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Palliation of Malignant Ascites

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Large-volume ascites accumulation is a common, problematic occurrence in patients with advanced malignancies and in patients with intraperitoneal spread of tumor. The mass effect of ascites accumulation can cause symptoms of painful abdominal distention, early satiety, and nausea. In extreme cases, vomiting secondary to the fluid causing external gastric or bowel compression and obstruction may occur. Additionally, patients often complain of shortness of breath, limited mobility, and lower extremity edema. These symptoms not only are distressing, but also adversely affect quality of life.

PATHOPHYSIOLOGY

The most common cause of ascites is cirrhosis (75% of patients). Ten percent of cases are due to malignancy, 3% are due to cardiac failure, 2% are due to tuberculosis, and the remainder are due to other causes [1]. The cause of ascites in cirrhotic patients has been well described [2,3]. Portal hypertension develops secondary to resistance at the splanchnic and arteriolar level, and the sinusoidal resistance is not relieved by the subsequent development of portosystemic collaterals. The ensuing development of portosystemic shunting and an increase in cardiac output leads to potential lethal complications, including renal failure, gastroesophageal varices, ascites, and hepatic encephalopathy.

The cause of ascites development in oncology patients differs from patients with cirrhosis. In 50% of patients with malignancies, ascites development is secondary to invasion of the parietal or visceral peritoneum; 15% are due to liver invasion and portal venous compression, 15% are a combination of the first two, and the remaining 20% are attributed to chylous ascites secondary to lymphatic invasion [4]. Most patients with malignant ascites have epithelial carcinomas as the source. Only 20% of patients have malignancies of unknown origin; 80% are from the breast, ovaries, colon, endometrium, gastrointestinal tract, or pancreas [5].

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Differentiating between malignant and nonmalignant causes of ascites production traditionally has been done by sending fluid for cytology and laboratory chemistries to determine if it is exudative or transudative. The difference between the albumin concentration in serum and ascitic fluid is termed the *serum–ascitic fluid albumin gradient* (SAAG). If the SAAG is greater than 1.1 g/dL, it is termed a "high" SAAG, and if it is less than 1.1 g/dL, it is termed a "low" SAAG. A high SAAG occurs in portal hypertension, which may be related to either liver disease or cardiac disease. When the SAAG is greater than 1.1 g/dL, the concentration of total proteins in ascitic fluid helps to distinguish cardiac causes from hepatic causes. In cardiac disease, the total protein concentration in ascitic fluid is usually greater than 2.5 g/dL, whereas in liver disease, it is less than 2.5 g/dL. A low SAAG typically is associated with carcinomatosis, tuberculosis, pancreatic ascites, and nephritic syndrome. Fifteen percent of cirrhotic patients have low SAAG ascites, however, and 20% of oncology patients have high SAAG ascites [6–11]. Several other tests have been described to help differentiate between malignant and nonmalignant ascites. Ascitic fluid can be sent for lactate dehydrogenase and for cholesterol. An ascites lactate dehydrogenase level greater than 250 μg/mL and a cholesterol level greater than 70 mg/dL are associated with malignancy [6,12–14]. Oncology patients who have comorbidities of cirrhosis, liver invasion by tumor, congestive heart failure, or cardiac compromise secondary to chemotherapy need further evaluation of ascites to help differentiate the cause because medical management may be appropriate.

Cirrhotic patients with symptomatic ascites who undergo frequent paracentesis for symptom relief typically are monitored closely for hypotension. Most of these patients undergo paracentesis at a slow rate with or without concomitant administration of plasma expanders, such as albumin, to maintain homeostasis. Lethal hypotensive episodes after paracentesis typically do not occur in oncology patients because of the different physiologic mechanism of ascites accumulation. Large-volume paracentesis of 5 L/d is recommended as safe [5], but this is a conservative recommendation, and larger volumes can be removed safely if necessary for patient comfort.

MANAGEMENT OPTIONS

Treatment options for malignant ascites should be developed with a goal of palliation of symptoms that is best suited for the patient. Most patients with advanced disease have a life expectancy of only a few weeks to a few months. Although breast and ovarian cancer patients often have longer survival times [15], palliation of symptoms still should be the goal. Medical therapies, such as diuretics, and sodium and fluid restriction are not effective in most oncology patients. The small percentage of patients with cirrhotic/portal compression as a cause of refractory ascites may find the restrictiveness of medical management unpalatable at the end of life. Available procedure-based therapies should be discussed openly, and the patient should be given the choice of medical versus nonmedical options. The following therapies are discussed in

more detail: paracentesis, pigtail catheter (all-purpose drain) placement, tunneled catheter placement, port placement, and shunt creation/placement.

Paracentesis

Paracentesis is the most common and effective therapy used by physicians for effective palliation of ascites symptoms [16]. Drainage of large-volume ascites can be accomplished without ultrasound guidance in an outpatient or office setting. Many hospitals offer paracentesis in various departments, including the gastrointestinal laboratory, ultrasound unit, and interventional radiology suite. Using ultrasound guidance is important in patients with loculated pockets of fluid or in patients with postsurgical abdomens in which fluid is walled off.

Paracentesis is a safe procedure. Rare complications that may occur include infection, bowel perforation, and hemorrhage. Paracentesis offers the advantages of a quick, simple, low-risk procedure with immediate symptom relief. Symptom relief is temporary, and as the patient's disease progresses, requisite trips to the hospital for the procedure increase as well. Patients are left with the fatigue of frequent hospital visits or waiting as long as possible between procedures until the ascites symptoms are no longer tolerable and the needle-stick pain that occurs with each procedure.

Pigtail Catheter Placement

Pigtail drainage catheters are used for a wide variety of indications, including percutaneous abscess drainage [17], evacuation of pleural effusions [18], and percutaneous biliary and renal drainage procedures. For management of ascites, catheters typically are placed under ultrasound or fluoroscopic guidance. This can be done as an outpatient procedure or during hospital admission. After placement, the catheters can be capped and drained intermittently via gravity drainage bag or vacuum bottles. Alternatively, they can be attached immediately to gravity drainage bags for continuous drainage.

Complications of pigtail catheter management for ascites occur in 35% of patients [19] and include peritonitis, accidental removal, leakage around the drain, and catheter occlusion. Good results have been obtained when pigtail catheters are used to treat symptomatic ascites associated with ovarian hyperstimulation syndrome [20]. Drains were placed in healthy young women for an average duration of less than 2 weeks. There has been speculation that infection rate may vary with continuous drainage as opposed to intermittent drainage. O'Neill and colleagues [21] attributed their four cases of peritonitis to the intermittent technique, whereas Richard and colleagues [22], Barnett and colleagues [23], and Rosenberg and colleagues [24] had no cases of peritonitis secondary to intermittent drainage technique. Infection rates in pigtail catheters are more likely secondary to the duration the catheter is in place, and these catheters should be used in patients with a life expectancy in weeks rather than months.

Tunneled Catheter Placement

Tunneled catheters have been used for vascular dialysis, apheresis, and peritoneal dialysis for many years. The catheters have Dacron cuffs that reside in the

subcuticular tunnel. The tissues heal and scar around the cuff, preventing a conduit for bacterial growth along the catheter. The catheters are designed to have one, two, or three cuffs. The third cuff is located near the tunnel exit site and impregnated with an antimicrobial agent.

Dialysis Catheters

Silastic peritoneal dialysis catheters now are being used effectively in management of malignant ascites [21,23,25,26]. The catheters are inserted into the largest area of ascites in an outpatient setting, usually by radiologists [27] under ultrasound or fluoroscopic guidance (Fig. 1). The catheters can be managed at home by the patient or primary caregiver via intermittent gravity drainage, intermittent vacuum bottle drainage, or continuous gravity drainage.

Complications are similar to the complications seen with peritoneal dialysis catheters, including cellulitis, peritonitis, and catheter occlusion. Another

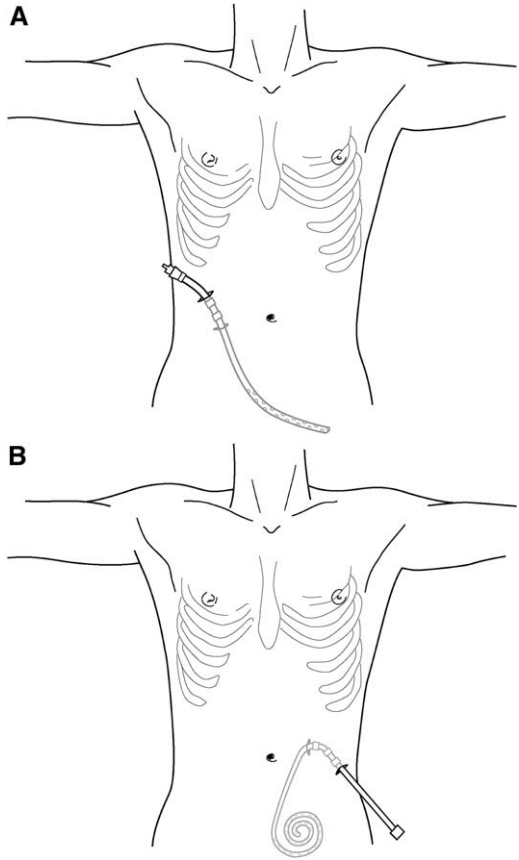

Fig. 1. (*A* and *B*) Dialysis catheters with two or three Dacron subcuticular cuffs. The superficial cuff closest to the exit site can be impregnated with antimicrobial chemicals.

common problem is leakage of ascites around the catheter tunnel until the cuff heals in properly. This leakage can be minimized by keeping the ascites well drained and pressure off of the tunnel until the cuff is well healed in the tunnel.

Pleurx Catheter

The Pleurx (Denver Biomedical, Denver, Colorado) catheter is a single-cuff, tunneled, 16Fr Silastic catheter that is approved by the Food and Drug Administration (FDA) for the drainage of malignant pleural effusions. FDA approval for malignant ascites was obtained in November of 2005. It has a one-way rubber valve rather than a clamp device to close the system and a line attached to vacuum bottles to access the catheter (Fig. 2). The valve remains sealed even if the cap becomes dislodged, and the catheter is open only when the valve is accessed. Patients and caregivers can be taught to perform the drainage at home without nursing assistance.

Placement of the Pleurx catheter is similar to that of the tunneled dialysis catheters. Problems with tunnel leakage have been resolved by puncturing the peritoneum superior and lateral to the umbilicus, then creating the subcuticular tunnel medially and superiorly (Fig. 3). In patients in whom fluid is located in the lower pelvis, a "C" curved tunnel can be created to help prevent fluid leakage (Fig. 4). Patients are instructed to perform drainage every day for the first 2 weeks to keep pressure off of the tunnel tract while it is healing. Patients are instructed to perform drainage subsequently as needed for comfort. Complications are similar to the complications associated with other tunneled catheters [22,24,28] and include infection, occlusion, and malpositioning.

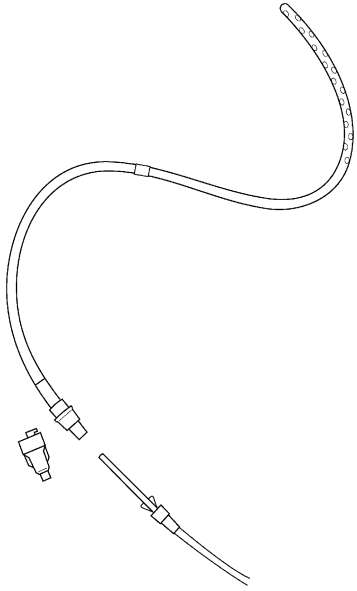

Fig. 2. Pleurx system with access line to go through the one-way safety valve.

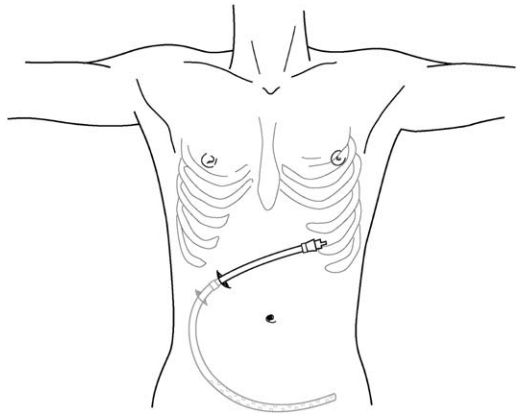

Fig. 3. Access to peritoneal cavity is obtained superior to umbilicus, and a tunnel is created further superior and medial to avoid leakage through tunnel.

Abdominal Port Placement

Venous arm and chest ports for chemotherapy delivery have been used by oncologists for years. When venous access is obtained, a tunnel is made for the catheter portion of the port, and a subcuticular pocket is created for the port well to reside. To help prevent infection, the whole system is subcuticular, and access is achieved through the skin with a noncoring needle. Some centers now place these types of ports in the abdomen to drain malignant ascites.

One published series of abdominal port placement in nine patients used either 6F or 8F vascular access ports [29]. A high complication rate was seen

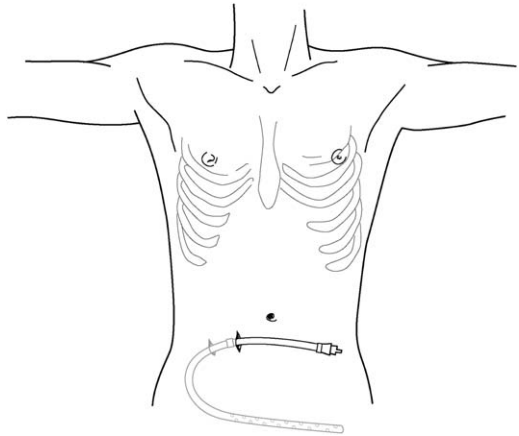

Fig. 4. "C" curved tunnel for when catheter must be placed in the lower pelvis to help prevent tunnel leakage.

with three cases of bacterial peritonitis, a case of catheter occlusion, and wound dehiscence. Additionally, ascites formation around the port made it difficult to palpate and prevented access. Other investigators addressed these issues [30,31] by using a port system designed for peritoneal access and by careful anatomic placement of the port. The port base they used was larger so that it could be palpated more easily, and it was attached to a 16F catheter with a Dacron cuff similar to that present on dialysis catheters. The larger, cuffed catheter not only allows for faster drainage time, but also should have fewer tunnel leaks after healing occurs around the cuff. It is recommended that the port hub be placed over the ribs to give undersupport to the port base when accessed (Fig. 5). The complication rate was similar to that seen with the external tunneled catheters previously described. The disadvantages to using a port are the requisite nursing support for home drainage because the port is accessed with a noncoring needle under sterile technique and the associated pain of needle access that occurs with each drainage attempt.

Shunt Creation

Peritoneovenous shunts

The shunting of ascitic fluid back into the main circulatory system can be accomplished through placement of Silastic catheters, such as the Denver or LeVeen [32], through peritoneovenous shunts (PVS), or through surgical manipulation such as transjugular intrahepatic portosystemic shunts (TIPS). Traditionally, PVS placement has been done under general anesthesia by surgeons in the operating room using large venous cutdowns. More recently, interventional radiologists have placed PVS successfully using minimally invasive techniques under conscious sedation [33–36].

Advantages of PVS placement include retention of protein-rich ascitic fluid and avoidance of external drainage devices, making it more acceptable to

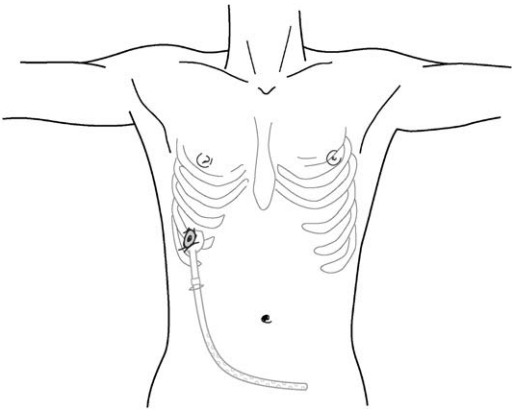

Fig. 5. Large peritoneal port placed over ribs to provide stable base for needle access. Note peritoneal port (as opposed to vascular port) with subcuticular Dacron cuff.

patients and their family members. The disadvantages are not trivial, however. PVS are prone to failure secondary to occlusion [37] and have been associated with pulmonary edema [32,38,39], thrombosis of major veins [38,40], seroma formation and leaks [38,41], and disseminated intravascular coagulation [39,42]. Patients must be evaluated carefully for body habitus, cardiac and renal status, and preexisting coagulopathy. PVS placement may not be available at local medical centers. Success and complication rates are tied directly to the learning curve associated with any complex procedure. A site with little experience in placing PVS may be more likely to experience a higher complication rate.

Transjugular intrahepatic portosystemic shunts

TIPS creation as a treatment for refractory ascites has been well described [43] and is described in detail in a separate article in this issue. TIPS is an effective treatment for intractable ascites because it reduces portal hypertension and improves sodium excretion and diuretic response. TIPS creation also is associated with the development of hepatic encephalopathy. Many studies have compared TIPS for treating refractory ascites versus repeated paracentesis. Saab and colleagues [44] conducted a Cochrane Database review of four trials that compared TIPS with paracentesis in treating refractory ascites [45–48]. They concluded that TIPS and paracentesis showed similar mortality and major complications except for the increase in hepatic encephalopathy in TIPS patients.

TIPS is efficacious in only a small percentage of oncology patients with liver invasion/portal compression as the underlying mechanism of ascites formation. Even in the few patients in whom TIPS may be helpful, careful consideration must be given to the benefits of ascites symptom management versus the risk of TIPS placement and subsequent complications of hepatic encephalopathy.

RECOMMENDATIONS

Effectively managing the symptoms associated with malignant ascites accumulation is problematic and challenging. No single method has been developed that works satisfactorily for all patients. Effective management has been a frustrating problem for many physicians and their patients.

Paracentesis is the most common therapy used to provide immediate symptom relief from large-volume ascites. It is a simple, low-risk procedure and is the therapy of choice when ascites first develops. It also is an excellent choice for symptom relief for ascites development between chemotherapy sessions. Many oncology patients, especially patients with ovarian and breast cancer, have temporary resolution of ascites accumulation after chemotherapy has been initiated or a new regimen begun. If chemotherapy is effective at resolving ascites development, paracentesis is the procedure of choice as a "bridge" between regimens. If the tunneled catheters were to be used immediately, they would need to be removed between each regimen because of the risk of infection and then replaced. PVS also are much more prone to failure if ascites is not present to keep them open and functioning. Paracentesis is the procedure of choice until all available chemotherapy options fail to address ascites accumulation.

After first-line therapies are exhausted, patients typically are left with paracentesis as the treatment option for symptom relief. Many patients find the pain with each procedure unpalatable and the frequent trips to the hospital fatiguing. They often wait as long as possible until the symptoms are no longer tolerable before scheduling their next procedure. Often, patients progress to needing drainage several times per week to maintain satisfactory comfort levels. Often at this point patients seek other alternatives to paracentesis. The least invasive methods for palliating ascites symptoms are tunneled catheters or port placement. TIPS and PVS placement require centers that are proficient at these procedures and either a general anesthetic or monitored sedation. PVS placement should be reserved for patients who cannot tolerate external drainage for psychological or physical reasons.

The choice of tunneled dialysis catheter, peritoneal port, or Pleurx placement may be dictated by what is available at local medical centers or by patient preference. Tunneled peritoneal catheters are easily placed as an outpatient. They have an open, clamp system with Luer-Lok access for drainage that can be performed at home by the patient or a family member. If vacuum bottles are unavailable, the significant time it would take for gravity drainage into bags may not be desirable for many patients. Peritoneal ports have a similar complication rate to other tunneled devices and can be placed as an outpatient. Drainage requires nursing support, however, for sterile preparation and noncoring needle access (and the associated pain with each access). The Pleurx catheter also is placed as an outpatient. It has a closed, one-way valve access system and comes with vacuum bottles and access lines. Previously, the bottles were 500 mL, but now 1-L bottles are available. A multicenter trial evaluating abdominal placement of the Pleurx catheter in patients with malignant ascites was completed to obtain FDA approval for this indication. Preliminary results show low complication rates similar to that published by Rosenberg et al [24] and Reisfield and Wilson [26], and FDA approval was obtained in November of 2005. Blood protein and chemistry levels were evaluated before placement of the catheter and at 12 weeks after ascites drainage of 2 L/d. There were no statistically significant changes in laboratory values for these patients, despite frequency of drainage [49].

Patients who are near death with less than several weeks to live can be kept comfortable with simple pigtail catheter drainage attached to gravity drainage bags. Most patients would like to travel, participate in family events, work, and go about the remainder of their lives without having to make frequent trips to the hospital for symptomatic drainage or are dependent on family members taking time off from work to get them to their drainage appointments. These patients benefit most from external drainage techniques. For patients who cannot tolerate external drainage, PVS may be an alternative.

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