Thromboembolism After Hip and Knee Arthroplasty: Diagnosis and Treatment

Craig J. Della Valle, MD, David J. Steiger, MD, and Paul E. Di Cesare, MD

Abstract

Postoperative thromboembolism is a potentially lethal complication. Its diagnosis may be difficult, as the classic clinical signs and symptoms are often absent, making a high index of suspicion imperative for diagnosis. Anticoagulant therapy is effective in reducing morbidity and mortality due to thromboembolism, but is associated with a substantial rate of bleeding complications in the immediate postoperative period. Inferior vena cava filters constitute an alternative to anticoagulant therapy, but are also associated with a substantial complication rate. The appropriate use of diagnostic tests combined with clinical suspicion can guide the orthopaedic surgeon in deciding which patients require treatment for thromboembolism.

J Am Acad Orthop Surg 1998;6:327-336

Thromboembolism is the most frequent serious complication following major orthopaedic surgery. Without prophylaxis, deep venous thrombosis (DVT) develops in approximately 50% of patients who undergo elective total hip arthroplasty, and pulmonary emboli develop in as many as 20%, 2% of whom suffer fatal pulmonary embolism (PE).[1] Patients undergoing total knee arthroplasty are at especially high risk for DVT, with rates reaching 84% in the absence of prophylaxis; however, lower rates of PE (7%) and death have been reported.[2] Despite modern prophylaxis, the incidence of venous thrombosis in elective total joint arthroplasty is still high, with venographically confirmed proximal DVT developing in 2% to 12% of patients. The high incidence of DVT and subsequent PE makes it the most common cause of death following total joint arthroplasty.

Patients are predisposed to venous thrombosis if they fulfill the elements of Virchow's triad: venous stasis, endothelial injury, and hypercoagulability. Venous stasis occurs secondary to long periods of immobilization in the operating room and delayed, limited, or impaired postoperative ambulation. Endothelial injury can be caused either directly, by surgical trauma to the deep veins of the lower extremity and the surrounding soft tissues, or indirectly, by hematoma formation and thermal injury (e.g., from electrocautery or during cement polymerization). Torsion of the deep venous system itself during extremity manipulation has also been demonstrated. A transient postoperative hypercoagulable state is hypothesized to exist as part of the normal host response to surgical insult.

Additional risk factors that may predispose patients to postoperative thromboembolism are listed in Table 1. A thorough preoperative history and physical examination are essential to identify those at particularly high risk. Intraoperative tourniquet time after total knee arthroplasty has not been shown to be an independent risk factor for postoperative thrombosis.[2,3] The use of postoperative continuous passive motion has not been shown to reduce the incidence of postoperative thromboembolism.[4]

Diagnosis

The diagnosis of DVT and PE may be difficult to make, as clinical signs and symptoms are neither sensitive nor specific for diagnosis.[1-5] Given the high incidence of

Dr. Della Valle is a Resident, Department of Orthopaedic Surgery, Hospital for Joint Diseases Orthopaedic Institute, New York, NY. Dr. Steiger is Director, Special Care Unit, Department of Medicine, Hospital for Joint Diseases Orthopaedic Institute; and Assistant Professor, Department of Medicine, New York University Medical Center, New York, NY. Dr. Di Cesare is Director, Musculoskeletal Research Center, Co-Director, Surgical Arthritis Service, Department of Orthopaedic Surgery, Hospital for Joint Diseases Orthopaedic Institute, and Assistant Professor, Department of Orthopaedic Surgery, New York University Medical Center.

Reprint requests: Dr. Di Cesare, Musculoskeletal Research Center, Department of Orthopaedic Surgery, Hospital for Joint Diseases Orthopaedic Institute, 301 East 17th Street, New York, NY 10003.

Table 1
Risk Factors for Postoperative Thromboembolism

Prior thromboembolism
Advanced age
Malignant condition
Obesity
Varicose veins
Congestive heart failure
Hypercoagulable state
Prolonged immobilization
Estrogen usage
Extended operative time
Extensive intraoperative trauma
Bilateral procedures

thromboembolism after orthopaedic procedures and the often clinically silent nature of the disease, effective prophylaxis is the cornerstone of preventing morbidity and mortality.[6]

Symptoms and Signs

Fewer than one third of patients with DVT present with the classic syndrome of calf discomfort, edema, venous distention, and pain on forced dorsiflexion of the foot (Homans sign). Thrombi can be clinically silent, detectable only by screening tests, if they are not entirely occlusive and venous outflow is maintained. In one study,[1] the diagnosis was confirmed by venography in fewer than half of patients with suspected DVT. Normal postoperative pain, swelling, and impaired gait patterns that lead to muscular strain add to the low specificity of clinical diagnosis in the postoperative period.

Pulmonary embolism classically presents as pleuritic chest pain and dyspnea, although the clinical presentation varies according to the severity of vascular obstruction and the patient's preexisting cardiopulmonary status. In the study by Manganelli et al,[5] dyspnea and chest pain were each noted in 60% to 80% of patients with angiographically documented PE, with the combination of the two present in only 40%. True pleuritic chest pain is rare and is associated only with pulmonary infarction seen with massive PE.[5] Patients may also present with vague symptoms of cough, diaphoresis, palpitations, altered mental status, and apprehension. Massive PE can present as syncope or sudden death. Pulmonary infarction occurs in a small percentage of patients with PE, leading to pleural irritation, hemoptysis, and an audible pleural friction rub. Clinical signs, although similarly nonspecific, may be suggestive of PE. The most common finding is tachypnea, which was reported in 85% of cases in the study by Manganelli et al[5]; tachycardia, rales, and fever were noted in 50% of patients, and neck vein distention (secondary to acute cor pulmonale) occurred in 30%. Given the limited accuracy of clinical signs in alerting the physician to the presence of thromboembolism, even vague symptoms or signs, such as unilateral lower-extremity swelling, altered mental status, or otherwise unexplained tachycardia, should be investigated.

Initial Patient Evaluation

Tests utilized in the initial evaluation of the patient with suspected PE include chest radiography, electrocardiography, and arterial blood gas analysis. Although not sufficiently specific to diagnose PE, the results from these tests may be characteristic of PE or may serve to identify alternative causes for symptoms (e.g., myocardial ischemia, pulmonary edema, and pneumonia), for which alternative interventions could be lifesaving.

Chest Radiography

Plain radiographs of the chest are imperative in the evaluation of cardiorespiratory symptoms. In the assessment of the patient with suspected PE, radiography serves to rule out other causes of hypoxia, such as pneumonia, severe atelectasis, pneumothorax, and congestive heart failure. In the postoperative setting, a relatively clear chest radiograph in the presence of severe hypoxemia is highly suggestive of PE. Such "classic" findings as focal hyperlucency of the lung parenchyma (Westermark sign) and enlargement of the descending pulmonary arteries are rarely seen.

Electrocardiography

The classic findings of "S1Q3T3" or a new incomplete right bundle branch block are rare, although they may be seen with massive PE. Tachycardia is frequent, as is ST-segment depression and T-wave inversion in V_1-V_2 secondary to right-ventricle strain. Findings consistent with acute myocardial infarction indicate an important alternative cause for dyspnea and chest pain postoperatively.

Arterial Blood Gas Analysis

An arterial blood gas sample should be obtained from all patients in whom PE is suspected. Absolute determinations of oxygen content, oxygen saturation, and carbon dioxide content should be made. The pulmonary alveolar-arterial oxygen gradient ($P[A–a]O_2$) should also be determined, with use of the following formula: $P(A–a)O_2 = (150 – 1.25\ [PaCO_2]) – PaO_2$. (Both $PaCO_2$ and PaO_2 are measured in millimeters of mercury in samples obtained while the subject is breathing room air. The upper limit of normal for $P[A–a]O_2$ is 20 mm Hg.)

Unfortunately, no combination of blood gas results has been identified that reliably excludes PE.[7] Most patients with pulmonary emboli are hypoxic (PaO_2 <80 mm Hg), hypocapnic ($PaCO_2$ <35 mm Hg), or have a high $P(A–a)O_2$ (>20

mm Hg), although in one study,[7] 38% of those without a prior history of cardiopulmonary disease had normal values despite angiographically proven PE. Older patients may have unrecognized preoperative hypoxemia, which further clouds the clinical picture. Serial measurements can help to assess functional recovery once treatment for PE has been instituted.

Pulse oximetry cannot be substituted for an arterial blood gas measurement. Hyperventilation may result in a normal oxygen saturation even in the presence of a substantial $P(A–a)O_2$. A low oxygen saturation may be useful in recognizing hypoxemia that warrants further evaluation.

Advanced Imaging Studies

The diagnosis of thromboembolism is made by combining the clinical suspicion of PE or DVT with the results of advanced imaging studies. The appropriate screening test for a patient with suspected DVT or PE must be individualized on the basis of the reliability of the test, the clinical situation, the risk of performing the test, and the availability and cost of the test. The risks of not pursuing further evaluation must also be considered. An algorithm for utilizing advanced imaging studies in the evaluation of a patient with suspected PE is presented in Figure 1.

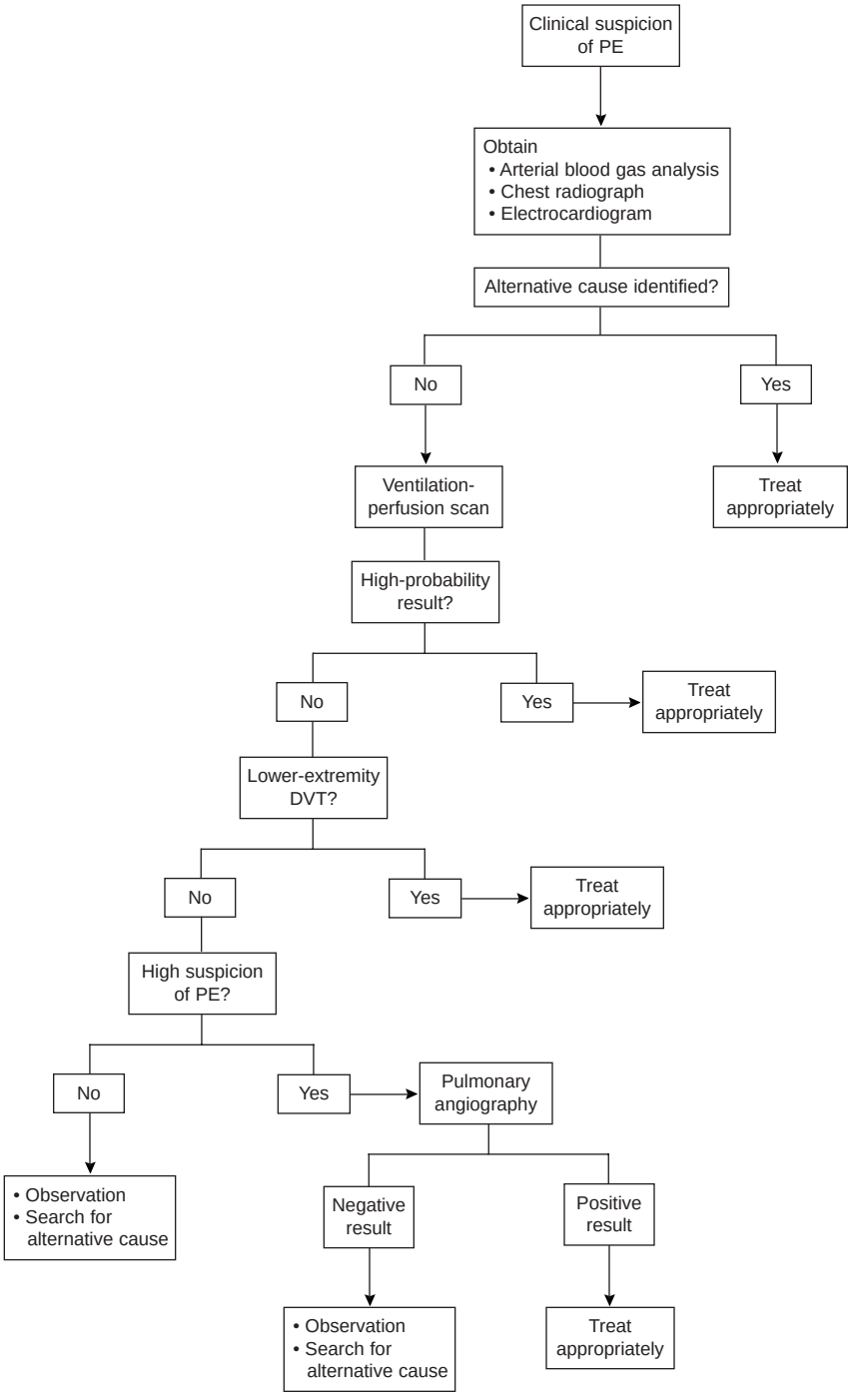
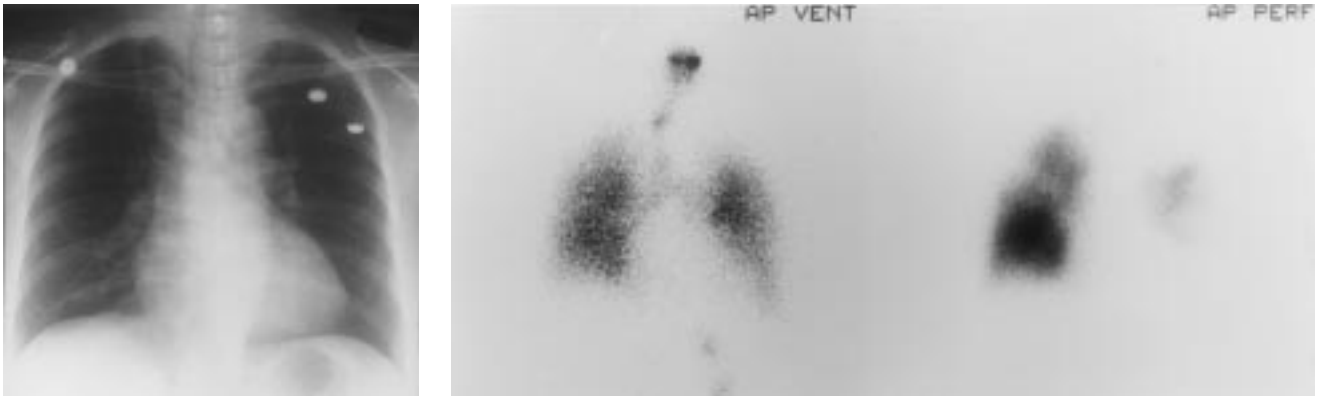


Fig. 1 Algorithm for evaluation and treatment of suspected PE.

Ventilation-Perfusion Scanning

Ventilation-perfusion ($\dot{V}/\dot{Q}$) scanning is the noninvasive test of choice for diagnosing PE. Patients inhale a radioactive aerosol (technetium-99m, xenon-133, xenon-127, or krypton-81), and the ventilation scintigrams obtained are compared with perfusion scintigrams obtained after intravenous injection of Tc-99m macroaggregated albumin. Normal scans have no perfusion defects. Areas of pneumonia or local hypoventilation theoretically produce a "matched defect," in which both ventilation and perfusion are deficient. Areas that are ventilated without associated regional perfusion (a "mismatched defect") are suspected of being the site of PE (Fig. 2). On the basis of criteria that have evolved from comparisons between $\dot{V}/\dot{Q}$ scans and pulmonary angiogram find-



A B

Fig. 2 **A,** Normal chest radiograph of a patient noted to be hypoxic postoperatively. **B,** Ventilation-perfusion study of the same patient. Perfusion scan (right) reveals multiple perfusion defects, including wedge-shaped defects in the right upper lobe and almost the entire left lung field. Ventilation scan (left) appears normal.

ings, scans are interpreted either as normal or as indicating a high, intermediate, or low probability of the presence of PE. In general, interobserver agreement on grading of $\dot{V}/\dot{Q}$ scans is greater than 94% for high-probability and normal scans and as low as 70% for intermediate- and low-probability scans.[8]

The Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) Study, reported in 1990,[8] compared the results of $\dot{V}/\dot{Q}$ scans and angiography in 755 patients and reported that a normal $\dot{V}/\dot{Q}$ scan effectively excluded angiographically documented PE in more than 96% of patients (96% negative predictive value). The positive predictive value of a high-probability scan was 88%, with a specificity of 97% and a sensitivity of 41%. Thus, a high-probability scan usually indicates the presence of PE; however, fewer than half of the patients with PE in that study had a high-probability scan. When the results of high-, intermediate-, and low-probability scans were considered together, the sensitivity increased dramatically to 98%; however, the specificity dropped to 10%. The negative predictive value of a low-probability scan was 84%; however, 12% of the patients with a low-probability scan were found to have PE.

Combining the physician's clinical assessment with the results of a $\dot{V}/\dot{Q}$ scan improves the probability of reaching the correct diagnosis. In the PIOPED Study,[8] in cases in which there was a high-probability scan and a high level of clinical suspicion, the rate of PE was 96%; in those in which there was a low level of clinical suspicion and a high-probability scan, the rate of angiographically confirmed PE was 56%. Similarly, a low level of clinical suspicion and a low-probability scan correctly excluded PE 96% of the time, but in cases in which there was a low-probability scan and a high level of clinical suspicion, the rate of angiographically proven PE was 40%.

Ventilation-perfusion scanning identifies those patients who are most likely and least likely to have suffered acute PE. When there is a high clinical suspicion of PE, a high-probability $\dot{V}/\dot{Q}$ study is diagnostic and mandates treatment. A normal or low-probability study combined with a low level of clinical suspicion makes the diagnosis of PE unlikely. A search for lower-extremity DVT is recommended, as it may obviate the need for pulmonary angiography in patients with intermediate- or low-probability $\dot{V}/\dot{Q}$ scans. Surprisingly, however, a large number of high-probability $\dot{V}/\dot{Q}$ scans are associated with normal duplex studies of the lower extremities. Patients with low- or intermediate-probability scans and a negative evaluation for lower-extremity DVT should undergo pulmonary angiography if clinical suspicion is high; in the PIOPED Study,[8] the risk of PE in these subsets of patients was 30% and 14%, respectively.

Pulmonary Angiography

Pulmonary angiography is considered the standard against which all other tests for diagnosis of PE are judged. However, the invasive nature of the procedure limits its usefulness as a screening tool. The femoral or antecubital vein is cannulated, and a catheter is directed via fluoroscopy through the right atrium and ventricle and into the pulmonary arteries, where iodinated contrast material is injected to visu-

alize the pulmonary vascular tree, starting in the areas of highest suspicion and including magnified oblique views if necessary. An intraluminal filling defect or an abrupt cutoff in a pulmonary artery is diagnostic (Fig. 3). Although not all emboli will be detected, large, clinically significant emboli will be identified.

In one large series,[9] the technique was associated with a 3.5% overall rate of complications, including cardiac perforation, endocardial or myocardial injury, arrhythmia, cardiac arrest, and contrast reactions. Death (incidence, 0.2%) was most frequently attributed to acute cor pulmonale in patients with pulmonary hypertension and elevated right ventricular end-diastolic pressures (>20 mm Hg) who were unable to tolerate the volume of contrast injections. An advantage of pulmonary angiography is that one can concomitantly insert an inferior vena cava (IVC) filter if indicated.

Although pulmonary angiography is considered the definitive diagnostic tool for PE, image quality can be impaired by respiratory and cardiac motion. In one large study,[8] interobserver agreement in angiogram interpretation was found to be 92% for the presence of PE and 83% for the absence of PE, with an 89% rate of agreement on indeterminate studies. In the same study, a normal angiogram was found to all but exclude the possibility of PE. Unfortunately, not all hospitals have the personnel to perform this technically demanding and costly procedure. Anticoagulants must be discontinued before pulmonary angiography to avoid bleeding complications.

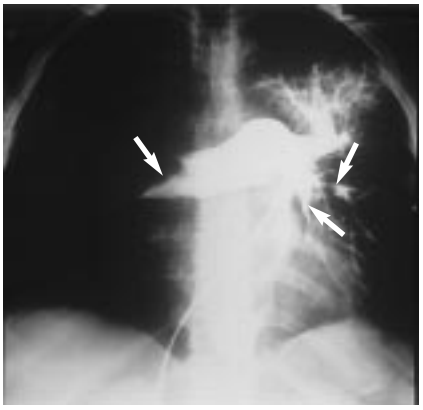


Fig. 3 Pulmonary angiogram revealing emboli (arrows) involving the segmental branches of the pulmonary artery supplying the lower left and lingular lobes and a large embolus occluding the right main pulmonary artery. (Courtesy of Peter Schlossberg, MD, New York.)

Recent Developments in Pulmonary Imaging

Given the limitations of $\dot{V}/\dot{Q}$ scanning and the invasive nature of pulmonary angiography, there has been considerable interest in developing alternative imaging methods to improve the speed, accuracy, and safety of diagnosing PE. Helical (spiral) and electron-beam computed tomography (CT) have improved visualization of the pulmonary vascular tree, allowing acquisition of volumetric image data. This technology allows multiplanar reconstruction and three-dimensional image production while simultaneously providing faster scanning times. Visualization of pulmonary segmental vessels is now possible with a sensitivity of 65% to 100% and a specificity of 89% to 100% for diagnosing PE.[10] Magnetic resonance (MR) imaging of the pulmonary vascular tree is also being developed and may allow sequential imaging of the lower-extremity venous system (to evaluate for pelvic and lower-extremity DVT) within a single examination.

Duplex Ultrasonography of the Lower Extremity

Duplex ultrasonography is the screening test of choice for evaluating patients for DVT. It is noninvasive and painless, requires no radiation, and can be performed at the bedside (if necessary) for about one third the cost of venography. Each venous segment from the common femoral vein at the inguinal ligament to the popliteal vein distally is examined for the presence of echogenic thrombus and compressibility. The addition of color Doppler imaging to confirm spontaneous flow improves the ability to determine the presence or absence of clot. Augmentation of flow with calf compression or toe dorsiflexion excludes major distal occlusion. Demonstrations of respiratory phasicity and cessation of flow with the Valsalva maneuver are indirect indicators of abdominal and pelvic venous patency.

This technique is more technically demanding and less sensitive in the calf than in the thigh, and the ability to directly image the deep veins of the pelvis is limited; however, occlusive iliac thrombus should be detectable on the basis of abnormal Doppler signals. The technique is highly operator-dependent, and accuracy improves with experience. An advantage of ultrasonography is the ability to reveal alternative causes, such as hematoma and superficial phlebitis, which may cause physical signs and symptoms similar to those of DVT.

Controlled trials of venography compared with duplex ultrasonography in patients with symptomatic DVT have yielded sensitivity and specificity values of 89% to 100%.[11] Sensitivity is decreased when duplex ultrasonography is used as a screening tool in postoperative patients who have undergone hip or knee surgery and are asymptomatic (average sensitivity, 62%; specificity, 97%; positive predictive value, 66%).[12] However, it should be borne in mind that these values vary greatly between centers.[13,14] Thrombi that are missed tend to be small, nonocclusive, and located in the calf. Although ultra-

sonography is less sensitive than venography, an outcome analysis of the data on 1,022 symptomatic patients who had normal studies revealed that only 5 patients had adverse sequelae of untreated DVT.[15]

As many as 50% of patients may have persistent abnormalities of the deep venous system after treatment. Therefore, patients with DVT who are receiving anticoagulant therapy should undergo repeat ultrasonography at 3 to 6 months to establish a baseline appearance of the venous system should symptoms or signs recur.

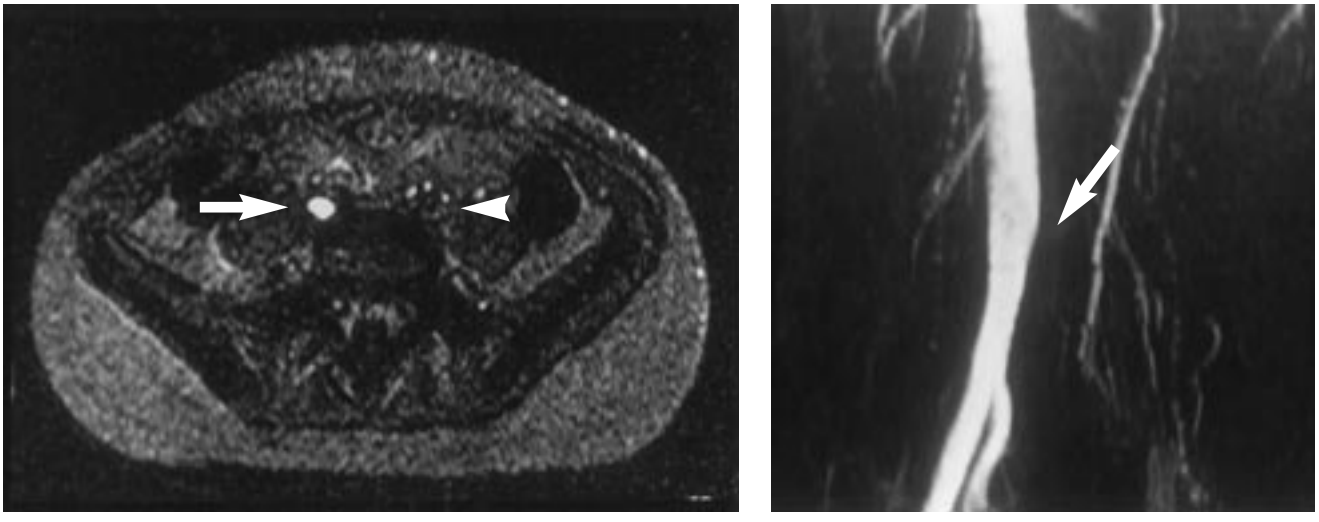
Venography of the Lower Extremity

Venography is the "gold standard" imaging study for the diagnosis of DVT in the calf and thigh, allowing an anatomic depiction of the venous system of the lower extremities. Venograms are obtained after the retrograde injection of 100 to 150 mL of iodinated contrast material into a dorsal pedal vein at the same time that radiographs of the lower extremity are obtained. The presence of well-defined filling defects in well-opacified veins is accurate for the detection of DVT. Negative studies reliably exclude DVT in the veins distal to the common iliac vessels.

Cost- and procedure-related morbidity, including patient discomfort, sequelae related to the use of iodinated contrast material, and the potential to induce DVT formation, make venography less than ideal as a screening test. Patients with poor venous access often cannot successfully undergo venography. Venography is indicated if the results obtained with noninvasive modalities are equivocal, if there are technical limitations to a study, or if DVT is suspected in areas where ultrasonography is known to be inaccurate. The detection of pelvic thrombosis is poor (due to the dilution of contrast medium by unopacified tributaries of the deep pelvic veins) unless direct femoral vein puncture is undertaken.

MR Imaging of Lower-Extremity and Pelvic Veins

Magnetic resonance imaging has been used increasingly to diagnose DVT in the thigh and particularly in the pelvis, where it has been shown to have greater sensitivity and specificity than venography.[16] With use of a gradient-echo technique, normally flowing blood is depicted as high-intensity signal (white), and areas of thrombus or reduced flow are visualized as lower-intensity signal (dark) (Fig. 4). Fast spin-echo techniques partially correct for artifacts adjacent to metallic implants, and excellent visualization of the thigh and pelvic vasculature has been reported after total hip arthroplasty.[17] Using venography via direct puncture of the femoral vein as the standard modality for specifically evaluating the deep pelvic veins, the sensitivity and specificity of MR venography were found to be 100% and 95%, respectively, and the sensitivity and specificity of standard venography utilizing retrograde filling from a dor-



A B

Fig. 4 MR venogram of the pelvis. **A,** Axial two-dimensional time-of-flight venogram (repetition time, 600 msec; echo time, 10 msec) shows occlusive thrombus (arrowhead) of the left common femoral vein and normal signal intensity on the right (arrow). **B,** Corresponding maximum-intensity projection shows complete occlusion (arrow) of the left common iliac vein; the right iliac vein appears normal. (Courtesy of Glenn Krinsky, MD, New York.)

sal pedal vein were found to be 78% and 100%. False-positive findings can occur, however, as areas of vascular bifurcation cause disturbed flow that can mimic a filling defect.

The diagnostic performance of MR imaging is equal to that of venography in the thigh but is inferior in the calf (sensitivity, 87%; specificity, 97%). When compared with duplex ultrasonography, MR imaging offers increased sensitivity in areas of known difficulty, such as the pelvic veins, common femoral vein, and superficial femoral vein in the adductor canal.

Magnetic resonance imaging has the advantages of being noninvasive, allowing simultaneous visualization of both lower extremities, and requiring no injection of contrast material and thus not being limited by poor venous access. Nevertheless, MR imaging has its own contraindications, including severe claustrophobia and the presence of cardiac pacemakers, certain valvular and otologic implants, cerebral aneurysmal clips, loose metal fragments, and certain IVC filter devices. The possibility of concurrently imaging the pulmonary tree for suspected PE is being investigated. Because of its high cost and limited availability, MR venography is not an ideal screening tool, although it can be extremely useful when pelvic thrombi are suspected and in other situations in which clarification is necessary.

Cuff-Impedance Plethysmography and I-125 Fibrinogen Scanning

Although used extensively both alone and in combination in the past, cuff-impedance plethysmography and I-125 fibrinogen scanning are reportedly less sensitive and specific than previously believed, with a high rate of false-positive results.[10] The routine use of these modalities is thus not recommended. Furthermore, the radiopharmaceutical agent needed for fibrinogen scanning is no longer available commercially in the United States because of concerns about infectious disease transmission.

Treatment

Anticoagulant Therapy

Continuous intravenous heparin administration followed by oral anticoagulation with warfarin for 3 months in cases of isolated DVT and 6 months in cases of PE is standard treatment.[18] Anticoagulation prevents further thrombus formation while allowing the fibrinolytic system to dissolve clots that have already formed. In the one study of PE in which intravenous heparin was compared with no treatment, the mortality rate of those untreated was 26%, compared with 0% in the treatment group.[19] Mortality rates of less than 2% have been reported for patients who received appropriate anticoagulation therapy for PE after hip and knee arthroplasty.[2,3,20]

The risk of developing PE is higher when there are larger and more proximal areas of DVT, with PE developing in 20% to 50% of patients with proximal DVT but no or few clinically significant emboli developing in patients with isolated calf thrombi.[3,21,22] Proximal extension of isolated calf vein thrombosis has been reported to occur in 10% to 20% of patients; therefore, patients with known isolated calf thrombi should be monitored with serial ultrasonography for 10 to 14 days, and anticoagulation therapy may be withheld unless proximal extension is identified.

Heparin acts by binding to antithrombin III, potentiating its inhibitory effect on thrombin and activated factor X. Heparin should be administered in an initial bolus of 80 units per kilogram of body weight, followed by continuous intravenous infusion of 18 U/kg per hour. The hourly dose is then titrated to prolong the activated partial thromboplastin time (APTT) to 1.5 to 2.5 times the control value. With use of a weight-based formula (Table 2), the therapeutic threshold is reached more rapidly, and recurrent thromboembolism is reduced,[23] as failure to exceed 1.5 times the APTT within 24 hours is associated with a significantly (P=0.02) increased (5 to 15 times) risk of both early and late recurrent thromboembolism.

There is a wide variability in patient response to heparin, necessitating individual dose titration and frequent monitoring. Heparin therapy is continued for 5 to 10 days, while warfarin therapy is initiated with a goal international normalized ratio (INR) of 2.0 to 3.0. In cases of massive PE or iliofemoral vein thrombosis, prolonged heparin therapy is indicated. In one randomized trial,[18] the rate of recurrence of thrombosis was 20% in patients treated with oral anticoagulants alone, compared with 6.7% in those treated with initial heparin therapy followed by oral anticoagulation. This effect may be not only a function of the delayed anticoagulant effect of oral agents (peak effect at 36 to 72 hr) but also in part a secondary thrombogenic effect that warfarin initially has via inhibition of the natural anticoagulants protein C and protein S. Continuous intravenous infusion of heparin is associated with fewer bleeding complications than intermittent intravenous infusion.[24]

After heparinization, patients must be monitored closely for major bleeding at the operative site as well as at distant sites. In the first 5 postoperative days, there is a substantial risk of hemorrhage and subsequent wound hematoma that can lead to wound dehiscence, neurapraxia, and deep sepsis. Rates of local wound hematoma formation have been reported to be as high as 25%,[20] and a 4% incidence of major bleeding episodes has been associat-

Table 2
Weight-Based Dosage of Intravenous Heparin*

APTT, sec	Dose Change, U/kg/hr†	Additional Action
<35	(<1.2) +4	Rebolus 80 U/kg
35-45	(1.2-1.5) +2	Rebolus 40 U/kg
46-75	(1.5-2.5) –0	None
76-90	(2.5-3.0) –2	None
>90	(>3.0) –3	Stop infusion for 1 hr

* Initial bolus of 80 U/kg/hr, followed by 18 U/kg/hr delivered by continuous intravenous infusion; APTT repeated 6 hr after change in heparin dose.
† Values in parentheses are number of times greater than control value.

ed with full heparinization followed by oral warfarin therapy. Patients who sustain a major complication after anticoagulation that necessitates its discontinuation should be considered for IVC filter placement.

The platelet count should be monitored, as mild thrombocytopenia is relatively common, and severe heparin-induced thrombocytopenia with pathologic thrombosis can occur. After orthopaedic surgery, most patients have a transient decrease in platelet count, followed by an increase above preoperative levels. Heparin-induced thrombocytopenia typically occurs after 5 or more days of treatment and is caused by heparin-dependent immunoglobulin G (IgG) antibodies, which activate platelets through their Fc receptor. Recurrent venous or arterial thrombosis can occur in the form of PE, extensive deep venous thrombosis, stroke, myocardial infarction, and lower-extremity arterial or aortic occlusion with subsequent distal ischemia. Rates of heparin-induced thrombocytopenia have been reported as 2% to 5% for patients who have undergone orthopaedic procedures.[25]

Severe heparin-induced thrombocytopenia and associated pathologic thrombosis is less common but more clinically important, given its significant rate of morbidity, including the need for amputation, and mortality. If thrombocytopenia (platelet count, <100,000) develops after 5 or more days of heparin administration for treatment or prophylaxis of thromboembolism, the medication should be discontinued, and the patient should undergo testing for heparin-dependent IgG antibodies. Patients who test positive must undergo reevaluation for thromboembolism, as clot extension and the development of new thromboses are common, and IVC filter placement should be considered. Once heparin therapy is discontinued, platelet counts typically rebound rapidly (within 2 to 5 days), and anticoagulation with warfarin should be instituted. Platelet transfusion is contraindicated.

As with heparin, the dose-response relationship of warfarin varies widely, and doses must be individualized and monitored carefully. Warfarin can be started on the first day of heparin therapy. Once the dose required for adequate anticoagulation has been determined, the INR should be monitored weekly. Hull et al[26] found that in patients with proximal DVT, 3 months of warfarin therapy (INR, 2.0 to 3.0) reduced the incidence of recurrent thromboembolism from 47% to 2%. A higher rate of recurrence was seen in patients who stopped warfarin before the 3-month period had elapsed; a significantly higher rate was seen in those who had been treated with subcutaneous heparin (P=0.001). In another study, the same researchers found that increased levels of anticoagulation (INR, 3.0 to 4.5) increased the rate of bleeding complications from approximately 3% to 22% without increased efficacy.[27] Patients with recurrent thrombosis despite anticoagulation, hypercoagulable states, or continued risk factors for thromboembolism should be considered for indefinite anticoagulation therapy. Patients receiving warfarin prophylaxis at the time of acute DVT or PE should receive heparin if the INR is less than 2.0 and should be considered for IVC filter placement if the INR is greater than 2.0.

The use of low-molecular-weight heparins (administered subcutaneously on a weight-adjusted basis) as agents for treating established DVT has been investigated. A meta-analysis of the various trials[28] revealed that low-molecular-weight heparins offer increased efficacy with a lower rate of complications compared with intravenous heparin therapy. However, most of these trials excluded patients who had recently undergone surgery or had received a low-molecular-weight heparin or warfarin before the study period. Low-molecular-weight heparins are currently not approved by the Food and Drug Administration for the treatment of postoperative thromboembolism.

Patients who have had a thromboembolic complication are at greater risk for recurrence if they undergo another surgical procedure within the next 6 months.[27] If further surgery is planned, patients should undergo preoperative cardiac echocardiography (to rule out pulmonary hypertension) and pulmonary function tests (to demonstrate adequate pulmonary reserve).

If nonelective surgery is necessary and those tests reveal poor cardiopulmonary reserve, a preoperative IVC filter should be considered.

Inferior Vena Cava Filters

Inferior vena cava filters can be placed percutaneously under fluoroscopic guidance, via either the femoral or the internal jugular vein. They should be placed below the renal veins at approximately the level of the third lumbar vertebra. These devices have been advocated for a subset of patients who have contraindications for anticoagulation, have had a significant complication secondary to anticoagulation for diagnosed thromboembolism, have sustained recurrent thromboembolic events despite adequate anticoagulation, or are at high risk for mortality in the event of additional pulmonary emboli. The prophylactic use of IVC filters has been advocated by some authors for patients undergoing elective orthopaedic procedures who are considered to be at high risk (i.e., those in whom DVT or PE developed despite appropriate prophylaxis in the past).[29]

Pulmonary embolism can recur after filter placement, in the form of small clots that pass through the filter or clots that bypass the filter as collateral venous circulation develops in cases in which vena cava occlusion has occurred. In addition, filter malpositioning, tilting, or migration may allow clots to pass, or a thrombus may propagate above the filter if large emboli are trapped within it. A 0% to 1.5% incidence of recurrent symptomatic or fatal PE has been reported in orthopaedic patients who underwent IVC filter placement. Similarly, in a summary of 13 case series,[30] 26 recurrent pulmonary emboli and 8 deaths secondary to PE were reported among 1,094 patients who had undergone Greenfield filter placement (incidence rates of 2.4% and 0.7%, respectively).

Complications related to filter placement include insertional problems (local hematoma, wound infection, vagal nerve injury, pneumothorax, air embolism, stroke), distal filter migration or tilting, filter malposition, insertion-site thrombosis, vena cava occlusion with subsequent lower-extremity edema, and, rarely, phlegmasia cerulea dolens (complete venous outflow obstruction with subsequent arterial spasm, reduced tissue perfusion, and the possibility of venous stasis ulceration, compartment syndrome, and gangrene that may require amputation). In one study,[30] death was directly related to filter insertion in 3 of 2,557 patients (0.12%).[30] Late perforation of the vena cava and aorta has also been described. However, only three reported instances of adverse clinical outcomes owing to vena cava penetration have been reported.

Although insertion-site thrombosis may occur, the Greenfield filter is designed to preserve lateral flow around entrapped clots so as to facilitate clot lysis and maintain IVC patency. The Greenfield device has long-term IVC patency rates of 95% without continued oral anticoagulation therapy and, accordingly, a 5% rate of symptomatic venous insufficiency. In an 18-month follow-up of 66 orthopaedic patients who underwent insertion of a Greenfield filter, none had evidence of filter migration, postphlebitic syndrome secondary to IVC occlusion, or chronic symptomatic extremity edema.[29] Temporary filters (both removable and resorbable) are being developed to avoid the late sequelae that may follow their insertion.

Anticoagulation therapy, if not contraindicated, is recommended for patients after filter placement, as the underlying thrombotic process is not altered by filter placement. Effective anticoagulation should decrease the incidence of thrombus propagation and/or recurrence, as well as insertion-site DVT and caval thrombosis. In a study of orthopaedic patients who were found to have symptomatic PE within 2 weeks of total joint arthroplasty, placement of IVC filters was found to be safe and effective, with a lower complication rate than that for intravenous heparin therapy.[31]

Summary

The high risk of thromboembolic complications after orthopaedic procedures is well documented. Many of these events may be clinically silent until they become life-threatening, and appropriate prophylaxis and a high level of clinical suspicion must be present to avoid morbidity and mortality. Duplex ultrasonography of the lower extremities and $\dot{V}/\dot{Q}$ scanning provide adequate sensitivity and specificity for evaluating patients for thromboembolism in the postoperative period. Newer imaging modalities (e.g., high-resolution CT angiography and MR pulmonary angiography and lower-extremity venography) show promise of improving the accuracy of diagnosis of thromboembolic phenomena.

Initial treatment includes intravenous heparin followed by oral warfarin for 3 to 6 months. An IVC filter is indicated when anticoagulation is contraindicated, when recurrent thromboembolism has developed despite adequate anticoagulation, when there is a complication secondary to anticoagulant therapy, or when the patient is considered to be at high risk for mortality if additional emboli develop. These devices provide effective prophylaxis against recurrent PE, with a 5% rate of complications. The decision in the early postoperative period to administer anticoagulant therapy or to proceed with IVC filter insertion is a difficult one and must be made on a case-by-case basis.

References

1. Haake DA, Berkman SA: Venous thromboembolic disease after hip surgery: Risk factors, prophylaxis, and diagnosis. *Clin Orthop* 1989;242:212-231.
2. Stulberg BN, Insall JN, Williams GW, Ghelman B: Deep-vein thrombosis following total knee replacement: An analysis of six hundred and thirty-eight arthroplasties. *J Bone Joint Surg Am* 1984;66:194-201.
3. Lotke PA, Ecker ML, Alavi A, Berkowitz H: Indications for the treatment of deep venous thrombosis following total knee replacement. *J Bone Joint Surg Am* 1984;66:202-208.
4. Lynch AF, Bourne RB, Rorabeck CH, Rankin RN, Donald A: Deep-vein thrombosis and continuous passive motion after total knee arthroplasty. *J Bone Joint Surg Am* 1988;70:11-14.
5. Manganelli D, Palla A, Donnamaria V, Giuntini C: Clinical features of pulmonary embolism: Doubts and certainties. *Chest* 1995;107(suppl 1): 25S-32S.
6. Zimlich RH, Fulbright BM, Friedman RJ: Current status of anticoagulation therapy after total hip and total knee arthroplasty. *J Am Acad Orthop Surg* 1996;4:54-62.
7. Stein PD, Goldhaber SZ, Henry JW, Miller AC: Arterial blood gas analysis in the assessment of suspected acute pulmonary embolism. *Chest* 1996;109: 78-81.
8. The PIOPED investigators: Value of ventilation/perfusion scan in acute pulmonary embolism: Results of the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED). *JAMA* 1990;263:2753-2759.
9. Mills SR, Jackson DC, Older RA, Heaston DK, Moore AV: The incidence, etiologies, and avoidance of complications of pulmonary angiography in a large series. *Radiology* 1980; 136:295-299.
10. Gefter WB, Hatabu H, Holland GA, Gupta KB, Henschke CI, Palevsky HI: Pulmonary thromboembolism: Recent developments in diagnosis with CT and MR imaging. *Radiology* 1995;197: 561-574.
11. Burke B, Sostman HD, Carroll BA, Witty LA: The diagnostic approach to deep venous thrombosis: Which technique? *Clin Chest Med* 1995;16:253-268.
12. Wells PS, Lensing AWA, Davidson BL, Prins MH, Hirsh J: Accuracy of ultrasound for the diagnosis of deep venous thrombosis in asymptomatic patients after orthopedic surgery: A meta-analysis. *Ann Intern Med* 1995; 122:47-53.
13. Davidson BL, Elliott CG, Lensing AWA, et al: Low accuracy of color Doppler ultrasound in the detection of proximal leg vein thrombosis in asymptomatic high-risk patients. *Ann Intern Med* 1992;117:735-738.
14. Woolson ST, McCrory DW, Walter JF, Maloney WJ, Watt JM, Cahill PD: B-Mode ultrasound scanning in the detection of proximal venous thrombosis after total hip replacement. *J Bone Joint Surg Am* 1990;72:983-987.
15. Vaccaro JP, Cronan JJ, Dorfman GS: Outcome analysis of patients with normal compression US examinations. *Radiology* 1990;175:645-649.
16. Evans AJ, Sostman HD, Knelson MH, et al: Detection of deep venous thrombosis: Prospective comparison of MR imaging with contrast venography. *AJR Am J Roentgenol* 1993;161:131-139.
17. Potter HG, Montgomery KD, Padgett DE, Salvati EA, Helfet DL: Magnetic resonance imaging of the pelvis: New orthopaedic applications. *Clin Orthop* 1995;319:223-231.
18. Brandjes DPM, Heijboer H, Büller HR, de Rijk M, Jagt H, ten Cate JW: Acenocoumarol and heparin compared with acenocoumarol alone in the initial treatment of proximal-vein thrombosis. *N Engl J Med* 1992;327:1485-1489.
19. Barritt DW, Jordan SC: Anticoagulant drugs in the treatment of pulmonary embolism: A controlled trial. *Lancet* 1960;1:1309-1312.
20. Patterson BM, Marchand R, Ranawat C: Complications of heparin therapy after total joint arthroplasty. *J Bone Joint Surg Am* 1989;71:1130-1134.
21. Moser KM, LeMoine JR: Is embolic risk conditioned by location of deep venous thrombosis? *Ann Intern Med* 1981;94(pt 1):439-444.
22. Lotke PA, Steinberg ME, Ecker ML: Significance of deep venous thrombosis in the lower extremity after total joint arthroplasty. *Clin Orthop* 1994; 299:25-30.
23. Raschke RA, Reilly BM, Guidry JR, Fontana JR, Srinivas S: The weight-based heparin dosing nomogram compared with a "standard care" nomogram: A randomized controlled trial. *Ann Intern Med* 1993;119:874-881.
24. Glazier RL, Crowell EB: Randomized prospective trial of continuous vs intermittent heparin therapy. *JAMA* 1976;236:1365-1367.
25. Warkentin TE, Levine MN, Hirsh J, et al: Heparin-induced thrombocytopenia in patients treated with low-molecular-weight heparin or unfractionated heparin. *N Engl J Med* 1995;332:1330-1335.
26. Hull R, Delmore T, Genton E, et al: Warfarin sodium versus low-dose heparin in the long-term treatment of venous thrombosis. *N Engl J Med* 1979;301:855-858.
27. Hull R, Hirsh J, Jay R, et al: Different intensities of oral anticoagulant therapy in the treatment of proximal-vein thrombosis. *N Engl J Med* 1982;307:1 676-1681.
28. Lensing AWA, Prins MH, Davidson BL, Hirsh J: Treatment of deep venous thrombosis with low-molecular-weight heparins: A meta-analysis. *Arch Intern Med* 1995;155:601-607.
29. Vaughn BK, Knezevich S, Lombardi AV Jr, Mallory TH: Use of the Greenfield filter to prevent fatal pulmonary embolism associated with total hip and knee arthroplasty. *J Bone Joint Surg Am* 1989;71:1542-1548.
30. Ballew KA, Philbrick JT, Becker DM: Vena cava filter devices. *Clin Chest Med* 1995;16:295-305.
31. Bicalho PS, Hozack WJ, Rothman RH, Eng K: Treatment of early symptomatic pulmonary embolism after total joint arthroplasty. *J Arthroplasty* 1996; 11:522-524.