Long-term venous access

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The use of multidrug chemotherapy and bone marrow transplantation in cancer treatment has made the utilization of reliable, long-term venous access (LTVA) an essential component of cancer therapy. The placement of LTVA devices not only permits the delivery of these complex therapeutic regimens but also drastically improves patients’ quality of life.

Indications
No definitive guidelines are available for utilization of central venous access. There are several important factors to consider when deciding upon LTVA device placement:

- the frequency and duration of therapy
- the frequency of blood draws
- the nature of therapy (eg, delivering vesicating agents into a central vein decreases the risk of extravasation)
- the need for supportive therapies (eg, total parenteral nutrition or systemic antibiotics)
- the need for stem-cell collection, plasmapheresis, and bone marrow reinfusion
- patient preference

Patient selection
LTVA should always be considered an elective procedure. Therefore, before an LTVA device is placed, the patient should have recovered from acute infections and the treatment of complications. If there is an absolute need for immediate central venous access before such times, a temporary percutaneous central venous access catheter can be placed. A history of vascular access catheter insertion, deep venous thrombosis of an upper extremity or central vein, thoracic surgery, neck surgery, irradiation, or mediastinal and thoracic disease should alert the surgeon to possible changes in normal venous drainage. Physical examination, documenting the integrity of the skin, changes in the skin secondary to previous surgical treatment and reconstruction, sites of previous central venous access catheter insertions, evidence of venous obstruction (presence of venous collaterals in the skin of the chest, unilateral arm swelling, or superior vena cava syndrome), and pulmonary reserve, should be performed in every patient. If there is any evidence of venous obstruction or a history of multiple previous central venous access catheters, the physical examination should be complemented with a formal venous imaging study. Duplex Doppler ultrasonography can visualize the patency and flow of the neck and arm veins. Intrathoracic veins and the right atrium are not well visualized by duplex Doppler ultrasonography but are better visualized with transesophageal echocardiography. This can be utilized preoperatively or intraoperatively. CT and MRI are useful for documenting the presence of thrombosis and the patency of major intrathoracic veins. Venography is still the gold standard for studying venous anatomy. Venography should be performed whenever the clinical situation warrants it and noninvasive venous imaging studies fail to provide a definitive diagnosis. This can be utilized preoperatively or intraoperatively. Chest radiography can disclose important information (such as the presence of pleural effusions, lung metastases, mediastinal adenopathy, and mediastinal tumors) that can modify selection of a site for LTVA placement.

Contraindications and precautions
Neutropenia A neutrophil count < 1,000/mm$^3$ is a relative contraindication to the placement of an LTVA device, since patients with neutropenia may have a higher incidence of septic episodes. The use of prophylactic antibiotics may reduce the incidence of infection in patients with a low absolute neutrophil count (ANC). Thrombocytopenia and platelet dysfunction are frequently encountered in the cancer patient. Preoperative platelet transfusion to approximately 50,000/ mL may allow the catheter to be safely placed with a reduction in the risk of bleeding complications. In those patients with thrombocytopenia refractory to platelet transfusions, venous cutdown may be a
safer approach for catheter placement. **Clotting factor abnormalities** Many cancer patients have abnormalities in their clotting factors secondary to malnutrition or chemotherapy. Correction with vitamin K or fresh frozen plasma may be necessary. **Active infection** The presence of an active infection represents an absolute contraindication to the placement of an LTVA device. In those patients with an active infection who require long-term antibiotic treatment, a temporary central venous access catheter or a peripherally inserted central venous catheter is preferable. **LTVA device selection** Two types of LTVA devices are available. There are tunneled external catheters that have skin surface access (Hickman, Broviac, Groshong, Quinton). Likewise, there are subcutaneous implanted ports (Port-A-Cath, Infusaport). Both types of central venous access devices are available with different lumen diameters and numbers. Peripherally placed central venous access devices, such as the PAS (peripherally accessed system) port or PICC (peripherally inserted central catheter), have become popular because of their ease of placement. PICC devices can be placed by specially trained nursing personnel. Important differences between tunneled external catheters and subcutaneous implanted ports are outlined in Table 1. **General considerations** An important general consideration in the selection of an appropriate LTVA device is that the infusion flow resistance depends on the catheter length and lumen diameter. Likewise, catheters with a split valve at the tip (Groshong catheter) are less reliable for blood drawing. **Frequency of device access** Subcutaneous implanted ports are preferred in patients who require intermittent device access for treatment or blood drawing. Tunneled external catheters are preferred in patients who require continuous or frequent device access for treatment, blood drawing, or delivery of supportive therapies (parenteral nutrition, blood product transfusion, pain medication) or who are receiving therapy that would be potentially toxic if extravasated into the subcutaneous tissue. Peripherally placed devices are used mainly in patients who require single, continuous, infusional therapy (systemic antibiotics, hydration, pain medication), as is seen frequently for palliation. **Number of lumens** The choice of the number of lumens should be based on the intensity and complexity of the therapy. **Specially designed catheters** There are specially designed catheters for hemodialysis or apheresis treatment. These catheters are shorter in length and have a lumen that is larger in diameter and is staggered at the tip to prevent recirculation. These catheters have a higher incidence of kinking, and, thus, care should be taken to avoid sharp angles at the skin exit site. In patients who already have an LTVA device in place and require short-term access for apheresis or stem-cell collection, consideration should be given to placing a temporary percutaneous hemodialysis or apheresis catheter rather than replacing the existing LTVA device. **Insertion technique** Placement of LTVA devices is best performed in a surgical suite or an appropriate interventional radiology suite to minimize the incidence of infections. Most procedures are performed on an outpatient basis or immediately prior to a scheduled admission. Local
anesthesia and short-acting barbiturates and sedatives are safe and provide excellent patient comfort and sedation. The use of intraoperative fluoroscopy is strongly recommended to document appropriate device placement and to prevent potential complications. The most common technique used in LTVA device placement is the percutaneous method of Seldinger, using the subclavian or internal jugular vein. Alternatively, a venous cutdown of the cephalic, external jugular, internal jugular, or saphenous vein can provide appropriate access for central venous device placement.

**Placement of tunneled external catheters**

For the percutaneous approach, the patient is placed supine and in the Trendelenburg position. Patients who cannot tolerate the Trendelenburg position frequently can have their device placed through a venous cutdown approach. A rolled sheet placed vertically in the small of the back is preferred by some to rotate the tips of the shoulders posteriorly. The region of the anterior chest, neck, and shoulders is prepared and draped in a sterilized fashion. The skin overlying the anticipated venipuncture site is infiltrated with a local anesthetic. **Vein penetration** The venipuncture needle is carefully and slowly advanced, bevel up, into the vein, while the attached syringe is aspirated (without Luerlock). If the vein is unable to be accessed after multiple attempts with the venipuncture needle, the contralateral side should not be approached during the same session without documenting the absence of complications. **Guidewire placement** Once easy flow of blood into the syringe confirms vein penetration, the bevel is rotated downward, the syringe is disconnected with out allowing introduction of air through the venipuncture needle, and a flexible J guidewire is advanced through the venipuncture needle. Fluoroscopy should be used to confirm the placement of the tip of the guidewire within the right atrium. Atrial arrhythmia may be seen when the guidewire is advanced into the right atrium. If pulsatile blood flow is noted upon introducing the venipuncture needle (indicating an arterial puncture), the venipuncture needle should be withdrawn and local pressure applied for 5-10 minutes (see section on "Complications"). Resistance to the advancement of the guidewire is usually due to misdirection of the guidewire into a secondary vein or migration of the guidewire outside the vein. Fluoroscopy will confirm the guidewire’s position. If the guidewire is suspected to be outside the vein, the venipuncture needle and the guidewire should be removed together, as a unit, to prevent shearing of the guidewire. If the guidewire is suspected to be in the wrong vein tributary, the venipuncture needle can be removed and a 16-gauge angiocatheter can be placed over the guidewire prior to readjusting the position of the guidewire. **Catheter placement** The anticipated skin exit site and subcutaneous tunnel for the external catheter are infiltrated with a local anesthetic. The catheter is then advanced along the subcutaneous tunnel from the anticipated skin exit site to the venipuncture site. The catheter is measured and custom cut to reach the junction between the superior vena cava and right atrium (approximately at the fourth anterior intercostal space). The catheter cuff is positioned midway in the subcutaneous tunnel. The dilator and peel-away introducer sheath are slowly and carefully advanced over the guidewire under fluoroscopy. The guidewire is gently and slightly withdrawn and advanced while the dilator and peel-away introducer sheath are advanced over the guidewire to confirm that they are indeed threading over the guidewire and that the guidewire has not migrated outside the vessel. The dilator and guidewire are then withdrawn from the peel-away introducer sheath. The catheter is then advanced through the peel-away introducer sheath and the tip of the catheter is advanced to the junction of the superior vena cava and right atrium. Difficulties in advancing the catheter through the peel-away introducer sheath usually imply that the peel-away introducer sheath is bent. This occurs most frequently during subclavian vein approach if the venipuncture is attempted too medially and through the costoclavicular ligament. If the catheter cannot be advanced through the peel-away introducer sheath, repeat venipuncture in a more lateral position may be necessary. The catheter should never be handled with sharp instruments. Only nontoothed forceps should be used, if needed. **Confirmation of catheter position** Prior to removal of the peel-away introducer sheath, the catheter position should be confirmed by fluoroscopy. Failure to position the fluoroscopic beam perpendicular to the patient will give a false impression of the catheter's position. At the completion of catheter placement, the entire catheter should be examined with fluoroscopy to confirm its position and to rule out any kinking that would prevent normal functioning. Catheter infusion (looking for impedance to inflow/infusion) and withdrawal (looking for interruption of flow on blood return) should be tested in the surgical suite prior to heparinization of the catheter lumen. A chest x-ray should be obtained in the recovery room to rule out complications and as a record of catheter position. Lastly, ultrasonography may be used during catheter placement to aid in vein localization for venous access and to determine the position of the catheter tip. **Placement of subcutaneous implanted ports**

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Catheter, except for the creation of a subcutaneous port pocket. To prevent wound disruption, the subcutaneous port pocket should permit no tension in the placement of the port. The port is sutured to the muscular fascia to prevent port migration and is placed over the rib cage to provide easy access. **Device care** Subcutaneous implanted ports require flushing with a heparin solution (2-3 mL; 100 U/mL) after each use or monthly during periods of nonuse. During continuous infusion therapy, the noncoring (Huber) access needle should be replaced every third to fifth day. **Tunneled external catheters** require more frequent care. The exit site is cleaned with an antiseptic agent, and an occlusive dressing is applied. This is generally done daily; however, some now advocate only biweekly cleanings and dressing changes. Hickman catheters are generally flushed daily with a heparin solution (2-3 mL; 100 U/mL) or after each use, and protective caps are replaced biweekly. However, some now advocate only biweekly flushing with a heparin solution (2-3 mL; 100 U/mL). Groshong catheters generally only require weekly flushing with 5 mL of a saline solution.

**Complications During device insertion**

Complications during device placement are generally related to the method of insertion and the experience of the operator. **Pneumothorax** is the most common complication of the percutaneous insertion technique, especially via the subclavian vein approach. The incidence of pneumothorax has been reported in most series to be approximately 1%-5%. It appears to be more frequently seen in nutritionally compromised and emaciated patients. Its incidence has also been thought to be related to the number of attempts required to access the vein and to the experience of the operator. Utilization of a venous cutdown approach eliminates the risk of pneumothorax. Pneumothorax is usually recognized on a postoperative upright chest x-ray. The ability to detect a small pneumothorax on chest x-ray can be aided by performing an expiratory film. Delayed pneumothorax can develop several hours to several days after attempted percutaneous device insertion. If the pneumothorax is small (<5%), the patient can be followed with subsequent chest x-rays, and the air occupying the pneumothorax can be left in place to be reabsorbed. Use of 100% oxygen can aid in reabsorption of a pneumothorax. Patients with a larger pneumothorax are generally treated by placement of a chest tube that is connected to a closed suction system or a Heimlich valve (one-way valve). **Iatrogenic arterial puncture** occurs most frequently with the percutaneous internal jugular approach and less frequently with the percutaneous subclavian vein approach. Pulsatile flow confirms an arterial puncture. In this instance, the venipuncture needle should be removed and the vessel compressed for 5-10 minutes. If an arterial puncture is initially unrecognized and the guidewire is passed into the vessel, a position of the guidewire to the left of the thoracic spine on fluoroscopy should alert the operator's suspicions for the occurrence of this complication. In a patient with a persistent left vena cava, the guidewire will also be seen to the left of the spine on fluoroscopy. An intraoperative venogram may help to confirm the diagnosis. **Hemothorax as a result of injury to major vessels** is seen less than 1% of the time. It can be life-threatening, however, when it does occur. During the percutaneous approach, injury to one of the major vessels with the venipuncture needle, guidewire, or dilator and peel-away introducer sheath may result in a hemothorax. Careful attention to insertion technique and use of fluoroscopy will help to prevent this complication. Utilization of a venous cutdown approach is much less likely to injure a major vessel. Most patients who develop a hemothorax can be treated with a large-bore, laterally placed chest tube connected to a closed suction system. Many of these closed suction systems have a blood re-infusion collecting system. Thoracotomy may be indicated in certain circumstances [in patients with ongoing bleeding (>500 mL/hr) or with a massive hemothorax (>1,500 mL)]. **Local hematomas** can occur frequently in thrombocytopenic patients or coagulopathic patients. They are best treated by local compression. Adequate replacement of platelets and clotting factors prior to device placement can help prevent these complications. **Catheter tip malposition** is usually recognized and corrected at the time of catheter placement with the use of intraoperative fluoroscopy. However, catheters situated in the azygos vein or the right internal mammary vein can look strikingly similar to catheters situated in the superior vena cava in an anterior-posterior projection under intraoperative fluoroscopy. Frequently, these catheters do not withdraw blood easily and the catheter tip does not move with the cardiac rhythm. Lateral rotation of the intraoperative fluoroscope and utilization of intraoperative venography can help to differentiate this sometimes subtle finding. **Other device-related complications**

**Catheter compression, fracture, and embolization** can occur when a catheter placed by the percutaneous subclavian approach is inserted too medially along the clavicle at the medial costoclavicular ligament. In such cases, the catheter may become chronically compressed between the clavicle and the first rib. This can be recognized radiographically as a “pinch-off sign.” Chronic compression of the catheter may result in structural fatigue of the catheter wall that may eventually...
cause fracturing and distal embolization of the catheter. This can be prevented by ensuring that the venipuncture site is situated more laterally on the clavicle as well as 1-2 cm below the clavicle. If this problem is recognized during catheter placement, the catheter should be removed and then placed through a different venipuncture site. **Device malfunction** can be divided into two types: (1) inability to withdraw blood from a device and (2) inability to infuse into a device. Inability to withdraw blood from a device, despite retaining the ability to infuse into the device, is most frequently caused by a fibrin sheath at the tip of the catheter that produces a one-way valve effect. Less frequently, it is due to a catheter tip positioned against the side wall of the vein. In patients with this problem, a Valsalva maneuver or repositioning of the patient can sometimes result in a successful blood withdrawal. Inability to both withdraw blood from and infuse into a device can result from many mechanical causes, such as catheter tip malposition, catheter kinking, catheter intraluminal thrombosis, intraluminal precipitation of medications, or venous thrombosis. A simple chest x-ray can identify some of these mechanical causes. Venography and venous duplex Doppler ultrasound imaging are also useful. Thrombolytic therapy, using tissue plasminogen activator (tPA) or alteplase (recombinant tPA), can help to restore the ability to withdraw blood from a device or to clear a device from intraluminal thrombosis or intraluminal precipitation of medications. Usually 1-2 mg of tPA in 1-2 cc of sterile water is instilled into the device, left in place for 1-2 hours, and then aspirated. Alternatively, 2.5-cc aliquots (diluted to 1 mg/mL) of alteplase can be used in a similar fashion. This may be repeated daily for several days until total patency is restored. Likewise, chemical occlusion of a device resulting from precipitation of chemotherapeutic agents, poorly soluble salts (calcium, magnesium, or phosphates), or antibiotics (amikacin [Amikin], vancomycin) can be successfully treated with instillation of 0.2-1.0 mL of 0.1 N hydrochloric acid. The solution is irrigated in and out of the device for 2 minutes, left in place for 1 hour, and then aspirated. This may be repeated daily for several days until total patency is restored. No side effects or metabolic acidosis has been associated with hydrochloric acid at these doses. **External catheter damage** External catheters can be damaged at the site of a catheter clamp or at a suture site. The use of needleless connections for infusions and irrigations should prevent needle damage to external portions of the catheter. Most external catheters have repair kits to replace any damaged external portion of the catheter. **Drug extravasation** into the subcutaneous tissues can occur with subcutaneous implanted ports when there is inappropriate placement or accidental dislodgment of the Huber access needle from the implanted port. This may result in chemical cellulitis, tissue necrosis, and loss of soft tissues in the area of extravasation. Clinical signs of extravasation include pain, burning, soft-tissue swelling, skin erythema, and skin vesicle formation at the infusion site. If drug extravasation is suspected, the infusion should be stopped and the Huber access needle should be immediately withdrawn. Management depends on the type of drug infused and the amount of drug extravasated. **Venous thrombosis** occurs more commonly than believed. The incidence of venous thrombosis varies in multiple studies, ranging from 0% to 65%. The incidence of venous thrombosis is higher in patients in whom the catheter tip is placed in the innominate vein or proximal superior vena cava as compared with the distal superior vena cava/right atrial junction. Ideally, the catheter tip should be positioned at the superior vena cava/right atrial junction and should be free floating. The incidence of venous thrombosis is higher in patients with multiple-lumen catheters than in those with single-lumen catheters. The incidence of venous thrombosis is higher in patients in whom the device was placed percutaneously than in those who underwent a venous cutdown approach. Preexisting hypercoagulable states predispose patients to the development of venous thrombosis. Ipsilateral arm swelling, pain, and development of collateral veins in the skin overlying the chest wall should alert the clinician to the possibility of venous thrombosis. Venography, venous duplex Doppler ultrasound imaging, and CT/ MRI scan can establish the diagnosis and the site of the obstruction. Proplyaxis In one prospective randomized study, cancer patients without abnormal clotting parameters were randomized to receive either 1 mg/day of warfarin or placebo for 90 days following insertion of a central venous access device. Venous thrombosis (documented by superior vena cava venograms) occurred in 37.5% of the placebo group (n = 40) as compared with 9.5% of the treatment group (n = 42). There was no prolongation of coagulation parameters in the treatment group. However, a recent study showed a high incidence of INR (international normalized ratio) abnormalities in patients receiving fluorouracil-based chemotherapy regimens who were maintained on 1 mg/day of warfarin. They recommended that such patients should have periodic monitoring of the prothrombin time and INR. In another prospective randomized study, cancer patients were randomized to receive either 2,500 IU/day of subcutaneous low-molecular-weight heparin (Fragmin) or no antithrombotic prophylaxis for 90 days following insertion of a catheter. Venous thrombosis (documented by superior vena cava venograms) occurred in 62% of the no antithrombotic
prophylaxis group (n = 13) as compared with 6% of the anticoagulation group (n = 16). Treatment should be directed toward prevention of pulmonary embolism, avoidance of clot propagation, prevention of the postphlebitic syndrome, and preservation of the LTVA device, if possible. With these objectives in mind, the LTVA device should be removed only if it is no longer necessary or if initial therapy for venous thrombosis fails. The patient can be initially treated with systemic heparinization or subcutaneous low-molecular-weight heparin followed by conversion to oral anticoagulation with warfarin. The LTVA device may be kept in place as long as the patient is asymptomatic and there is no contraindication to anticoagulation. Anticoagulant therapy should be continued for at least 3 months.

Device-related infections
Device-related infections can be divided into device-related bacteremia and site infections. Site infections consist of subcutaneous catheter tunnel infections and subcutaneous port pocket infections. In general, device-related infections are thought to be greater for tunneled external catheters than subcutaneous implanted ports and greater for multilumen catheters than single-lumen catheters. However, considerable controversy on this topic exists in the literature, since various studies examining device-related infection rates differ significantly with respect to patient characteristics, device maintenance schedules, and diagnostic criteria for defining a device-related infection. Differing device-use patterns and patient medical illness acuity are thought to explain the difference in device-related infection rates between tunneled external catheters and subcutaneous implanted ports and between multiple-lumen catheters and single-lumen catheters. It is controversial whether utilization of perioperative antibiotics for LTVA device placement decreases the incidence of device-related infections. Some studies have evaluated the addition of antibiotics (such as vancomycin) to the standard heparin-flush solution administered through LTVA devices to prevent device-related infections. Such results should be viewed with caution, however, in light of the increased incidence of vancomycin-resistant organisms in the hospital inpatient population.

Device-related bacteremia
Device-related bacteremia is a potentially life-threatening complication, especially in the immunocompromised patient. The infection generally is caused by gram-positive cocci (coagulase-negative staphylococci) or enteric gram-negative bacilli (*Enterobacteriaceae*, *Escherichia coli*, and *Pseudomonas* species). Less frequently, device-related bacteremia is caused by fungi (*Candida* species). The incidence of fungal infection is significantly higher in immunocompromised patients. Criteria for diagnosis of device-related bacteremia vary among institutions. Some institutions utilize quantitative analysis of blood culture results, whereas others utilize qualitative analysis of blood culture results. Quantitative analysis involves comparing the number of colony-forming units seen in blood drawn through the device to blood drawn through the periphery. Usually, a 5- to 10-fold increase in the number of colony-forming units from blood drawn from the device as compared with concomitant peripheral cultures (or in the absence of positive peripheral cultures, > 1,000 colony-forming units from blood drawn from the device) signifies device-related bacteremia. Qualitative analysis involves comparing positivity and negativity of blood cultures drawn from both the device and the periphery. Usually, simultaneous positive blood cultures drawn from both the device and the periphery, along with clinical relevance, signifies device-related bacteremia. Management If device-related bacteremia is suspected, appropriate systemic antibiotic coverage should be instituted after device and peripheral blood cultures are obtained. Antibiotic selection should be reassessed after organism identification and antibiotic sensitivities are available. Up to 70% of cases of device-related bacteremia can be successfully treated with a course of appropriate systemic antibiotics. The indications for device removal are the persistence of positive blood cultures after an appropriate course of systemic antibiotics, hypotension or severe systemic compromise, infections caused by *Candida* species, or recurrent infections caused by the same organism after successful systemic antibiotic therapy.

Site infections
Site infections consist of subcutaneous catheter tunnel infections and subcutaneous port pocket infections. They can be superficial or deep. These infections are usually caused by gram-positive cocci (coagulase-negative staphylococci). Swelling, tenderness, and warmth over the site usually indicate a site infection. In the neutropenic patient, fever is often the only symptom. Swab culture of the skin exit site of the external catheter or the skin around the Huber access needle overlying the implanted port can sometimes identify the offending organism. Management Local care at the skin exit site of the tunneled external catheter or removal of the Huber access needle from the subcutaneous implanted port and systemic antibiotics can be effective for most superficial site infections. Deep-seated subcutaneous catheter tunnel infections and subcutaneous port pocket infections may require device removal for successful eradication of the infection. Site infections caused by *Candida* species usually require device removal.
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