Portomesenteric Intervention in the Cancer Patient

A review of patient selection and treatment approaches.

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Portomesenteric venous stenosis and occlusions are complex problems that can develop in patients with pancreaticobiliary cancers. They can be caused by external compression from tumors or lymph nodes or by direct tumor invasion in the portal system leading to tumor thrombus, or they can be a result of previous surgery or radiation therapy. Portomesenteric stenosis causes increased venous pressures in the mesentery and spleen, resulting in abdominal ascites, thrombocytopenia, and formation of abnormal collateral vessels, the latter of which can lead to gastrointestinal (GI) bleeding when located near luminal surfaces. It also results in decreased venous inflow into the liver, which causes liver dysfunction and atrophy.

The most common clinical symptoms of portomesenteric stenosis or occlusion are ascites and GI bleeding. Additional symptoms that may be related to portomesenteric hypertension are GI malabsorption and associated weight loss, nausea, and abdominal pain, which can be postprandial but is less severe than that seen in arterial mesenteric ischemia. However, pain, weight loss, nausea, and abdominal pain are common symptoms in patients with GI malignancies and are therefore more difficult to directly attribute to symptoms of portal vein pathology.

The development of symptoms related to portal vein stenosis (PVS) is dependent on the acuity of the etiology and the patient's ability to develop sufficient nonluminal collaterals. In some patients, collateral formation is robust enough such that the patient is completely asymptomatic from a complete portal vein occlusion, whereas some patients with 50% luminal stenosis develop florid ascites. Because prognoses from PVS progression vary, treatment algorithms are difficult to determine in patients with asymptomatic PVS.

The severity of the anatomic abnormality can vary from mild, non–flow-limiting stenosis to complete portomesenteric thrombosis and can be further complicated by the presence of intrahepatic parenchymal disease due to cirrhosis or chemotherapy-induced liver disease. Complicating this problem further is that the severity of stenosis may not correlate with clinical symptoms. Therefore, treatment decisions in these patients need to be personalized, taking into account symptom severity, individual anatomy, and patient goals of care. This article describes some general approaches we have taken in these patients and techniques that we have found to be safe and effective.

PATIENT SELECTION

The decision to intervene on patients with portomesenteric pathology has to be first and foremost based on the patients' goals of care. Although it is important to question invasive procedures in patients who may be near the end of life, it is equally important not to exclude them from invasive interventions that can result in significant palliation for the remainder of their lives and/or nominally extend their lives such that they can exert control over the dying process. A review of our experience found that 2-year survival in these patients was only 31%. However, patients experienced significant palliation of symptoms, with 87% of their remaining life free of the presenting symptom (ascites

or GI bleeding), a statistic we defined as mean fraction of remaining life palliated.[1]

Portal Vein Thrombosis Without Underlying Stenosis

In patients with portal vein thrombus without underlying stenosis, the etiology of the thrombus is not related to a disruption of venous blood flow into the liver (inflow) as is seen in patients with extrahepatic venous stenosis or occlusions. Rather, patients may be prothrombotic for various reasons or have intrahepatic disease with reduced venous blood flow out of the liver (outflow). Cancer generally confers considerable increased risk for portomesenteric venous thrombosis (PMVT) compared to the general population (relative risk [RR], 5.3). This is especially true in patients with hepatocellular carcinoma (RR, 124), cholangiocarcinoma (RR, 77), and pancreatic malignancies (RR, 28).[2] In noncirrhotic patients with PMVT, the standard of care is therapeutic anticoagulation for 6 months.[3] The use of anticoagulation in cirrhotic patients and those with chronic PMVT is more controversial and made on a case-by-case basis. Either way, we do not offer intervention to asymptomatic patients with PMVT without inflow obstruction but rather recommend systemic anticoagulation if there are no contraindications.

Asymptomatic Patients

It is not standard of care to intervene on patients with PVS without related symptoms. However, in symptomatic patients, portal vein stenting has been shown to reduce symptoms related to portomesenteric hypertension, increase liver size, and possibly prolong survival compared to patients with PVS who are not treated.[1] Therefore, treating patients with portal vein stenting to prevent the development of total occlusion and potential symptoms thereof is intriguing. To that end, we have a prospective trial at our institution of portal vein stenting available to patients without symptoms but with at least 75% stenosis of the portal vein on imaging. Outside of a trial, patients in this category should be offered observation/expectant management.

Symptomatic Patients

The severity of symptoms and their effect on patient quality of life must be considered prior to offering intervention for symptomatic portomesenteric stenosis or occlusion. In our experience, patients with mild to moderate symptoms have longer durability of symptom relief, while severely symptomatic patients often have more extensive thrombosis or occlusion and higher rate of reocclusion and symptom recurrence.

Although portal vein stenting or transjugular intrahepatic portosystemic shunt (TIPS) without thrombosis is often performed as an outpatient elective case, more invasive procedures such as thrombectomy or sharp recanalization are typically reserved for severely symptomatic, hospitalized patients or those who require patency to preserve future transplant or surgical options. When the decision to intervene has been made, attention can then be turned to approach and technique. Cancer patients with symptomatic portomesenteric pathology can usually be classified into one of the following categories:

- Inflow limitation (type 1)
  - Without thrombus (type 1A)
  - With nonocclusive thrombus limited to the extrahepatic portal vein (type 1B)
  - With extensive thrombosis (type 1C)
- Outflow limitation (type 2)
  - Without thrombosis (type 2A)
  - With nonocclusive thrombus limited to the extrahepatic portal vein (type 2B)
  - With extensive thrombosis (type 2C)
- Combined inflow and outflow limitation with or without thrombosis (type 3)

APPROACH TO SYMPTOMATIC INFLOW DISEASE

Inflow disease to the liver can be caused by stenosis anywhere in the central portomesenteric system. Stenoses/occlusions can be extrahepatic, intrahepatic, or both and can involve the splenic vein, superior mesenteric vein (SMV), or portal vein, either alone or in combination. The location of the stenosis and vessels involved depends on the tumor origin and presence of regional lymph node metastasis. The most common location seen in patients with pancreatic cancer is extrahepatic PVS adjacent to the pancreatic head and involving the splenic-SMV confluence. Lesions in the pancreatic body or tail often thrombose the splenic vein, and as an isolated occlusion, they are relatively well tolerated and often asymptomatic. Patients with hilar cholangiocarcinoma often present with normal SMV and splenic vein but with stenosis of the main portal vein extending into the liver to include the right and left portal veins and even to the anterior and posterior sectoral branches. Extrinsic compression caused by lymph node metastasis is far less common but can present with stenosis in any extrahepatic location.

The approach to treating patients with type 1 disease is to relieve the presenting symptom. In the case of ascites or mesenteric collaterals, the priority for treatment is to maintain inline flow from the normal portion of

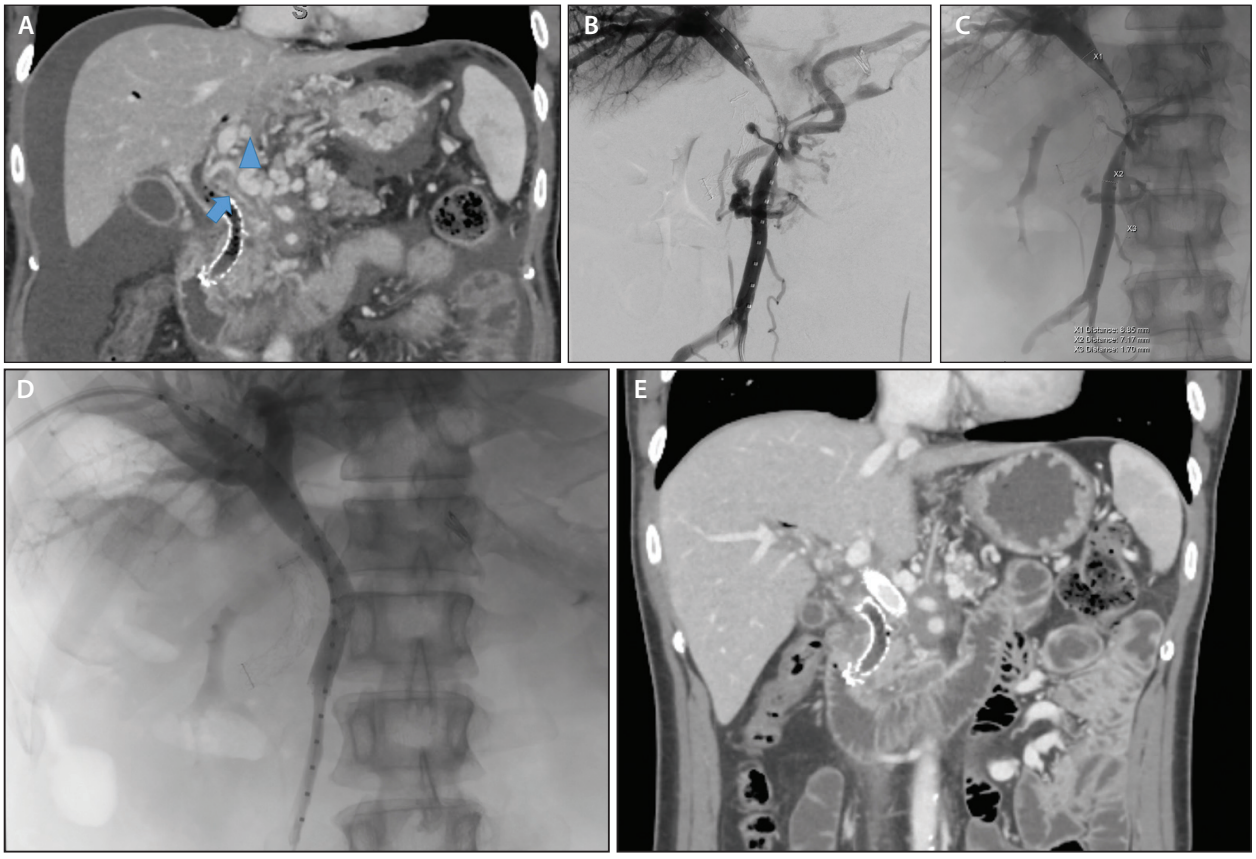

Figure 1. A 50-year-old man with locally advanced pancreatic cancer and ascites requiring weekly paracentesis due to near-total occlusion of the portal vein (arrow). Prehepatic portal hypertension manifested as ascites, thickening of the bowel wall, and development of multiple mesenteric collaterals (arrowhead) (A). Simultaneous digital subtraction angiography (DSA) from the 5-F measuring catheter in the SMV and the 7-F sheath in the main portal vein showing near-total occlusion of the SMV-portal junction, with prominent varices but no thrombus (B, C). DSA from SMV after placement of 10-mm X 8-cm Protégé stent. Note there is no filling of the collaterals (D). CT performed 9 months later showed a patent portal vein stent, an increase in liver volume, a normal-appearing bowel, and resolution of ascites (E).

the SMV or its proximal branches to a normal intrahepatic portal vein with good outflow. Although less common, GI bleeding from sinistral portal hypertension related to occlusion of the splenic vein with poor collateralization to the inferior mesenteric vein (IMV) and SMV is a situation often seen in postsurgical patients with local recurrences, and it may require preservation or restoration of patency of the splenic to portal vein. With the exception of the previous scenario, as long as IMV to SMV collaterals exist, the inflow is best restored by focusing on SMV patency. In these cases, we do not hesitate to cover a patent or stenosed splenic vein origin as long as collaterals exist to the SMV. An alternative plan is to put parallel stents in place in a Y configuration, deploying splenic-to–portal vein and SMV-to–portal vein stents simultaneously, usually using 7- or 8-mm stents for the portal vein to accommodate both. Although we have used this approach, the patency duration is shorter using this technique, and we prefer placing larger stents (12 or 14 mm) from the SMV to the portal vein and allowing splenic decompression via IMV/SMV collaterals.

Type 1A: Inflow Limitation Without Thrombus

From a technical perspective, treating type 1A patients is straightforward (Figure 1); we treat them via transhepatic access. It is important in any case of transhepatic or transplenic access to ensure all ascites is drained during and after the procedure. Although the parenchymal tract is closed with coils and/or glue, hemostasis still depends on clot formation at the organ surface. If ascites is present, clot cannot readily form

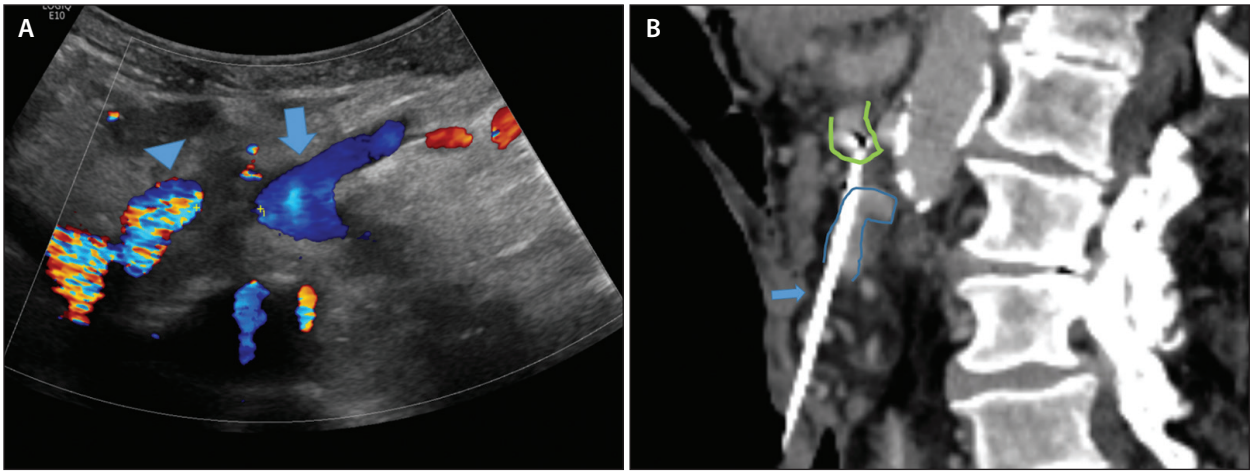

Figure 2. A chronically occluded SMV in a 68-year-old man with recurrent life-threatening GI bleeding 2 years after undergoing the Whipple procedure. Blind ending of the SMV (arrow) and portal vein (arrowhead) can be seen. Attempts at conventional crossing were not successful (A). The needle (arrow) was passed from the anterior abdomen into the SMV (blue line), then out through the occlusion and into the portal vein (green line) (B). In-room arterial and venous phase CT were performed after portal vein access was achieved and reconstructed to sagittal plane.

and hemostasis cannot be easily achieved. Therefore, in the presence of ascites, we place an intraperitoneal drainage catheter immediately adjacent to the access entry site and leave it open during the case and for 12 hours postoperatively to evaluate for any postprocedural bleeding.

In the absence of thrombosis, access is easily achieved in a peripheral portal vein branch using ultrasound and is confirmed with contrast injection. Although the segment of access is usually operator preference, in patients with cholangiocarcinoma or another cause of intrahepatic stenosis, stenting may be required to extend into the posterior or anterior sectoral branches; therefore, attention to the segment of access can be critical. In patients without outflow limitation, we do not favor intervention via TIPS access. We typically secure access with a 7-F, 23-cm sheath, allowing for use with most noncovered self-expanding and balloon-expandable stents.

Crossing the stenosis or occlusion is the next technical hurdle. In cases of complete chronic occlusion, advanced crossing techniques employed in any vascular system can be employed. On occasion, needle-based sharp recanalization can be used to cross long-standing chronic SMV occlusions in patients with clinically recalcitrant and life-threatening bleeding (Figure 2). After venography, we typically measure venous pressures to calculate a pressure gradient across the lesion. This can also be helpful if coexisting intrahepatic parenchymal disease is suspected and may indicate a need for concurrent TIPS. Stent selection is based on the length and shape of lesion. We prefer not to use covered stents as a first-line device, although they may be used in cases of portal vein rupture. For short focal stenoses, we typically opt for an uncovered 10-mm–diameter balloon-expandable stent (Visi-Pro, Medtronic), with postdilation up to 12 mm in some cases. For longer or more tortuous lesions, we typically use a 10-, 12-, or 14-mm self-expanding stent (Protégé, Medtronic), with postdeployment dilation to 10 or 12 mm. In some cases, we use an 8-mm stent when the inflow target vessels are particularly small. However, it is important to review imaging prior to the development of stenosis to identify the original diameter of the target vein. Oftentimes the "normal" SMV on angiography is diminutive but was substantially larger on previous imaging. Stent size selection should take this historical information into account because stents are typically upsized at least 2 mm from the diameter seen on angiography on the day of the procedure (Figure 1C and 1D). Stent length is determined in the usual fashion. In benign (postsurgical or radiation-induced) stenosis close to a bifurcation, a balloon-expandable stent can be used for precise stent deployment without covering the bifurcating branch. However, this is not advised for malignant external compression because it is important to extend the stent well into normal vessels to account for anticipated continued tumor progression, even at the expense of "covering" a bifurcation. Particularly in cholangiocarcinoma, this means that you are stenting across the left portal vein.

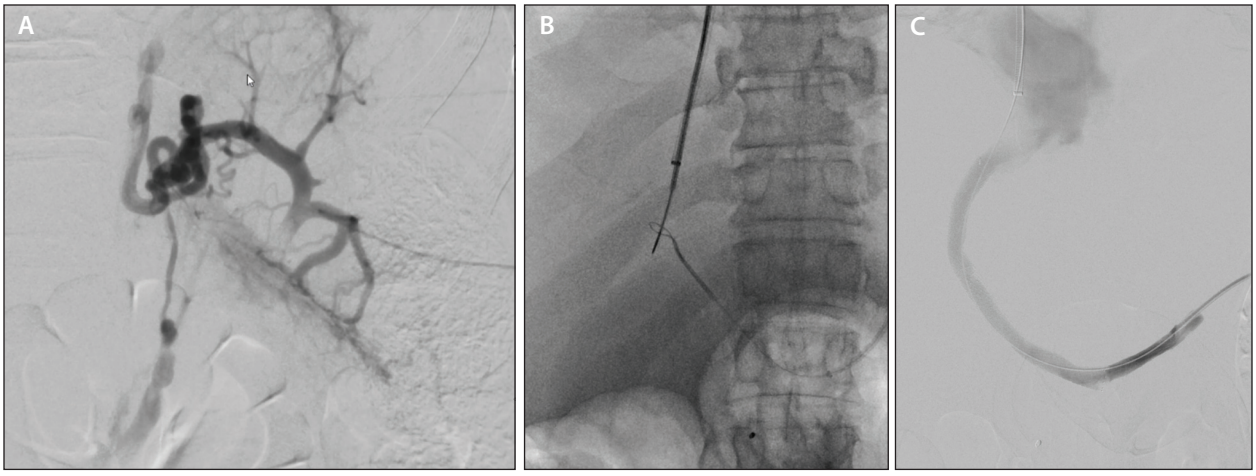

Figure 3. Transplenic DSA in a 58-year-old man with total portomesenteric thrombosis and GI bleeding showing total occlusion and poorly formed collaterals (A). TIPS access was achieved by targeting a transplenic snare (B). Completed TIPS (C).

Type 1B: Inflow Limitation With Partial Thrombosis

The approach to patients with inflow limitations with partial thrombosis (type 1B) is similar to that of patients without thrombosis because there is usually preserved intrahepatic portal flow and access is readily achieved from a transhepatic approach. The main difference in technique compared to that used for type 1A patients is the additional use of thrombectomy devices and intraprocedural anticoagulation. The goal of this procedure is to establish patency with a reasonable chance of durability, and therefore brisk inflow and outflow are required through the stent. The presence of thrombus can limit either of these goals, and in these situations, we attempt to remove existing clot prior to stenting. Our typical tools for this are the AngioJet Solent Proxi (Boston Scientific Corporation) and the Indigo CAT6 or CAT8 (Penumbra, Inc.), with the CAT8 necessitating upsizing to an 8-F sheath. For small-burden thrombus, we do not use thrombolytics. However, when performing mechanical thrombectomy, we heparinize the patients with a goal activated clotting time of 220 to 280 seconds. The approach to stent placement is similar to patients in the type 1A category. We typically do not plan to transfuse these patients during the procedure.

Type 1C: Inflow Limitation With Extensive Thrombosis

Symptomatic patients with inflow limitation and extensive or complete portal thrombosis (type 1C) are more challenging to treat. Even if the operator is able to clear and open the portal vein into the liver, the extensive portal thrombosis itself becomes a pseudo-outflow obstruction and will result in short-term stent failure and rethrombosis if not either significantly improved or bypassed. For this reason, these patients should also be consented for TIPS as part of the revascularization procedure.

Access in these cases is more variable. Our preference is transplenic access because segmental splenic veins are typically patent even in the setting of widespread intra- and extrahepatic portal vein thrombosis. Furthermore, a transplenic approach allows the operator to select multiple intrahepatic portal vein branches for thrombectomy or angioplasty. Thrombectomy is performed using the same previously outlined devices. When the CAT8 is needed or stenting needs to extend into the SMV rather than the splenic vein, we establish access into a thrombosed peripheral intrahepatic portal vein branch by targeting a vascular snare under fluoroscopy or by establishing TIPS access, oftentimes again by using a snare in the thrombosed portal vein as a target (Figure 3). In the setting of acute widespread thrombus, we occasionally use a small amount of alteplase (5 mg in a 50-mL solution) for power-pulse spray mode. We do not use indwelling lysis catheters for prolonged alteplase infusions. If enough of the intrahepatic portal vein is cleared such that there is good outflow, we placed a stent in the portal system to restore inflow without creating a TIPS; in cases of poor outflow, we establish outflow via a TIPS. Intraprocedural heparinization is vital during portal vein intervention where there is preexisting thrombus.

For transhepatic and transplenic access, we typically close the transparenchymal tract with coils. In transplenic cases or when the patient requires uninterrupted anticoagulation, a small glue cap is added to the coil pack at the organ edge (Figure 4).

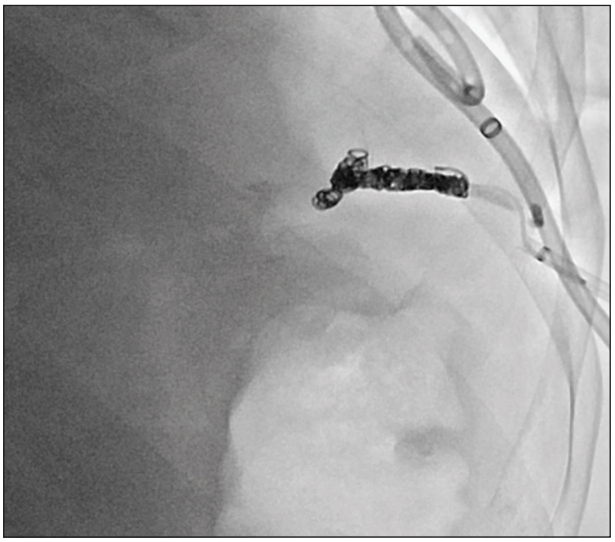

Figure 4. Transplenic access closure. Note the presence of the intraperitoneal drainage catheter adjacent to the access site, detachable 4-mm Ruby coils (Penumbra, Inc.), and n-butyl cyanoacrylate:Lipiodol (Guerbet LLC) 1:1 glue cap.

APPROACH TO SYMPTOMATIC OUTFLOW AND COMBINED INFLOW-OUTFLOW DISEASE

Both cirrhosis-related and chemotherapy-induced liver disease are important causes of portal hypertension in patients with cancer. The same indications for TIPS creation for patients without cancer apply to these patients (ascites refractory to medical management or GI bleeding), with the added caveat of ensuring that it makes sense to go forward given the stage of disease and the patient's goals of care. Additionally, TIPS creation may be complicated by the presence of intrahepatic tumors in the expected path of the shunt. However, there is often a path to the portal system from one of the three hepatic veins, which is not a contraindication. Our center has previously reported a series of nine patients who underwent TIPS creation through tumor without procedure-related hemorrhage or overt vascular tumor seeding.[4] The technical approach to TIPS is otherwise the same as in patients without cancer. Although success rates are similar, rates of encephalopathy in cancer patients have been noted to be higher than those without malignancy.[4,5]

Portal vein thrombosis in the setting of cirrhosis or other parenchymal outflow obstruction is a challenging problem. In asymptomatic or minimally symptomatic patients, we recommend anticoagulation alone. In more symptomatic patients or patients who worsen with anticoagulation, we consider TIPS in combination with portal thrombectomy/reconstruction. If there is only partial thrombosis, we attempt access via TIPS if there is some intrahepatic portal vein flow.

Severe thrombosis should be treated as a combined inflow-outflow case (type 3) by combining transplenic and TIPS access and using thrombectomy, angioplasty, stenting, and TIPS creation. In these cases, we remove as much clot as possible and place a stent in areas of persistent clot to ensure good inflow in addition to the TIPS stent. We often plan to transfuse one unit of red blood cells for extensive thrombectomy. At a minimum, blood should be readily available for transfusion.

COMPLICATIONS AND POSTPROCEDURE CARE

In our experience, transhepatic and transplenic interventions have a low incidence of intraprocedural complications. In 104 patients who underwent transparenchymal access in the past 3 years, there has been one refractory tract bleed with unplanned transfusion and two portal vein ruptures. In portal vein rupture after recanalization and stenting, both cases were successfully managed with short covered Viabahn stents (Gore & Associates). There is some variability in operator preference for anticoagulation in our practice, but in general, if a patient has clot in the portal system, intraprocedural heparinization and postprocedural full-dose low-molecular-weight heparin (1 mg/kg) or apixaban (5 mg by mouth twice daily) are used. For portal vein stenting and no clot, we do not use full intraprocedural anticoagulation and start the patient on prophylactic dose apixaban (2.5 mg by mouth twice daily) after stent placement. We do not use anticoagulation for standalone TIPS.

CONCLUSION

Portomesenteric disease in patients with cancer is a complex problem, and treatment requires consideration of the disease state and the patient's goals of care. In appropriately selected patients, portomesenteric intervention including TIPS, portal vein stenting, and portal thrombectomy/reconstruction have low rates of complications and can provide important symptom palliation in patients with cancer. ■

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