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New Technology Applications

Thrombolysis of Acute Deep Vein Thrombosis

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Treatment of deep vein thrombosis traditionally has focused on preventing the potentially life-threatening complication of pulmonary embolism rather than on removing or reducing the thrombus. Although treatment with anticoagulants may prevent thrombus propagation, the body's intrinsic thrombolytic system is left to attempt clot dissolution. Because this natural process is generally ineffective in its ability to fully recanalize a proximal vein, the risks of recurrent thrombosis as well as the disabling complication of postthrombotic syndrome increase. Moreover, the long-term consequences of postthrombotic syndrome include pain, disability, and, for many, a significant decrease in the quality of life. Recent technology using high-frequency, low-power ultrasound, or mechanical thrombectomy with catheter-directed delivery of a thrombolytic drug directly into the clot is available and showing promise. Nurses are caring for patients who receive endovascular interventions with lytic infusions. The nursing challenge is to provide safe and effective patient care.
Key words: *catheter-directed*, *deep vein thrombosis*, *low-power ultrasound*, *lytic care*, *thrombectomy*, *thrombolysis*

ALTHOUGH the exact incidence of deep vein thrombosis (DVT) is unknown, published figures estimate the annual incidence to be as high as 2 million people in the United States alone.[1] Caucasians and African Americans have a significantly higher incidence than do Hispanic persons and Asian Pacific Islanders.[2] Moreover, the incidence of DVT in high-risk patients, including those sustaining a traumatic injury and orthopedic surgery, patients with cancer, or hospitalized patients on bed rest, is significant. Massive pulmonary embolism (PE) is the major sequela of DVT, resulting in as many as 100,000 deaths in the United States each year, with significant long-term morbidity from recurrent thrombosis and postthrombotic syndrome.[3] Pulmonary embolism is the leading cause of preventable in-hospital mortality.[4]

Although life-threatening complications necessitate the need to prevent DVT and/or effectively treat the problem, more recent attention is focusing on long-term outcomes. As much as 50% of veins show residual disease after acute DVT, and these chronic venous changes affect the valvular system, resulting in venous hypertension.[4] Better known as postthrombotic syndrome, this complication is associated with limb edema, pain, skin hyperpigmentation, muscle fatigue, and chronic venous stasis ulcers. These conditions can occur from months to years following acute DVT and adversely affect quality of life through immobility and long-term disability.[5] Phlegmasia cerulea dolens, a complication associated with severe venous engorgement and obstruction, poses the risk of arterial insufficiency with ischemia and eventual gangrene.[6]

Traditionally, the treatment of DVT has focused on preventing the acute complication of pulmonary emboli through anticoagulation

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rather than removing or reducing the thrombus. A more recent therapeutic intervention using systemic intravenous thrombolytics drugs was superior to anticoagulation, but bleeding complications limited its wider use. Coupled with interventional radiological percutaneous catheter placement, clot-directed delivery of thrombolytic agents has dramatically affected the care of individuals with DVT. Nurses are confronted with caring for patients who receive endovascular interventions with catheter-directed drug infusion therapy. The nursing challenge is to provide safe, effective care with vigilance for complications of therapy.

PATHOPHYSIOLOGY—VIRCHOW'S TRIAD

In 1856, Rudolf Virchow, a Prussian-born physician, described the relationship between thrombosis and emboli. He is credited with identifying 3 factors predisposing patients to vascular thrombosis. Better known today as Virchow's Triad, these factors include changes or damage to a vessel wall, such as inflammation or trauma; changes in the volume or pattern of blood flow that would occur with immobility, dehydration, shock, or heart failure; and changes in the constituents of blood or hypercoagulability. Risk factors for DVT are given in Table 1.

Table 1. Risk factors for DVT

Vessel wall factors
Inflammation
Vasculitis including secondary to systemic disorders such lupus erythematosis
Surgery
Trauma
Bone fracture
Intravenous access devices
Circulating factors (Stasis)
Bed rest
Immobilization
Long plane or car trips
Increased age
Obesity
Pregnancy
Varicose veins
Dehydration
Heart failure
Hypercoagulability
Drugs including estrogens and estrogen receptor modulators
Malignancy
Inherited thrombophilic disorders: deficiencies of Protein C or Protein S, Protein C resistance, prothrombin variant 20210A, elevation on coagulation factors VIII and XI
Acquired thrombophilia

While these predisposing factors contribute to the development of venous thrombosis, so also is the body's natural balance between thrombogenesis and thrombolysis. According to Weiner,[7] any disruption in the interrelationship between these 2 processes can result in life-threatening intravascular thrombus formation or bleeding. Plasmin, the protein responsible for clot lysis, is the primary component of the fibrinolytic system. As a proteolytic enzyme, plasmin is found in the general circulation as an inert precursor known as plasminogen. Plasminogen is also found in the body bound to fibrin in a thrombus. Endogenously, tissue plasminogen activator released by vascular endothelium converts fibrin-bound plasminogen to active plasmin within a thrombus. Moreover, the administration of exogenous forms of plasminogen activators can form plasmin for the purpose of digesting thrombi. Drugs such as streptokinase (Streptase) and urokinase (Abbokinase) combine with plasminogen to systemically activate plasmin for fibrinolysis. Newer generation, more specific tissue plasminogen activators (*t*-PA) such as alteplase (rt-PA; Activase) were designed to preferentially activate fibrin-bound plasminogen at the site of a thrombus, theoretically avoiding systemic activation and increased bleeding.

THE DIAGNOSIS OF DVT

A detailed history and physical examination can facilitate the clinical diagnosis of DVT. In

many cases, however, incomplete venous obstruction renders an individual asymptomatic. An acute PE accompanied by dyspnea, tachypnea, hypoxia, and apprehension may be the first and only manifestation.

Acute DVT often is anatomically organized into calf vein thrombosis, known as infrapopliteal, and those involving the popliteal vein and above, referred to as proximal DVT. Individuals presenting with proximal occlusions may have large, formed thrombi in the veins of the lower extremities, including the caval, iliofemoral, and femoral-popliteal vessels. These large and extensive thrombi are not amenable to breakdown by the body's intrinsic fibrinolytic system. In addition to creating a higher risk of pulmonary emboli, proximal DVT may be associated with unilateral swelling, pain, and tenderness of the affected extremity, although swelling alone may be the only presenting manifestation.[8] Less commonly, a positive Homans' sign, which is discomfort in the calf muscles on forced dorsiflexion of the foot, occurs. However, the Homans' sign is an unreliable and nonspecific indicator of DVT, since this finding is often found in other conditions such as cellulitis and venous insufficiency.[9] The later and more disabling manifestations of postthrombotic syndrome, including persistent pain, limb edema, and venous stasis ulcers, often accompany poorly resolved proximal venous thrombi.

Given the difficulty in diagnosing DVT solely on the basis of the initial clinical presentation, providers must rely on diagnostic and laboratory testing as well as tools that stratify patients into risk categories. Anand et al[10] report on a clinical prediction guide known as the *Well's Model of the Clinical Pretest Probability of DVT*. Their tool includes a scoring component for stratifying patients with suspected DVT into low, moderate, or high pretest probability categories, which simplifies management for patients with suspected DVT. The scoring guide uses specific combinations of risk factors, symptoms, and physical signs in combination with the results of noninvasive diagnostic test results to guide further diagnostic testing and treatment.[10]

Imaging studies have been evaluated for their specificity and sensitivity in the diagnosis of DVT. Although venography with contrast was once the standard for DVT diagnosis, allergic reactions, contrast-induced complications, and technical disadvantages have limited its clinical usefulness.[11] Noninvasive alternatives include ultrasonography, impedance plethysmography, and magnetic resonance imaging (MRI).

The venous Doppler ultrasound extremity study, also known as venous duplex ultrasound, is a noninvasive diagnostic test widely used today because of its low risk and diagnostic sensitivity and specificity. The procedure involves the recording of sound waves via a transducer to obtain information about the patency of the venous vasculature in the upper or lower extremities. Blood flow direction and velocity can be assessed in real time, and the presence of blood flow obstructions identified. Doppler compression ultrasound is combined with the Doppler flow assessment. A transducer facilitates the detection of thrombus via compression of a vein. Noncompressibility is the major determinant for venous thrombosis.[12] Major advantages of this procedure include safety, accessibility, and low cost as well as the absence of ionizing radiation or contrast material. Similarly, impedance plethysmography is a noninvasive diagnostic test used in the diagnosis of acute DVT. This procedure provides an indirect assessment of blood volume changes by measurement of its electrical impedance. The technique involves using a series of cuff inflation and deflation measurements to estimate venous capacitance and outflow. While disadvantages to ultrasonography and impedance plethysmography include difficulty identifying calf vein thrombi and nonobstructing thrombi, ultrasonography is more accurate when the two are compared.[9] National guidelines recommend that patients with moderate to high clinical pretest probability of DVT receive a duplex ultrasound with compression as the first test to diagnose DVT.[13]

Magnetic resonance imaging uses magnetic fields and radio waves to produce multidimensional images of bones and organs as well as blood vessels. When vessels are involved, this scanning method is referred to as magnetic resonance angiography or venography and has the ability to show thrombi as filling defects. Similar to other MRI procedures, careful screening of patients prior to the scan is necessary for any implanted devices such as pacemakers, ear implants, intrauterine devices, or artificial heart valves as well as internal metal, including combat shrapnel. If contrast medium is planned, an allergy history is imperative, as is an assessment of renal function. During the procedure, the patient must be able to lie still in a confined space, and all external metallic objects must be removed before the patient enters the scanning room. Although noninvasive, this procedure is costly. As technology improves and wider accessibility to the equipment is established, MRI may play a greater role in the evaluation of venous thromboembolic disease.[14] Additional new techniques using magnetic resonance direct thrombus imaging (MRDTI) are on the horizon for detecting both DVT and PE.[12] Unlike current technology, which captures filling defects, MRDTI directly visualizes acute thrombi and demonstrates a high degree of accuracy for diagnosing DVT.[15]

Laboratory evaluation of venous thromboembolism is an adjunct as a diagnostic marker for DVT.[12] D-dimer plasma assays have been well studied for their usefulness in hypercoagulability disorders and are currently incorporated into national guidelines and the clinical algorithm for patients with suspected DVT. A positive D-dimer indicates the presence of abnormally high levels of fibrin degradation products. This commonly occurs in disease processes accompanied by significant thrombus formation such as sepsis, disseminated intravascular coagulation, and PE. Research by Curtin et al[16] supports the D-dimer assay as an initial test in combination with a pretest probability assessment. According to national guidelines, a negative D-dimer in patients with low clinical pretest probability of DVT may have the diagnosis of DVT excluded and no further testing is required.[13] Although the D-dimer testing requires a blood sample, there are different assays available with varying sensitivities and specificities.

GOALS OF DVT THERAPY---A FOCUS ON POSTTHROMBOTIC SYNDROME

The primary goals of DVT management focus on the relief of acute symptoms with the restoration of venous flow, the prevention of thrombus propagation, and the prevention of embolization or recurrence. An equally critical goal that focuses on the preservation of valve function to curtail the future development of venous insufficiency and postthrombotic syndrome is gaining increasing attention.[17] According to Eclavea and Patel,[18] venous thrombi that are not dissolved by the body's intrinsic fibrinolytic system are invaded by connective tissue cells, which are incorporated into the vein wall, forming scar tissue that may damage or destroy vein valves. This outcome is the primary contributor to postthrombotic syndrome. Kahn and Ginsberg[19] report that approximately 20% to 50% of patients with DVT develop postthrombotic syndrome with severe disease including venous stasis ulcers occurring in up to 10% of cases. Yet, to date, most research surrounding DVT management centers on thrombus recurrence and bleeding. A paucity of evidence exists regarding the clinical endpoint of postthrombotic syndrome.[20] The most relevant factor in the development of postthrombotic syndrome is valvular incompetence, which results in venous reflux.[20] Moreover, outflow obstruction caused by incomplete recanalization results in additional chronic venous hypertension and edema.[18] Valve incompetence occurs not only as a consequence of acute DVT but is also determined by the rate of recanalization and recurrent thrombotic events.[20] These findings play a vital role in providing effective treatment of DVT. Maintaining valve integrity and rapidly removing venous obstruction may decrease the incidence of postthrombotic syndrome.[20,21]

CONVENTIONAL TREATMENT STRATEGIES—ANTICOAGULATION AND FILTERS

Established therapy for acute DVT focuses on anticoagulation, which is delineated in national guidelines and standards of care. Initially unfractionated heparin administered intravenously was the drug of choice, but the need for prolonged hospitalization and frequent laboratory monitoring of clotting times led to more common treatment with subcutaneous low-molecular-weight heparins (LMWH).[22] According to national guidelines, the use of LMWH is the preferred heparin for initial anticoagulation in most patients with DVT.[13] Both enoxaparin and tinzaparin are federal Food and Drug Administration– (FDA) approved drugs for venous thromboembolism treatment. Heparin, however, does not pharmacodynamically act on existing thrombi. Rather, its action is to combine with antithrombin III to inhibit new thrombus formation and propagation by inactivating activated factor X and inhibiting the conversion of prothrombin to thrombin. In addition to heparin, oral anticoagulation with warfarin is initiated after 24 to 48 hours, and the dose titrated to maintain a target international normalized ratio (INR) of 2.5.[11] Although the pharmacodynamics of coumarin anticoagulants differs from that of heparin by inhibiting vitamin K–dependent coagulation factors, warfarin works similarly to suppress new clot formation and propagation. National guidelines specify that heparin should be given for at least 4 to 5 days, and until the INR is 2.0 or higher for 2 consecutive days.[11,13] In addition, current guidelines recommend continuing warfarin for 3 months if the DVT is caused by a transient risk factor such as surgery or estrogen use. For idiopathic or medical risk factors, anticoagulation should continue for 6 to 12 months. In some patients with thrombophilic disorders, indefinite anticoagulation is warranted. While anticoagulation therapy does fulfill some of the goals of DVT therapy, including a decrease in thrombosis recurrence rate, it does not promote lysis to reduce thrombus burden, nor does it restore valve function.[23]

Since 1967, filters have emerged in the management of DVT when partial interruption of the inferior vena cava (IVC) flow is indicated to prevent the occurrence of PE. Filters are indicated when anticoagulation is contraindicated, such as in major or multiple trauma. Filters also are indicated when a complication of anticoagulation arises, such as hemorrhage or heparin-induced thrombocytopenia, when failure of anticoagulation arises, and with free-floating iliofemoral or caval thrombi.[24] Currently, many IVC filters are FDA approved for use. Newer retrievable filters are also available, thus avoiding the known long-term complications of permanent filters and IVC occlusion. Although this intervention allays the life-threatening complication of PE, vena caval filters do not solve the problem of recurrent thrombosis nor prevent the long-term complication of PTS.

OTHER APPROACHES TO DVT MANAGEMENT—THROMBOABLATION

Systemic thrombolytic infusion

Other strategies in DVT management focus on restoring venous patency and valve preservation. Unlike anticoagulants, thrombolytic drugs classified as plasminogen activators convert plasminogen into the active protease plasmin. Activated plasmin cleaves fibrin. Eclavea and Patel explain, "Plasmin functions to disrupt the proteinacious fibrin cross-linked strands that provide the framework for platelet and red blood cell aggregation in a thrombus."[18(p64)] As compared with standard anticoagulation therapy, thrombolysis restores venous patency and valve function, and thus reduces the potential for future postthrombotic syndrome.[23]

Thrombolytic therapy first became available in 1978 with the commercial production of urokinase. Since then, cell culture techniques and recombinant DNA technology have enabled the development of many other agents that are used in the treatment

of thromboembolic occlusive disorders, including acute coronary syndrome, PE, stroke, and acute peripheral arterial occlusions. The thrombolytic drugs currently available vary in their fibrin specificity, antigenity, and plasma pharmacokinetics.[25] Newer generation drugs such as alteplase (Activase) and reteplase (Retavase) have a high fibrin specificity promoting the activation of plasminogen to plasmin that is localized to the fibrin clot.[26] While theoretically these agents were expected to significantly reduce bleeding potential, data from clinical trials did not universally support this outcome.[5,27]

When thrombolytics therapy for acute PE emerged in the 1990s, the use of systemic thrombolytics agents for DVT became possible.[28] A clinical review by Comerota and Aldridge[29] comparing systemic anticoagulation therapy with systemic thrombolytic therapy demonstrated improved clot resolution in patients with DVT who received lytic infusion therapy. Although few studies evaluated the long-term results of either therapy, patients who sustained successful clot lysis with lytic therapy demonstrated a reduction in postthrombotic symptoms with a significant functional benefit.[29] However, the risk of life-threatening severe bleeding complications, including intracranial bleeding and pulmonary emboli, limited the applicability of systemic therapy.[30]

Catheter-directed thrombolysis

The requisite for efficient clot-directed delivery of thrombolytic agents with less bleeding complications and the rapid development of catheter-based technology led to catheter-directed thrombolysis as a strategy for the treatment of DVT.[4] An interventional radiologist performs the procedure by gaining wire access to the thrombus via a percutaneous puncture and positions a multiholed catheter throughout the thrombus length to slowly infuse a thrombolytic agent.[4] Utilizing this technology, there is a reduction in the overall dose and duration of the lytic infusion.

A National Multicenter Registry was formed to evaluate catheter-directed thrombolysis for the treatment of symptomatic lower extremity DVT.[31] This prospective study involved 63 centers that submitted detailed case reports to a data-collection center. Results of the study indicated that catheter-directed thrombolysis was a safe and effective treatment for selected groups of patients. Most patients who were treated had acute DVT and thromboses involving the iliofemoral or femoral-popliteal vessels. Fortunately, significant complications were infrequent. Two deaths were reported, representing less than 1% of the study population, and included deaths from PE and intracranial hemorrhage.[31] Results from the National Venous Registry set the stage for the critical investigation of quality-of-life outcomes following catheter-directed thrombolysis. Patients who received catheter-directed urokinase reported better physical functioning, less health distress, and fewer postthrombotic symptoms than patients treated with anticoagulation alone.[32] Similarly, a prospective randomized multicenter trial, the Thrombolysis of Lower Extremity Deep Vein Thrombosis or Oral Anticoagulation trial, has as one of its outcomes to provide ongoing data supporting that early clot lysis is associated with significantly improved quality of life at 1 year.[4]

Although most early studies, including the National Multicenter Venous Registry, utilize urokinase, later studies compare future generation recombinant agents, including alteplase (rt-PA; Activase) and reteplase (Retavase), for catheter-directed delivery. This research supports that catheter-directed thrombolysis is safe and effective, regardless of the agent.[33] National guidelines from ICSI[13] support catheter-directed lytic therapy over systemic lytic therapy in patients with extensive iliofemoral disease who demonstrate vascular compromise. Currently, the National Institutes of Health (NIH) Clinical Center is recruiting patients to test the effectiveness of low-dose alteplase (rt-PA; Activase) in dissolving blood clots in deep leg veins.[34]

Thrombectomy

In addition to pharmacologic thrombolysis, mechanical interventions serve as old and

new treatment strategies. An open surgical thrombectomy is an uncommonly performed surgical procedure to remove a venous clot. It is performed through an incision and is generally reserved for patients who are refractory to other treatments or when thrombolytic therapy is contraindicated.[3] Besides the associated operative mortality risk, surgical thrombectomy has been associated with early rethrombosis rates and recurrent DVT.[18] The ICSI[13] indicates that a surgical thrombectomy should be considered only as a last option in those patients with extensive venous thrombosis who have contraindications to anticoagulation and lytic therapy.

Percutaneous mechanical thrombectomy (PMT), coupled with the introduction of motorized thrombectomy devices, generally has replaced the open surgical approach. This technology was designed primarily to eliminate the bleeding risks associated with catheter-directed thrombolysis. As an endovascular technique, PMT employs rotational or hydrodynamic (rheolytic) mechanisms to fragment and aspirate thrombi, thus reducing thrombus burden. Some available rotational devices that are available include the Amplatz mechanical thrombectomy device, Microvena; Trerotola percutaneous thrombolytic device, Arrow International; the Bacchus Fino device, Bacchus Vascular; and the Cragg thrombolytic brush, Microtherapertics. Hydrodynamic devices create high-speed saline jets that fragment the thrombus, thus allowing them to be aspirated.[3] Several devices that employ the rheolytic mechanism are the Oasis thrombectomy system, Boston Scientific/Meditech Corp; AngioJet, Possis Medical Inc; and the Hydrolyzer, Cordis.

PMT catheters often utilize mechanical clot removal in conjunction with thrombolytic drug infusions for more complete and rapid thrombus removal. Intraclot pulse spray-directed lytic (rt-PA) treatment also is being studied for its use in extensive venous thrombosis. A pilot study sponsored by the NIH Clinical Center is designed to evaluate the efficiency and safety of this treatment.[35] Advantages of the combination approach include lower lytic doses and infusion time, resulting in fewer hemorrhagic complications and cost savings. Major risks of PMT with lytic infusion include bleeding as well as potentially significant complications of PE from clot fragmentation and endothelial vessel damage resulting from mechanical injury.[36] Research evaluating the outcomes of PMT for DVT is limited, with no controlled trials comparing PMT with conventional therapy.

Ultrasound-facilitated thrombolysis

The use of ultrasound energy also is being harnessed for the dissolution of thrombotic occlusions. Ultrasound-enhanced systemic thrombolysis was effective in treating patients with acute ischemic stroke.[37] When combined simultaneously with a catheter-directed thrombolytic infusion, ultrasound technology is accelerating clot dissolution in the peripheral vasculature as well.

Although the mechanism responsible for its effect on thrombus dissolution is not completely known, one theory postulates that ultrasound energy may create a loosening in the fibrin mesh, thus facilitating the permeation of *t*-PA directly into the thrombus.[38] In addition, the more porous fibrin mesh provides a greater surface area upon which the lytic drug may work.[21] In an effect known as acoustic microstreaming, blood that is close to the occluding thrombus is agitated by the ultrasound waves to promote the effective mixing of the thrombolytic drug while effectively increasing the drug concentration that is in contact with the thrombus.[38] In addition to the loosening effect on the fibrin mesh, heat generated by the ultrasound also may be responsible for accelerating thrombolysis. Research supports that ultrasound-generated temperature elevation can increase the dissolution rate of thrombi.[38]

Advantages of ultrasound-facilitated thrombolysis in the management of DVT are reduced procedural time and the use of lower doses of lytic drugs, thus decreasing the potential for bleeding complications.[21] These factors favor this technology as an important

consideration when evaluating patients. EKOS Corporation manufactures the Lysus Infusion System drug delivery catheters that simultaneously deliver a thrombolytic drug and high-frequency, low-energy ultrasound into the clot. As endovascular techniques and catheter-directed thrombolysis continue to emerge as viable treatment strategies in selected patients with proximal DVT, nurses are challenged to provide safe and effective care.

NURSING CARE

Admission

There is a paucity of information surrounding the care of patients who receive endovascular procedures with combined thrombolytic infusions.[39,40] At the time of admission there must be a careful assessment of symptoms coupled with a risk factor evaluation to determine any identifiable cause. Virchow's triad, which focuses on the 3 mechanisms contributing to the development of acute DVT, provides a critical starting point in patient assessment. Although vessel wall injury, stasis of blood, and abnormal clotting individually may be the culprits, these mechanisms often interact with each other. In addition to assessing factors related to DVT, the nurse should question the patient about a medical or surgical history that would prohibit the use of a thrombolytic drug. Contraindications to lytic infusions may include a history of intracranial hemorrhage, known bleeding diathesis, recent major surgery or trauma, and active internal bleeding.[41]

For the newly admitted patient, baseline laboratory tests generally include a complete blood cell count (CBC), D-dimer, and coagulation studies in addition to a basic metabolic panel, which includes a vital assessment of renal function. In the setting of recurrent or unprovoked thrombosis, thrombosis occurring at an age less than 50 years, or idiopathic thrombosis, a hematology consultation as well as additional comprehensive thrombophilic screening tests may be warranted to identify inherited or acquired prothrombic abnormalities.[42] The nurse can anticipate a venous Doppler ultrasound with compression as the initial diagnostic procedure. For the patient with a significant proximal DVT involving the iliofemoral or deep femoral vein who will be treated with an interventional radiological procedure, the nurse also must anticipate and prepare the patient for venography. This necessitates a careful assessment for contrast allergy as well as renal function. When indicated in at-risk patients, prophylaxis strategies for contrast-induced nephropathy may ensue on the basis of hospital or physician protocols. Low-osmolar or iso-osmolar contrast media should be used.[43] Current evidence also supports periprocedural hydration with intravenous 0.9% isotonic saline or an isotonic sodium bicarbonate solution.[43] Although there is limited evidence that drugs are efficacious in the prevention of contrast-induced nephropathy, *N*-acetylcysteine or asorbic acid may serve as some renal protective strategies.[44]

On admission, the patient having an endovascular procedure with lytic therapy should have 2 peripheral intravenous catheters for medication administration. In some institutions, the antecubital vein is accessed, thus allowing blood draws for laboratory testing. Most patients also will have a foley catheter inserted to carefully monitor intake and output, postprocedure hemoglobinuria, and to facilitate the strict mobility restrictions once the endovascular lines are placed. Informed consent must be obtained by the interventional radiologist. On the basis of recommendations from the American Society of Anesthesiologists, the patient should have a 2-hour fast for clear liquids and a 6-hour fast for food prior to the scheduled procedure. Moreover, the patient will require education on what to expect both in the radiological suite and on the lytic unit. Teaching should include activity restrictions; an explanation of the monitoring procedures, including frequent vital signs; measures to control pain; and information on the expected course of therapy.

Interventional radiology

The registered nurse working in the interventional radiology (IR) department has a formidable role in caring for the patient who receives an endovascular procedure. Often the first person to greet the patient upon arrival in the department, the nurse has a primary role to ensure the patient's safety and comfort. Establishing a rapport that enables open communication and a calming environment attenuates the potentially frightening experience. Procedural sedation and analgesia generally are employed and include an opioid and benzodiazepine. Commonly used intravenous drugs are fentanyl and midazolam in doses sufficient to relax the patient and provide comfort while preserving spontaneous respiration and airway-protective reflexes. The nurse utilizes cardiac and pulse-oximetry monitoring with frequent documentation of the patient's status and vital signs from the time of arrival until all sedation has resolved and the patient has resumed his or her baseline status.[45] If available, capnometry can provide additional information regarding the early identification of hypoventilation during procedural sedation and analgesia.[46]

In most instances, the popliteal vein on the affected side is accessed, which requires assisting the patient into the prone position. After the site is appropriately prepped, the interventional radiologist begins the procedure by anesthetizing the site with a local anesthetic followed by using an introducer kit to access the vein. A contrast media then is injected via the popliteal vein to visualize the acute thrombosis. Based on the location and extent of the occlusion, a temporary, retrievable IVC filter may be required initially to prevent the life-threatening complication of pulmonary emboli. The interventional radiologist next places a #5 French multiside hole catheter over a standard guidewire into the thrombus. The length of the catheter varies depending on the extent of the occlusion, and digital images under fluoroscopy facilitate ideal catheter placement.

When correctly positioned, a continuous lytic infusion is initiated using an infusion pump. While the specific thrombolytic drug is based on institutional and physician preference, the lytic preparation, dosing, and administration should be guided by the manufacturer's recommendations as well as agency policy and procedure. Low-dose heparin is infused via a separate line through the side port of the introducer to maintain catheter patency. In addition, periprocedural anticoagulation with systemic heparin at a rate to maintain a therapeutic PTT is started via an upper extremity saline lock.

When ultrasound is utilized to facilitate catheter-directed thrombolysis, the system is initiated in the IR department. The control unit manufactured by EKOS supplies the electrical energy needed for ultrasound generation by a specifically manufactured catheter. Ultrasound output and temperature of both the catheter and control unit are monitored to ensure that the device functions within safe, preset parameters. The ultrasound machine is self-contained, and there are no user settings on the control unit or catheter. Because heat is generated with ultrasound, this technology requires a normal saline solution to be delivered via a "coolant" lumen of the catheter at a prescribed rate.

After the procedure, the IR nurse provides a detailed report to the registered nurse on the receiving unit. The patient also is informed that he or she can expect to return to the radiology department the following day for reevaluation of the thrombosis. The nurse then transports the patient to intensive care unit (ICU) or the lytic infusion care unit of the hospital. Patients receiving thrombolytics for peripheral occlusion must have a registered nurse and/or physician present at all times, including during transportation.

Intensive care/lytic unit

Policy and procedure should be the first steps to guide safe, effective care for a patient receiving a lytic infusion and an endovascular

intervention. Since the primary complications related to the procedure are hemorrhage and PE, the standard of care includes specific assessment requirements. The infusion site is checked every 15 minutes during therapy for bleeding or hematoma. Vital signs are checked every hour and include the patient's level of orientation to assess for signs of potential intracranial hemorrhaging. Continuous pulse oximetry is required, as is close monitoring for breathing changes, given that PE is a life-threatening complication of fibrinolysis. When a thrombolytic infusion is utilized, neurovascular checks are conducted hourly. The nurse also performs guaiac testing of urine and stool, and any intramuscular or subcutaneous injections are contraindicated for the duration of therapy and for 12 hours after the discontinuation of lytic therapy. The admitting surgeon and radiologist should be contacted in case of any significant change in baseline vital signs and/or respiratory or neurological status or with any signs of active bleeding or evidence of decreased perfusion. With the potential antigenity of some lytics, adverse reactions, such as fever, nausea, vomiting, or chills, also must be reported.

Pain is an important factor to consider in all patients with vascular disease. A compromise in perfusion to an extremity can cause "a recurring cycle known as ischemia-reperfusion syndrome, which is characterized by the generation of oxygen radicals, damage to vascular endothelium, activation of platelets, microvascular occlusion, and cellular damage."[47(p599)] The additional pathophysiologic processes specifically associated with venous occlusion include venous hypertension with subsequent edema and the compression of tissue in closed compartments.[47] These factors are major contributors of pain. The nurse should conduct a pain assessment at least every 4 hours and following the administration of any analgesic medication. Physician orders for pain management may include intermittent intravenous bolus injections of morphine, fentanyl, or hydromorphone, or these opioids may be administered as patient-controlled analgesia.[48] In either case, the nurse must carefully assess the adequacy of the prescribed medication regimen.

Besides pain management, positioning is critical for a patient receiving catheter-directed thrombolysis. To prevent bleeding or hematoma, strict bed rest is required with limited leg mobility. With groin access, the head of the bed should remain at less than 30°. When the patient has a popliteal access device, the knee must remain straight. Log rolling best facilitates turning for patients with vascular catheters and lytic infusions.

The nurse can expect postprocedure intravenous hydration in addition to laboratory follow-up of the creatinine level. Because full anticoagulation with systemic heparin is employed, PTT levels are routinely checked. Some physicians also routinely order follow-up CBC and DIC screens. Generally, the patient is maintained on clear liquids for the duration of therapy in the event that there is an emergent need for surgery or anesthesia.

The psychosocial aspects of the vascular patient in the ICU or lytic infusion unit cannot be underscored. The environment and equipment are unfamiliar to the patient, and alarms sounding can cause apprehension. In addition, pain and the required mobility restrictions can increase the patient's level of distress exponentially. The nurse plays a substantial role in providing comfort and decreasing anxiety. Generally with catheter-directed thrombolysis, the expected ICU length of stay and lytic infusion time may be as long as 72 hours. A benefit of newer approaches with ultrasound or PMT is decreased time to complete lysis, which equates to a shorter length of stay, less cost, and the potential for fewer complications.

Discharge

Catheter sheaths are removed when clot lysis is successfully achieved, and at least 2 hours after thrombolytic therapy is discontinued. Hospital policy should govern who is responsible for the removal of the lines. Despite the frequent necessity for ICU beds, patients must remain in the ICU and be carefully monitored with 15-minute site checks and

hourly vital signs for at least 2 hours after the sheath is removed. If significant swelling is present, an elastic bandage applied to the entire length of the limb with leg elevation is imperative.

After transfer to a general unit, patients usually remain hospitalized to achieve a therapeutic INR level. Discharge anticoagulation is maintained with warfarin or LMWH for up to a year, or longer when a thrombophilic disorder exists. A postprocedural venous Doppler examination typically is obtained prior to discharge and repeated at 3, 6, and 12 months for the first year, and then yearly. At each follow-up examination, the patient is carefully evaluated for PTS symptoms. Discharge teaching by the nurse is critical. Medication administration, including self-injection of subcutaneous heparin or instruction on the required INR follow-up for warfarin, is a priority. Fall-prevention strategies as well as measures to prevent bleeding should be reinforced with the patient prior to discharge. The nurse must also emphasize measures to prevent recurrent DVT.

SUMMARY

As endovascular technology advances, the treatment of acute proximal DVT is changing. Significant clinical trials are on the horizon to evaluate quality-of-life outcomes, the use of low-dose catheter-directed lytic infusions, and factors that affect the development of post-thrombotic syndrome. Currently, the NIH at www.clinicaltrials.gov reports 47 clinical trials recruiting patients for studies that involve venous thrombosis.

Nurses have key roles when caring for patients before, during, and after interventional radiological procedures with catheter-directed thrombolysis. Safe, effective care necessitates careful monitoring and vigilance for complications.

REFERENCES

1. Hirsh J, Hoak J. Management of deep vein thrombosis and pulmonary embolism. *Circulation*. 1996;93:2212–2245.
2. White R. The epidemiology of venous thromboembolism. *Circulation.* 2003;107:4–8
3. Augustinos P, Ouriel K. Invasive approaches to treatment of venous thromboembolism. *Circulation*. 2004;110:I-27–I-34.
4. Baldwin Z, Comerota A, Schwartz L. Catheter-directed thrombolysis for deep vein thrombosis. *Vasc Endovasc Surg*. 2004;38(1):1–9.
5. Perler B. Thrombolytic therapies: the current state of affairs. *J Endovasc Ther*. 2005;12:224–232.
6. Antani M. Catheter-directed thrombolysis for treatment of acute deep venous thrombosis. *Appl Radiol*. 2001;30(7):29–35.
7. Weiner B. Thrombolytic agents in critical care. *Crit Care Nurs Clin N Am*. 1993;5(2):355–366.
8. Waterbury L, Zieve P. Thromboembolic disease. In Barker L, Burton J, Zieve P, eds. *Principles of Ambulatory Medicine*. Philadelphia: Lippincott Williams & Wilkins; 2006:770–779.
9. Ramzi D, Leeper K. DVT and pulmonary embolism: part I. Diagnosis. *Am Fam Physician*. 2004;69(12):2829–2836.
10. Anand S, Wells P, Hunt D, Brill-Edwards P, Cook D, Ginsberg J. Does this patient have deep vein thrombosis? *JAMA*. 1998;279(14):1094–1099.
11. Bates S, Ginsberg J. Treatment of deep-vein thrombosis. *N Engl J Med,* 2004;351:268–277.
12. Merli G. Diagnostic assessment of deep vein thrombosis and pulmonary embolism. *Am J Med*. 2005;118(8A):3S–12S.
13. Institute for Clinical Systems Improvement. Venous thromboembolism. 2006. Available at: http://www.guidelines.gov/summary/summary.aspx?doc_id=8949&nbr=004871&string=venous±AND±thromboembolism. Accessed July 5, 2006.
14. Kanne J, Lalani T. Role of computed tomography and magnetic resonance imaging for deep vein thrombosis and pulmonary embolism. *Circulation*. 2004;109(12S1):I15–I21.
15. Fraser D, Moody A, Morgan P, Martel A, Davidson I. Diagnosis of lower-limb deep venous thrombosis: a prospective blinded study of magnetic resonance direct thrombus imaging. *Ann Intern Med*. 2002;136(2):89–98.
16. Curtin N, Highe G, Harris M, Braunstein A, Demattia F, Coss L. Extensive evaluation of the instrumentation laboratory IL test D-dimer immunoturbidimetric assay on the ACL 9000 determines the D-dimer cutoff value for reliable exclusion of venous thromboembolism. *Lab Hematol*. 2004;10(2):88–94.
17. Blum A, Roche E. Endovascular management of acute deep vein thrombosis. *Am J Med*. 2005;118(8A):31S–38S.

18. Eclavea A, Patel N. Thrombolytic therapy for acute iliofemoral deep vein thrombosis: past, present, and future. *Appl Radiol*. 2001;30(7):61–69.
19. Kahn S, Ginsberg J. The post-thrombotic syndrome: current knowledge, controversies, and directions for future research. *Blood Rev*. 2002;16(3):155–165.
20. Meissner M. Thrombolytic therapy for acute deep vein thrombosis and the venous registry. *Rev Cardiovasc Med*. 2002;3(2S):S53–S60.
21. Raabe R. Ultrasound-facilitated thrombolysis in treating DVT. *Endovasc Today*. 2006;5(4):75–79.
22. Nutescu E. Antithrombotic therapy for the treatment of venous thromboembolism. *Am J Manag Care*. 2003;9(5S):S103–S114.
23. Allie D, Ansel G, Arata M, et al. Combination therapy lysis and devices for DVT. *Endovasc Today*. 2005;4(4S):1–17.
24. Siskin G, Kwan B. Inferior vena cava filters. 2005. Available at: http://www.emedicine.com/radio/topic762.htm. Accessed July 5, 2006.
25. Cohen M, Arjomand H, Pollack M. The evolution of thrombotic therapy and adjunctive antithrombotic regimens in acute ST-segment elevation myocardial infarction. *Am J Emerg Med.* 2004;22(1):14–23.
26. Giannini D, Balbarini A. Thrombolytic therapy in peripheral arterial disease. *Curr Drug Targets-Cardiovasc Haematol Disord*. 2004;4:249–258.
27. Frangos S, Chen A, Sumpio B. Vascular drugs in the new millennium. *J Am Coll Surg*. 2000;191(1):76–92.
28. Meier G. Combination therapy with rheolytic thrombectomy and pharmacologic lysis in the treatment of DVT. In *30th Global: Vascular and Endovascular Issues, Techniques, and Horizons,* Veith Symposium; 2003; Cleveland, Ohio.
29. Comerota A, Aldridge S. Thrombolytic therapy for acute deep vein thrombosis. *Semin Vasc Surg*. 1992;5(2):76–84.
30. Schweizer J, Kirch W, Koch R, et al. Short- and long-term results after thrombolytic treatment of deep venous thrombosis. *J Am Coll Cardiol*. 2000;36(4):1336–1343.
31. Mewissen M, Seabrook G, Meissner M, Cynamon J, Labropoulos N, Haughton S. Catheter-directed thrombolysis for lower extremity deep venous thrombosis: report of a national multicenter registry. *Radiology*. 1999;211:39–49.
32. Comerota A. Quality-of-life improvement using thrombolytic therapy for iliofemoral deep vein thrombosis. *RevCardiovasc Med*. 2002;3(2S):S61–S67.
33. Grunwald M, Hofmann L. Comparison of urokinase, alteplase, and reteplase for catheter-directed thrombolysis of deep venous thrombosis. *J Vasc Interv Radiol*. 2004;15:347–352.
34. National Institutes of Health Clinical Center. Low-dose alteplase to treat blood clots in deep leg veins. 2006. Available at: http://www.clinicaltrials.gov/ct/show/NCT00082355?order=1. Accessed July 11, 2006.
35. National Institutes of Health Clinical Center. Treatment of acute deep vein thrombosis of the lower extremity with intraclot, pulse-sprayed recombinant tissue plasminogen activator, plus heparin and warfarin: a pilot study. 2006. Available at: http://www.clinicaltrials.gov/ct/show/NCT00001713?order=53. Accessed August 3, 2006.
36. Janssen M, Wollersheim H, Schultze-Kool L, Thien T. Local and systemic thrombolytic therapy for acute deep venous thrombosis. *Neth J Med*. 2005;63(3):81–90.
37. Alexandrov A, Molina C, Grotta J, et al. Ultrasound-enhanced systemic thrombolysis for acute ischemic stroke. *N Engl J Med*. 2004;351(21):2170–2178.
38. Polak J. Ultrasound energy and the dissolution of thrombosis. *N Engl J Med*. 2004;351(21):2154–2155.
39. Bussard M. Reteplase: nursing implications for catheter-directed thrombolytic therapy for peripheral vascular occlusions. *Crit Care Nurse*. 2002;22(3):57–62.
40. Frankenfield S, Pile A, Ware C. Learning about catheter-directed thrombolysis. *Dimensions Crit Care Nurs*. 2002;21(3):91–93.
41. Institute for Clinical Systems Improvement. Diagnosis and treatment of chest pain and acute coronary syndrome. 2005. Available at: http://www.guidelines.gov/summary/summary.aspx?ss=15&doc_id=8362&nbr=004683&string=thrombolytic±AND±drugs#s27. Accessed July 30, 2006.
42. Barger A, Hurley R. Evaluation of the hypercoagulable state. *Postgrad Med*. 2000;108(4):59–66.
43. Tepel M, Aspelin P, Lameire N. Contrast-induced nephropathy—a clinical and evidence-based approach. *Circulation*. 2006;113:1799–1806.
44. Pannu N, Wiebe N, Tonelli M. Prophylaxis strategies for contrast-induced nephropathy. *JAMA*. 2006;295(23):2765–2779.
45. Brown T, Lovato L, Parker D. Procedural sedation in the acute care setting. *Am Fam Physician*. 2005;71(1):85–90.
46. Godwin S, Caro D, Wolf S, et al. American College of Emergency Physicians Clinical Policy: procedural sedation and analgesia in the emergency department. 2005. Available at: http://www.guidelines.gov/summary/summary.aspx?doc_id=6495&nbr=004068&string=procedural±AND±sedation. Accessed July 31, 2006.
47. Johansen K. Pain due to vascular disease. In Loeser JD, ed. *Bonica's Management of Pain*. Philadelphia: Lippincott Williams & Wilkins; 2001:587–612.
48. Hatsiopoulou O, Cohen R, Lang E. Postprocedure pain management of interventional radiology patients. *J Vasc Interv Radiol*. 2003;14:1373–1385.