (Atrium Medical, Merrimack, NH) and a combination of self-expandable stent and a self-expandable stent-grafts (Viabahn, WL Gore, Phoenix, AZ) in 2 patients. Stents were dilated to profile using standard angioplasty balloons. Stent diameters ranged from 8–14 mm and lengths ranged from 1.7- 8 cm depending on diameter and length of the obstruction. A completion portogram was performed to confirm stent patency in all cases. If completion portogram showed residual thrombus, this was treated with additional intervention including mechanical thrombectomy, pulse spray thrombolysis and/or additional angioplasty. The transhepatic tracts were closed using 0.035” Nester coils (Cook medical, Bloomington, IN) (n = 16), and Mynx vascular closure
device (Cardinal Health, Dublin, OH) (n = 4). The trans-splenic access was closed with an 8 mm Amplatzer plug (Abbott, St. Paul, MN).

Technical success was defined by successful crossing of the obstruction, stent placement and dilatation and a completion portogram showing a patent portal vein with patent intrahepatic portal vein branches. Clinical success was defined by resolution of ascitic fluid and bowel wall edema by cross sectional imaging, symptomatic improvement in abdominal pain and/or bleeding control.

Management After Intervention And Follow-up

Patients were followed from date of stent insertion until latest clinical follow-up or patient’s death (2 weeks- 4 years). All patients were seen one week after intervention in the IR clinic for recognition of early complications. An abdominal ultrasound was done within a week after the procedure to assess stent patency.

All patients were followed in the surgical oncology clinic. Contrast enhanced CT scans were performed every 3–6 months to monitor disease progression. Indications for imaging studies was decided by the medical oncologist in consultation with the hepatobiliary surgeon and the interventional radiologists. The follow-up scans were reviewed by the interventional radiologist. If a stent abnormality was identified, the case was discussed and the possibility of stent revision was considered. Figures 2a-g illustrate the process of stent placement and follow-up in a patient who presented with acute portal vein thrombosis.

Statistical Analysis

Study results are presented in means and percentages. Statistical analysis was performed using SPSS version 26. Stent patency and patient survival are presented with Kaplan-Meier curves.

Results

Technical and Clinical success

The technical success rate was 100%. A transhepatic approach was used in 20 cases (95.2%); trans-splenic access in one. The trans-splenic access was used in a patient who presented with portal vein thrombosis after right lobectomy. The window for access to the portal vein in the left hepatic lobe was limited by post-surgical changes. Four patients had Yerdel class IV acute portal vein thrombosis 4–7 days after surgery. Two patients had a right lobectomy to remove metastases from cholangiocarcinoma and colon cancer, respectively. One patient had a distal pancreatectomy and splenectomy for a pancreatic carcinoma involving the tail of the pancreas and one patient had undergone a Whipple operation with portal vein reconstruction. The clinical presentation in these patients was abdominal pain, ascites and abnormal liver function tests. Obstruction of the portal venous system was chronic in the remaining 17 patients. In patients with chronic obstruction, 8 presented with a focal stenosis at the site of vascular
reconstruction 4–30 months after a successful Whipple, 6 patients had obstruction secondary to a non-resectable pancreatic carcinoma and 2 had recurrent pancreatic cancer after Whipple. One patient developed an intra-abdominal abscess 20 days after a Whipple, drained percutaneously. Patient presented bloody output through the percutaneous drain and an abscessogram showed a fistula from the abscess cavity to the portal vein. A balloon expandable I-cast stent-graft (Atrium Medical, Merrimack, NH) was placed to seal the fistula.

There were no acute stent occlusions. Primary stent patency was 95.2% 84% and 68% at 1, 3 and six months respectively (Figure # 3). All stent occlusions were caused by tumor progression. Two patients had stent occlusion 2 months after insertion; One patient underwent successful recanalization with restenting but there was no symptom improvement. The other patient had extensive disease progression and recanalization was not attempted. One patient had a stent occlusion five months after insertion. Extension of primary disease was identified on CT and stent revision was not attempted. A patient had stent occlusion 10 months after insertion. Stent revision was attempted but technically unsuccessful. Occlusion 17 months after insertion occurred in one patient, and no revision was attempted. One patient presented 20 months after stent insertion with recurrent ascites and abdominal pain. This patient had a successful revision with clinical improvement, however, 2 months after stent revision she developed variceal bleeding. Second revision that included TIPS creation was performed and bleeding was controlled but the patient died 2 months later from progressive disease.

Patient survival at 10 months was 40% (Figure # 4). Resolution of ascites and/or abdominal pain was seen in 17 patients (80.9%). Four patients with obstruction related to extrinsic compression by unresectable tumor reported no clinical improvement after stent placement.

Complications.

Complications were classified according to CIRSE guidelines. There were two major complications in this series: one death and one major bleed requiring transfusion. One patient died 2 days after an uneventful stent placement. The cause of death was not determined. The early death rate was 4.76%.

Portal vein perforation with massive bleeding was seen in one patient. The patient presented with abdominal pain, ascites and elevated serum bilirubin 5 days after resection of the right lobe of the liver. Contrast enhanced CT demonstrated acute portal vein thrombus. A trans-splenic approach was used to perform mechanical thrombectomy and thromboaspiration but thrombus removal was suboptimal. Pulse-spray infusion of 4 mg of alteplase was conducted using an 8 Fr Zelante device using the power pulse mode. Portogram after power pulse alteplase infusion showed massive extravasation from the main portal vein. This complication was managed with placement of a 13 mm x 5 cm Viabahn self-expandable stent-graft (W.L. Gore, Phoenix, AZ).

There were no bleeding complications from percutaneous tracts.

Discussion
This study describes the outcome of percutaneous portal and mesenteric vein stent placement to palliate portal and mesenteric vein obstruction in 21 consecutive patients with hepatobiliary malignancies. Management of portal vein obstruction in patients with hepatobiliary malignancies with endovascular stent placement has been described to be safe and effective (13). Based on our experience, indication for intervention is best decided through a multidisciplinary approach. Patient selection is essential to identify suitable candidates to undergo these procedures. The technical success rate, clinical improvement and stent patency in our group of patients concurs with the rates described in other reports (2, 6, 14). Stent placement was successful in all patients and clinical improvement was seen in 80% of our patients, similar to what has been reported elsewhere (2). Primary stent patency at 1, 3 and 6 months was 95%, 84% and 68% respectively. Six patients had stent occlusion and all were secondary to tumor progression. Stent selection is a challenge and there is no evidence that any type of stent works better for this indication (2, 8). Bare stents were used in most of the cases in the current series; and the indications for stent-graft insertion were: persistent thrombus in the main portal vein that could not be eliminated during the recanalization procedure, portal vein perforation with acute bleeding and erosion of the portal vein by an infected fluid collection (15). Anticoagulation does not seem to play a role in stent patency. In the current study, Lovenox at therapeutic doses was used in patients who had thrombosis in the portal vein but it is unclear if this improved or maintained stent patency. The findings on this series are similar to those reported recently, in a similar group of patients (16). A prospective trial to determine if anticoagulants are indicated or useful in these patients may not be feasible.

Patient survival is directly related to the course of the patient’s primary disease. There was only one patient who has survived more than 4 years after stent placement. This patient had acute portal vein thrombosis after pancreatoco-duodenectomy with vascular reconstruction. The thrombosis was identified by CT scan at post-operative day 5 and she underwent successful portal vein recanalization, thrombectomy and stent placement at post-operative day 7. Her clinical condition improved after the procedure; she received neo-adjuvant chemotherapy and had an excellent clinical outcome. No stent revisions were conducted on this patient. Early intervention may have participated in this patient’s prolonged survival.

There were two major complications, one related to the use of alteplase in a patient who presented with acute portal vein thrombus 5 days after right lobe resection. The complication was managed successfully with placement of a stent-graft. A very similar complication was reported by Kuban and Sheth in a review article (13). There was one early death but the cause of death could not be determined.

The results reported in this study support placement of stents to palliate portal vein obstruction in selected patients with hepatobiliary malignancies. The procedure was safe, with high technical success, acceptable clinical success and low complication rate. The procedure is useful especially in patients who present with ascites and respond to treatment. This represents a significant improvement in quality of life, even if life expectancy is not improved as survival is essentially dictated by the course of the primary malignancy.
The weakness of this report is that it is a retrospective study and may be affected by patient selection bias, however, the results presented here are similar to previous published reports and supports the application of this intervention in suitable patients. Results presented here support a multidisciplinary approach for the management of these patients. Early identification of the problem with intervention may be key in improving patient outcomes.

**Conclusion**

Endovascular recanalization with stent placement is safe. Clinical palliation was achieved in 80% of patients. Stent patency is acceptable and determined by disease progression.

**Declarations**

“Compliance with Ethical Standards”

1. **Ethics approval and consent to participate.**
   a. This was a retrospective study of a series of patients undergoing a clinically indicated procedure. Approval for retrospective chart review was granted by the IRB.
   b. This is a retrospective study, for this type of study formal consent is not required.
   c. **Informed consent:** Informed consent was obtained from all individual participants included in the study.

2. **Consent for publication:** For this type of publication, consent for publication is not required.

3. **Availability of data:** The data included in this study was obtained from patients charts in a retrospective fashion. The data is available upon request; there are no patient identifiers.

4. **Conflict of Interest:**
   a. Ferral is a consultant for Terumo
   b. All other authors declare no conflict of interest.

5. **Funding:** This study was not supported by any funding

6. **Authors’ contributions:**
   a. **Hector Ferral and Marc Alonzo:** Interventional radiologists who were the operators for the procedures. Main authors of the manuscript.
   b. **Robert Marsh:** Medical Oncologist and physician who managed the patients and referred the patients to the procedures. Editorial review of the manuscript.
   c. **Mark Talamonti:** Hepato-biliary surgeon who operated on the surgical patients and also referred patients to the procedures. Editorial review of the manuscript.
   d. **Jewell Datri:** Statistical evaluation of the data and editorial review of the manuscript.

7. **Acknowledgments:** Not applicable
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**Figures**

**Figure 1**

Portal Vein Access a. Ultrasound guided access to the portal vein. Image shows needle placement a peripheral branch of the right portal vein. Ascites provides a good window for needle access. b. Direct portogram through the 5 Fr dilator shows opacification of the main portal vein and peripheral branches. Notice contrast cut-off at the mid-portal vein, confirming obstruction.
Figure 2

a. Direct portogram via angiographic catheter immediately after recanalization in a patient with acute thrombosis shows moderate amount of thrombus in the lumen of the portal vein. b. Direct portogram with measuring catheter after crossing of the portal vein obstruction. Mesenteric venous branches leading to the main mesenteric vein are opacified. c. Direct completion portogram after stent placement shows a patent stent. Note that the left portal vein is not opacified. d. Direct portogram after left portal vein thromboaspiration shows partially patent intrahepatic branches of the left portal vein. e. Direct portogram after aspiration of left portal vein thrombus now shows a patent stent and intrahepatic portal vein branches with small amount of intraluminal thrombus. f. Coronal view of contrast enhanced CT scan three months after intervention shows a patent stent g. Axial view of contrast enhanced CT scan shows patent intrahepatic portal vein branches.

Figure 3

Kaplan-Meier curve depicts stent patency
Figure 4

Kaplan-Meier curve depicts patient survival