Total hip replacement is an operation that is particularly prone to thromboembolic complications with potentially life-threatening consequences. Johnson et al., in a series of 7959 total hip replacements performed between 1962 and 1973, reported that the overall prevalence of pulmonary embolism was 7.89 percent and that of fatal pulmonary embolism was 1.04 percent. Similarly, in 1974, Coventry et al. reported an overall prevalence of pulmonary embolism of 2.2 percent in a series of 1202 consecutive total hip replacements. In a subset of sixty-two patients who had received no prophylactic anticoagulation, the prevalence of fatal pulmonary embolism was 3.4 percent. However, the average duration of the operation was 2.4 hours, the average blood loss was 1650 milliliters, and the average volume of blood transfused was 1144 milliliters. Prophylactic anticoagulation with warfarin was started five days after the operation. Patients were managed with bed rest for an average of one week before walking was allowed, and they were discharged at an average of three weeks after the operation.

During the last three decades, substantial advances have been made in the understanding of the pathophysiology and the prevention of venous thromboembolism associated with total hip replacement. The prevalence of fatal pulmonary embolism with contemporary operative techniques in the absence of anticoagulant prophylaxis was reported to be 0.5 percent after 1162 total hip replacements. The rates of proximal deep venous thrombosis may be reduced by even more than 50 percent when epidural anesthesia is used. Many studies have demonstrated that epidural and spinal anesthesia are associated with a lower rate of postoperative deep venous thrombosis. The use of epidural or spinal anesthesia during total hip replacement reduces the risk of postoperative deep venous thrombosis by approximately 40 to 50 percent. The rates of proximal deep venous thrombosis may be reduced by even more than 50 percent when epidural anesthesia is used. This reduction in the rate of deep venous thrombosis is seen irrespective of the type of anesthesia.
postoperative anticoagulant prophylaxis. In a compilation of recent multicenter studies in Europe in which deep venous thrombosis was assessed with venography, Eriksson et al. verified that epidural anesthesia reduces the risk of deep venous thrombosis in patients who receive heparin, low-molecular-weight heparin, or hirudin (Table I). Epidural anesthesia also reduces the risk of pulmonary embolism. In a retrospective study performed at The Hospital for Special Surgery, the risk of in-hospital death due to pulmonary embolism decreased sixfold, from 0.12 percent (seven) of 5874 procedures performed with general anesthesia between 1981 and 1986 to 0.02 percent (two) of 9685 procedures performed with epidural anesthesia between 1987 and 1991 (p = 0.03).

Carefully controlled studies have demonstrated that regional anesthesia per se has no effect on platelet function or fibrinolysis during the operation. Rather, epidural anesthesia increases blood flow in the lower extremity during and immediately after an operation, thereby reducing the risk of deep venous thrombosis by minimizing venous stasis. Epidural anesthesia considerably increases blood flow to the foot but not necessarily to the muscle of the leg. However, if catecholamines with beta-agonist activity such as epinephrine are used, blood flow to the skeletal muscle is enhanced. In contrast, if beta agonists are not used, blood flow to the calf decreases with epidural anesthesia. In a series of 441 consecutive total hip arthroplasties performed by the same surgeon, with the patients under epidural anesthesia, the rate of proximal deep venous thrombosis was 2.4 percent when epinephrine was used and 9.3 percent when epinephrine was not used. In that study, the rates of deep venous thrombosis assessed with venography, were also found to be related to the duration of the operation. The overall rate of deep venous thrombosis was 10.0 percent when the duration of the operation was less than seventy minutes and 35.5 percent when it exceeded seventy minutes. Corresponding rates of proximal deep venous thrombosis were 3.3 percent and 13.3 percent, respectively.

Measurement of markers of thrombin generation (prothrombin “F1+2” and thrombin-antithrombin complexes) and fibrin formation (fibrinopeptide A) in circulating blood during total hip replacement demonstrated that activation of thrombogenesis does not begin in the initial phase of the operation (Fig. 1). Rather, it starts during the preparation of the femur and is most pronounced with implantation of femoral components with cement rather than without cement. It is also during this phase of the operation that femoral venous occlusion occurs. Presumably, tissue thromboplastin and other intramedullary procoagulants are released from the femoral canal into the obstructed femoral vein, thereby activating femoral venous thrombosis. Such femoral venous occlusion during femoral preparation has been demonstrated both in cadaver models and in vivo. Animal models of operative injury, thrombosis begins in five to ten minutes in a completely obstructed vein. Thus, it behooves the surgeon to minimize the duration of femoral venous occlusion during preparation of the canal and implantation of the component.

A low dose of heparin administered intraoperatively after implantation of the acetabular cup was found to suppress fibrin formation during insertion of the femoral component. In a dose-response study, ten units of unfractionated heparin per kilogram of body weight inhibited fibrin formation to a substantial degree, whereas twenty units per kilogram of body weight completely suppressed fibrin formation (Fig. 1). The virtue of this single intravenous dose of unfractionated heparin given approximately during the operation, thereby reducing the risk of deep venous thrombosis, assessed with venography, were also found to be related to the duration of the operation. In an animal model of femoral venous occlusion, thrombosis begins within five to ten minutes of a completely obstructed vein.

### Table I: Rates of Deep Venous Thrombosis Associated with Regional Block and General Anesthesia According to a Multicenter Study by Eriksson et al.

<table>
<thead>
<tr>
<th>Type of Prophylaxis*</th>
<th>Unfractionated Heparin (no. of patients)</th>
<th>Enoxaparin (no. of patients)</th>
<th>Desirudin (no. of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall rate of deep venous thrombosis</td>
<td>Patients managed with regional block anesthesia</td>
<td>67 (24.7%) of 271</td>
<td>83 (19.4%) of 428</td>
</tr>
<tr>
<td></td>
<td>Patients managed with general anesthesia</td>
<td>46 (39.0%) of 118</td>
<td>112 (32.8%) of 341</td>
</tr>
<tr>
<td>Rate of proximal deep venous thrombosis</td>
<td>Patients managed with regional block anesthesia</td>
<td>42 (15.4%) of 272</td>
<td>22 (5.0%) of 437</td>
</tr>
<tr>
<td></td>
<td>Patients managed with general anesthesia</td>
<td>27 (22.3%) of 121</td>
<td>36 (10.3%) of 350</td>
</tr>
</tbody>
</table>

*The patients managed with heparin received 5000 international units three times daily, those managed with enoxaparin received 40 international units three times daily, and those managed with desirudin received 15 milligrams daily.
middle of the operation is that the half-life is short (thirty to forty minutes), so the risk of intraoperative and postoperative bleeding is minimized. If intraoperative hypotension is used, no additional intraoperative bleeding is evident. Perhaps the most important aspect of these observations is that they introduce the concept of targeting anticoagulation for a short period of time during the operation in order to prevent the formation of clots rather than attempting to retard the extension of existing thrombi after the operation. In a series of 212 patients who had a total hip replacement under hypotensive epidural anesthesia with epinephrine, intraoperative administration of fifteen units of heparin per kilogram of body weight before femoral preparation, an expeditious operation, and postoperative use of aspirin, the rate of deep venous thrombosis, as determined with ultrasound screening, was 6 percent (3 percent had proximal thrombosis and 3 percent had distal thrombosis)\(^{28}\). There were no postoperative bleeding complications and no pulmonary emboli. This experience was expanded and at the time of writing included 1000 total hip replacements. There were five pulmonary emboli (none fatal) and no bleeding complications.

Hypotensive anesthesia may further contribute to the blunting of thrombogenesis by reducing blood loss, and the associated peripheral vasoconstriction and status, and by facilitating an expeditious operation\(^{61,106,109}\). Excessive bleeding and intravenous administration of fluid may dilute circulating anticoagulants such as anti-thrombin III, altering the coagulation profile and leading to a prothrombotic state\(^{62,76}\). The rate of deep venous thrombosis associated with hypotensive epidural anesthesia is 8 to 15 percent, which is substantially lower than the rate of 25 to 50 percent associated with normotensive anesthesia\(^{106,109}\).

Postoperative epidural analgesia provides excellent pain relief after total hip replacement and may further reduce the risk of deep-vein thrombosis\(^{30}\); however, we are not aware of any studies that have specifically addressed this question. Ultrasonic measurements after total hip replacement in patients who received epidural analgesia with use of 0.12 percent bupivacaine and fentanyl (five micrograms per milliliter) infused at ten milliliters per hour failed to demonstrate any augmentation of blood flow in the lower extremity\(^{64}\). Although epidural analgesia may not directly increase femoral venous blood flow, it may reduce the rates of deep venous thrombosis by enabling patients to perform flexion and extension exercises of the foot and then facilitating early walking.

The Food and Drug Administration issued an advisory against the concurrent use of low-molecular-weight heparin and epidural anesthesia in December 1997 because of thirty-eight cases of epidural hematoma associated with a neurological deficit\(^{32}\). It appears that it is unsafe to administer epidural anesthesia to a patient who has received low-molecular-weight heparin preoperatively or to use low-molecular-weight heparin postoperatively before removal of an epidural catheter. Low-molecular-weight heparin is suitable for use in patients receiving general anesthesia, provided that it is administered twelve hours after the operation.

**A ssessment of the R isks and B enefits of R outine T hromboprophylaxis A fter T otal H ip R eplacement**

Consensus conferences\(^{27,65,79}\) and numerous scientific and medicolegal publications have purported that total hip replacement is associated with a high risk of venous thromboembolism and a rate of fatal pulmonary embolism ranging from 1.0 to 3.4 percent. Consequently, guidelines suggest that prophylaxis be used for all patients having a total hip replacement; such sweeping recommendations should not be issued until there is clear evidence that the benefits of thromboprophylaxis outweigh the risks.

**Su rrogate O utcomes**

The widespread belief that the rate of fatal pulmonary embolism after total hip replacement is more than 1 percent is based on the findings of a few studies conducted mainly in the 1960s and early 1970s\(^{16,51}\). Moreover, the unique characteristics of the pattern and risk factors of deep venous thrombosis after total hip replacement preclude generalization of the findings of studies of venous thrombosis after other types of pro-

![Graph showing blood levels of fibrinopeptide A during hybrid total hip replacement. Fibrinopeptide A is a cleavage product when thrombin acts on fibrinogen to form fibrin. It has a half-life of five minutes. Note the increase in fibrinopeptide A, during insertion of the femoral component, in the group managed with saline solution and the significant suppression in both the group managed with ten units of unfractionated heparin per kilogram of body weight and the group managed with twenty units of unfractionated heparin per kilogram of body weight. The values are given as the average and the standard deviation. Event 1 = before epidural injection, event 2 = after insertion of the acetabular component, event 3 = after reaming of the femur, event 4 = after relocation of the hip, and event 5 = thirty minutes postoperatively. * indicates \(p = 0.0001\).](image)
A number of randomized controlled trials that subsequently were undertaken have demonstrated a substantial reduction in the prevalence of venographically evident thrombosis after total hip replacement with prophylactic anticoagulation. It is incorrect to assume that this reduction in the surrogate outcome of deep venous thrombosis necessarily leads to a decrease in the more important outcome of overall death rate. This assumption may be false if fatal pulmonary embolism is not very common and does not account for most deaths, if a decrease in the rate of venous thrombosis is not associated with a similar decrease in the rate of fatal pulmonary embolism, or if prophylaxis increases the risk of other causes of death. Evaluation of surrogate outcomes may lead to false conclusions.

Assessment of the Death Rate

Mortality after hip replacement may be assessed in different ways. The Report of the National Confidential Enquiry into Perioperative Deaths 1991/1992 is a large database that includes information on deaths after total hip replacement in the United Kingdom. The overall death rate of 0.35 percent (134 of 38,000 patients) was calculated on the basis of inpatient mortality within thirty days after hip replacement. Related outpatient deaths were ignored, and the death rate was potentially understated. A better way to assess the death rate is to consider events that occur each month after hip replacement as was done in the Oxford Record Linkage Study. In that study of about 12,000 patients managed between 1976 and 1985, the death rate increased threefold during the first month and an additional one and one-half-fold during the second postoperative month, which amounted to an excess death rate of about 0.5 percent. In another study, which was performed in Scotland, the death rates were compared before and after hip replacement. That study demonstrated an increased postoperative death rate for a few months, but thereafter the death rate was actually lower than it was for patients on the waiting list for total hip replacement; total mortality for the first year after hip replacement was the same as it was for the year before hip replacement. These findings suggest that hip replacement may have hastened a few deaths that would have occurred naturally during the subsequent year but did not actually increase the death rate during that year.

Meta-Analysis

An informal or opportunistic meta-analysis, not confined to randomized controlled trials, was undertaken in 1996 to review all of the English-language orthopaedic literature published between 1966 and 1995 that contained information about death or pulmonary embolism after total hip replacement. Information on 93,000 patients in 181 reports was analyzed with capture of deaths that occurred within three months after the operation. The patients were categorized according to the type of prophylaxis used: none, heparin, warfarin, aspirin, dextran, and other. The patients who were managed with no prophylaxis, placebo, or antiembolism stockings were included in the category termed none, and those managed with any form of heparin, heparinoid, or low-molecular-weight heparin, with or without stockings, were included in the heparin category. Similarly, patients who were managed with warfarin, aspirin, or dextran, with or without antiembolism stockings, were included in the categories so labeled. All patients in trials in which a combination of prophylactic regimens was used or in which the prophylactic regimen was unclear were included in the category named other. This category also included 745 patients managed with mechanical pumps, as this group was too small for a separate analysis.

A progressive decrease in the rate of fatal pulmonary embolism was observed over time, with a contemporary rate of 0.11 percent (confidence limits, 0.07 to 0.16 percent), which is an order of magnitude lower than that generally reported. This decrease in the rate of fatal pulmonary embolism was likely due to improvements in anesthetic techniques (such as regional anesthesia), operative techniques, and rehabilitation protocols. Because it is not always possible to determine the definitive cause of death even on postmortem examination, the rate of fatal pulmonary embolism may be inaccurate. Moreover, complications of therapy for the embolism or other comorbidities may result in a false event. Therefore, it is important to determine the overall death rate, as it represents an upper limit for the rate of fatal pulmonary embolism.

Like the rate of fatal pulmonary embolism, the overall death rate has decreased in the last few decades. The findings of the meta-analysis suggest that the current overall death rate is 0.38 percent (confidence limits, 0.29 to 0.47 percent), which is similar to the previously calculated death rate of 0.35 percent (confidence limits, 0.29 to 0.41 percent). Combining both sets of data yields a better estimate of the current overall death rate after total hip replacement of 0.36 percent (confidence limits, 0.31 to 0.40 percent).

The studies in the meta-analysis were categorized according to the type of prophylaxis and the rate of fatal pulmonary embolism. Information on fatal pulmonary embolism from only 22,000 patients precluded the determination of any significant difference among the groups with respect to the type of prophylaxis. Despite an encouraging trend, no prophylactic agent significantly decreased the rate of fatal pulmonary embolism compared with the rate for the group that received no prophylaxis: four fatal emboli (0.12 percent) were observed in 3432 patients who received no prophylaxis compared with two fatal emboli (0.04 percent) in 5162 patients who received prophylaxis with warfarin (p = 0.051).

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It is possible that some prophylactic agents do prevent fatal pulmonary embolism after total hip replacement, but the number of patients in the meta-analysis was too small to discern such a finding. Moreover, even if it is suspected that various pharmacological agents prevent fatal pulmonary embolism, it cannot be assumed that they decrease the overall death rate because of the issue of deaths related to the use of anticoagulants. Assuming that thromboprophylaxis prevents fatal pulmonary embolism, the number of lives saved is directly related to the rate of fatal pulmonary embolism. In contrast, the risk related to anticoagulant prophylaxis is finite and independent of the rate of fatal pulmonary embolism. Therefore, when the rate of fatal pulmonary embolism is high, the benefits outweigh the risks; when the frequency of fatal pulmonary embolism is low, the risks of anticoagulation outweigh the benefits.

Meta-analyses from other fields of medicine and surgery have demonstrated that aspirin and heparin prevent a proportion of fatal pulmonary emboli. However, the rate of fatal pulmonary embolism specific to total hip replacement in the absence of chemical thromboprophylaxis was about 0.1 percent; therefore, prophylaxis cannot decrease the rate of fatal pulmonary embolism by more than about 0.05 percent in this setting. The death rate resulting directly or indirectly from the complications of anticoagulants is not known. If the death rate is 0.05 percent or more, which is not inconceivable, then the use of these agents may actually be detrimental. Prophylactic agents therefore are best assessed by consideration of the overall death rate, accounting for both risks and benefits.

Similarly, no prophylactic agent has significantly decreased the overall rate of death. Therefore, it has been suggested that recommendations in favor of the routine use of thromboprophylaxis after total hip replacement are not justified. Likewise, proponents of this philosophy advocate that it is not negligent to use no prophylactic agents for routine total hip replacement. Notwithstanding this general approach, there is a subgroup of patients who are at a particularly high risk of fatal pulmonary embolism after a total hip replacement, such as those with a history of thromboembolism and primary and secondary hypercoagulable states; other chemoprophylaxis may be appropriate for this subgroup.

Conclusions from any meta-analysis may be unreliable. Assumptions and estimates of death rates may be flawed. Likewise, comparisons between different prophylactic regimens and between management with and management without prophylaxis may be biased for a number of reasons. In the absence of such aggregate analyses, larger trials of 30,000 patients in each arm would be required to demonstrate a real decrease in the overall death rate. Before the issuance of guidelines recommending the routine use of chemoprophylaxis, such large, randomized, controlled clinical trials or comparably-sized meta-analyses are necessary to demonstrate significance. However, such individual trials may be impractical to conduct.

The Risks and Benefits of Aspirin

There have been variable waves of enthusiasm, and a lack thereof, for the use of aspirin as prophylaxis against venous thromboembolism after total joint arthroplasty. The National Institutes of Health Consensus Conference on thromboembolic disease in 1986 did not include aspirin among the recommended agents. Nonetheless, to determine the best methods to protect patients from thromboembolic disease, it is necessary to carefully assess the risks and benefits. Until recently, the risks had not been clearly defined, and this contributed to the continued controversy. Recent studies have shown that the rate of fatal pulmonary embolism after total hip replacement is between 0.1 and 0.2 percent. This rate has been shown consistently by many investigators and appears to be unchanged by the form of prophylactic agent. Given that the risk of fatal pulmonary embolism is relatively low, it is important to assess the concurrent risk of hemorrhage when evaluating any antithrombotic prophylaxis because excessive bleeding is the principal anticipated adverse outcome. Indeed, over the years, the greatest attributes of aspirin have been its ease of use and safety; recommendations for its use are usually predicated on the lack of associated bleeding complications rather than on its proved efficacy. It is inexpensive, requires no monitoring, and is well tolerated in low doses.

The risks from bleeding complications vary according to the agents that are chosen. A major bleeding episode has been conventionally defined as one that causes death, intra-organ bleeding, or a reoperation. The morbidity after bleeding, to which operating surgeons are sensitive, has never been clearly defined. However, if only major bleeding episodes are considered, substantial rates of bleeding are found with some of the agents currently available for thromboembolic prophylaxis, such as enoxaparin, which is associated with a rate of 5.1 percent, and warfarin, which is associated with a rate of 2.3 percent. Lieberman et al., in a series of 1099 total hip arthroplasties, noted the risk of wound hematoma increased from 1.1 to 3.8 percent (p = 0.003) in a subset of 450 patients who were managed with warfarin and had a prothrombin time of more than seventeen seconds. In a meta-analysis by Imperiale and Speroff, the risks of a major bleeding episode after total hip replacement were compared among different methods of prophylaxis. The risk was 0.3 percent for the control group, 0.4 percent for the group managed with aspirin, 1.3 percent for patients
managed with warfarin, 1.8 percent for those who received low-molecular-weight heparin, and 2.6 percent for the group managed with unfractionated heparin.

Without evidence that specific agents reduce the risk of fatal pulmonary embolism (which is between 0.1 and 0.2 percent), it is necessary to ask if the increased risk of bleeding and the subsequent morbidity are worth the potential reduction in the rate of fatal pulmonary embolism. Because of these risks, there has been a resurgence of interest in the use of aspirin. It is well known that aspirin reduces the risk of heterotopic ossification and inhibits platelet function. In doses of less than 100 milligrams per day, the inhibition is dose-dependent; if more than 100 milligrams of aspirin is given per day, there is complete lifetime (approximately ten-day) suppression of platelet aggregation.

Clinical trials to assess the effectiveness of aspirin have been divided into arterial and venous studies. Although studies of the arterial effects of aspirin have demonstrated a clear efficacy in reducing mortality related to unstable angina by 60 percent and mortality related to cerebrovascular accident and transient ischemic attacks by 25 percent, studies of the venous effects of aspirin have been less conclusive. A large meta-analysis of antiplatelet prophylaxis against venous thromboembolism was recently reported by the Antiplatelet Trialists' Collaboration. A pooled analysis of fifty-three operative trials (only nine of which included the use of aspirin during elective orthopaedic procedures) demonstrated that fatal pulmonary embolism was reduced to 0.2 percent in the patients managed with aspirin compared with 0.9 percent in control subjects ($p = 0.0001$). In the studies of elective orthopaedic procedures (a total of thirteen trials with only nine involving use of aspirin), the prevalence of deep venous thrombosis was reduced to 37.5 percent in the patients who used aspirin compared with 53.2 percent in the control group. These findings may be considered to be comparable with those associated with the use of warfarin and fractionated heparin after knee arthroplasty, but they are clearly inferior to the results associated with the use of either regimen after hip arthroplasty with conventional forms of anesthesia. In one study, of 2592 total hip replacements performed with use of epidural anesthesia, between 1990 and 1994, 80 percent received aspirin postoperatively for prophylaxis. Warfarin was administered to the remaining 20 percent of the patients because they had additional predisposing factors for venous thromboembolism. The prevalence of venographically evident deep venous thrombosis was 10 percent, the prevalence of symptomatic pulmonary embolism was 1 percent, and the prevalence of fatal pulmonary embolism was 0.04 percent. Sarmiento and Goswami administered aspirin after 1492 total hip arthroplasies. A fatal pulmonary embolism occurred after two arthroplasties (0.13 percent), a nonfatal pulmonary embolism was diagnosed after fourteen (0.94 percent), and clinical evidence of deep venous thrombosis developed after fifteen (1.01 percent).

In summary, one must assess risks and benefits in order to determine the appropriate chemoprophylactic agents for the prevention of fatal pulmonary embolism. As the current rates of fatal pulmonary embolism are very low, inordinately large numbers of patients are needed to scientifically prove the benefit of one regimen compared with another. Therefore, one must compare the potential risk of fatal pulmonary embolism with the potential risk of increased bleeding. A spirin has accumulated an excellent track record on safety and its use may be indicated in conjunction with epidural or spinal anesthesia in patients with no additional predisposing risk factors for venous thromboembolism.

**Prophylaxis with Warfarin and Fractionated Heparin**

During the past three decades of total hip replacement in North America, the focus on thromboembolic disease has sharpened considerably. The recommendations of the National Institutes of Health Consensus Conference in 1986 endorsed the routine use of anticoagulant prophylaxis for thromboembolic disease after elective total joint replacement and treatment of fractures about the hip. A understandable preoccupation with bleeding complications was subsequently responsible for the slow acceptance of anticoagulant prophylaxis, but Paiement et al. documented the increasing use of pharmacological prophylaxis, which has had a favorable impact on thromboembolism-related mortality. In a recent series of 1638 patients who had a total joint replacement with routine anticoagulant prophylaxis, the overall mortality rate at six months was 0.79 percent; there were two fatal pulmonary emboli (0.12 percent), which accounted for only 15 percent of deaths from all causes. Despite this decrease in the mortality rate, with current methods of prophylaxis after total hip replacement the rate of venographically documented deep venous thrombosis has ranged from 15 to 26 percent for patients managed with warfarin and from 6 to 21 percent for patients managed with low-molecular-weight heparin; the rates of proximal thrombosis have been approximately 2 to 5 percent for either regimen.

Notwithstanding an apparent reduction in the prevalence of fatal thromboembolic disease with more widespread use of routine anticoagulant prophylaxis, venous thromboembolism remains the most common reason for emergency readmission after total joint replacement, and warfarin and fractionated heparin have each had varying degrees of popularity as prophylactic agents.

**Warfarin**

Coumadin (warfarin) is the most commonly used single agent for prophylaxis against thromboembolic
disease after total hip replacement in North America. In their landmark study concerning the rate of pulmonary embolism after 2012 hip replacements, Coventry et al. found that the occurrence of fatal pulmonary embolism was reduced from 3.4 percent in patients who did not receive anticoagulation to 0.05 percent in patients who were managed with warfarin prophylaxis. It is noteworthy that they delayed the start of prophylactic anticoagulation until the fifth postoperative day, presumably because of a concern about bleeding problems in the early postoperative period, and still observed a rate of bleeding complications of 4.1 percent in patients managed with warfarin. In a similar report of clinically evident pulmonary embolism after total hip replacement, Amszutz et al. administered warfarin for prophylaxis for three weeks postoperatively, even when this extended beyond the date of discharge from the hospital. After 3000 total hip replacements, they noted fourteen symptomatic nonfatal pulmonary emboli (0.5 percent), confirmed by ventilation-perfusion scan or angiography. In a follow-up survey conducted by mail, they identified five more symptomatic pulmonary emboli (0.17 percent) that occurred after discharge from the hospital in patients who had received warfarin for prophylaxis for an average of 11.6 days. None of the pulmonary emboli were fatal.

Early studies with rates of bleeding episodes ranging from 8 to 12 percent have suggested that the concern about hemorrhagic complications was justified. Occasionally, the episodes were severe enough to lead to death. More recent recommendations have favored reduced-intensity anticoagulation with a prothrombin-time ratio of 1.3 to 1.5 times control, or an international normalized ratio of 2.0 to 2.5, and such protocols have been associated with lower rates of bleeding. Amszutz et al. noted an overall rate of bleeding complications of 1.5 percent (forty-four of 3000 total hip replacements), with the rate decreasing from 4.7 to 1 percent after the target level for the prothrombin time was reduced from eighteen to twenty seconds to sixteen to eighteen seconds and a bedside flow sheet was implemented to monitor daily prothrombin times and warfarin dose. Of the forty-four major bleeding complications, thirty-six were wound hematomas and eight involved bleeding in the gastrointestinal or genitourinary tract; there were no related deaths.

In 1079 consecutive patients who had a primary or revision total hip replacement, Pellegrini et al. observed a rate of bleeding complications of 1.2 percent with use of a target range of 1.3 to 1.5 for the prothrombin-time index. In contrast, Paiement et al. reported that 4 percent (ten) of 268 patients had a major bleeding episode (nine had a wound hematoma and one had a gastrointestinal bleeding episode) during hospitalization; the overall rate of bleeding episodes, including so-called minor bleeding episodes, during hospitalization was 6 percent. After discharge from the hospital and during the twelve-week period of extended prophylaxis with warfarin, an additional 5 percent (thirteen) of the 268 patients had a so-called minor bleeding episode. In a similar study with a structured program of outpatient prophylaxis with warfarin after total hip replacement, Ries et al. reported a rate of bleeding complications of 3.2 percent in 125 patients managed with warfarin for four weeks following the operation, and no patient needed to be readmitted because of bleeding.

Non-wound-related bleeding complications in orthopaedic patients managed with anticoagulant therapy predominantly involve the gastrointestinal and genitourinary tracts. Orthopaedic studies of a few hundred patients, by design, possess adequate statistical power to investigate venographically documented thromboembolic disease with a prevalence of 20 percent. However, the lower prevalence of bleeding complications, which ranges from 1 to 5 percent, usually renders studies of this size insufficient to determine significant conclusions relative to rates of bleeding episodes associated with various anticoagulant therapies.

Physicians in the field of internal medicine have investigated predictors of major bleeding in medical patients managed with warfarin anticoagulation in the same age-ranges as patients managed with total hip replacement. The most common site of bleeding has been the gastrointestinal tract. Landefeld et al. identified the risk predictors of a major bleeding episode in 565 outpatients being managed with warfarin in a study that emphasized comorbid medical conditions and the intensity of the anticoagulant therapy. The rate of major bleeding episodes for outpatients managed with warfarin was 3 percent in the first month after discharge, with an incremental rate of 0.8 percent per month for each subsequent month of anticoagulant therapy. These data, from study populations that were considerably larger than those commonly enrolled in orthopaedic trials, suggest a rate of major bleeding complications of 4 to 5 percent in outpatients managed with warfarin for three months. These outpatient bleeding complications often escape recognition in clinical and cost-efficacy studies, as their cost is not directly attached to the index hospitalization during which the total joint replacement was performed.

Recent evidence has suggested that a combination of continuous epidural anesthesia and postoperative epidural analgesia with warfarin prophylaxis is associated with greater efficacy in the prevention of deep venous thrombosis than either modality used alone. In 322 consecutive unilateral total hip replacements, including 210 primary and 112 revision procedures, warfarin was used to prolong the international normalized ratio to a range of 2.0 to 2.5; this represents an extension of the previously published experience. An epidural catheter was placed preoperatively and was maintained for thirty-six to forty-eight hours postoperative.

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atively for pain management, with an infusion of bupivacaine and fentanyl. With an average inpatient stay of 4.7 days, contrast venography was performed for 258 patients before discharge. The overall rate of deep venous thrombosis, as detected on venography, was 8.9 percent (twenty-three of 258 patients), with seventeen thrombi in the calf (6.6 percent) and six in the thigh (2.3 percent). Counter to historical experience, all of the proximal thrombi were contiguous popliteal extensions of thrombi in the calf; there were no segmental femoral-vein thrombi. None of the twenty-three patients with venographic evidence of deep venous thrombosis, who were managed with twelve weeks of warfarin, had additional thromboembolic disease-related events or bleeding. All of the 235 patients who had normal venograms were discharged without additional anticoagulant prophylaxis. Two (0.8 percent) of these patients were readmitted because of symptomatic thromboembolic disease; one of them had deep venous thrombosis in the thigh after a bilateral Syme amputation, and the other had a nonfatal pulmonary embolism and was admitted to an outside hospital. There were no wound hematomas necessitating a reoperation and no other morbid bleeding events. These data confirmed the findings of Westrich et al., who observed an overall prevalence of deep venous thrombosis, as determined by venography, of 10.3 percent in 2037 patients who had had a total hip replacement with hypotensive epidural anesthesia in conjunction with aspirin as prophylaxis against thromboembolic disease. The rate of proximal deep venous thrombosis was 4.3 percent. Late symptomatic pulmonary embolism developed in eight (0.44 percent) of 1826 patients who had had negative findings on venograms.

The prevalence of deep venous thrombosis associated with a combination of warfarin and epidural anesthesia compares favorably with the results associated with any pharmacological regimen, including fractionated heparins, but without the associated bleeding complications. Both extended epidural analgesia, which is contraindicated with use of fractionated heparins, and early mobilization probably contribute to the low prevalence of deep venous thrombosis, and they improve on the 20 percent prevalence of deep venous thrombosis associated with warfarin prophylaxis alone. Most provocative is the observation that segmental proximal thrombi, known to account for as many as 50 percent of all deep venous thrombosis after total hip replacement, did not occur with this combined prophylaxis. Warfarin, in conjunction with continuous epidural anesthesia and analgesia and early mobilization of patients after total hip replacement, is an effective strategy of prophylaxis against thromboembolic disease without the risk of bleeding associated with newer preparations of fractionated heparin. All trials with use of these newer agents should include concurrent control groups and should regulate the type of anesthesia and the duration of hospitalization, as both may affect the prevalence of thromboembolic disease.

Fractionated Heparin

The introduction of fractionated heparin with a molecular weight in the range of 5000 daltons, compared with the average 15,000-dalton molecular weight of unfractionated heparin, has provided another alternative to conventional prophylaxis against thromboembolism. With an enhanced steric affinity for antithrombin III and activated factor X, the fractionated heparin molecule provides a more active agent at an earlier point in the clotting cascade than conventional heparin. Furthermore, by virtue of less binding of plasma protein, the fractionated heparins are more bioavailable, need no monitoring, and have been associated with a lower frequency of both idiosyncratic and autoimmune-mediated thrombocytopenia. All of these factors, including an ambitious marketing program by commercial parties, have contributed to their initial popularity.

The findings of numerous clinical studies have proved the efficacy of fractionated heparins in reducing the frequency of thromboembolism after total hip replacement compared with placebos and with unfractionated heparins. More recently, similar controlled studies comparing fractionated heparins with warfarin have demonstrated that the former have improved efficacy in the prevention of deep venous thrombosis, with overall rates in the range of 8 to 15 percent and rates of proximal deep venous thrombosis of less than 5 percent.

Although low-molecular-weight heparins offer anticoagulant prophylaxis without the need for attendant monitoring and periodic phlebotomy (notwithstanding the need to teach self-injection for outpatient use), the fractionated heparins are associated with a frequency of bleeding complications that exceeds that associated with warfarin therapy. In a meta-analysis of methods used for the prevention of deep venous thrombosis after hip replacement, Imperiale and Speroff identified a sixfold greater risk of “clinically important” bleeding in the patients managed with low-molecular-weight heparins than in the controls and a 50 percent greater risk than in patients managed with warfarin. Hull et al. observed a modest reduction in deep venous thrombosis in 795 patients who had had a total hip replacement. A analysis of the patients for whom data were available revealed that 23.2 percent (seventy-nine) of 340 patients who received warfarin and 20.8 percent (sixty-nine) of 332 patients who received Logiparin had deep venous thrombosis, but the difference between the groups was not found to be significant. However, this reduction was offset by an increase in bleeding complications. Major bleeding complications were observed in six (1.5 percent) of 397 patients managed with warfarin compared with eleven (2.8 percent) of 398 patients managed with Logiparin. The
prevalence of wound hematomas in the group managed with warfarin (ten of 397; 2.5 percent) was less than half that in the group managed with Logiparin (twenty-three of 398; 5.8 percent) \( (p = 0.03) \). In other studies with similar categorization of major and minor bleeding complications, investigators reported a greater frequency of bleeding events associated with use of fractionated heparins, but the groups were too small to provide sufficient statistical power to determine significant differences\(^{15,35,123} \). In a prospective, controlled trial comparing dalteparin with warfarin in 580 patients who had a total hip replacement, the overall prevalence of deep venous thrombosis, as detected on venography, was 15 percent in the patients managed with dalteparin compared with 26 percent in those managed with warfarin \( (p = 0.006) \), whereas the prevalence of proximal deep venous thrombosis was 5 and 8 percent, respectively \( (p = 0.185) \). The overall rates of major bleeding events were not found to be significantly different between the groups (2.2 and 1.4 percent, respectively). Nonetheless, more patients who received dalteparin required transfusion of red blood cells than did those who received warfarin (48 and 31 percent, respectively; \( p = 0.001 \)), and bleeding complications at the operative site were more than four times more frequent in the group that received dalteparin (4.4 percent) than in the group that received warfarin (1 percent) \( (p = 0.03) \). One patient who was managed with dalteparin had transient thrombocytopenia and needed a reoperation for evacuation of a draining hematoma.

Colwell et al., in a multicenter study of 156 centers, compared the prevalence of clinically evident venous thromboembolic disease after total hip replacement in groups receiving either adjusted-dose warfarin (1495 patients) or thirty milligrams of enoxaparin every twelve hours (1516 patients) as prophylaxis\(^{15} \). All clinically suspected events were confirmed by objective testing. The pharmacological prophylaxis was administered for an average of 6.5 days in each group, and venous thromboembolic events were monitored for three months after discharge from the hospital. At the time of the most recent follow-up, confirmed venous thromboembolism was noted in 3.6 percent of the patients managed with enoxaparin and 3.7 percent of those managed with warfarin. Thromboembolic events were more common during hospitalization in the group that received warfarin (1.1 percent) than in the group that received enoxaparin (0.3 percent) and were more frequent after discharge from the hospital in the group that received enoxaparin (3.4 percent) than in the group that received warfarin (2.6 percent). Clinically important bleeding occurred in eighteen (1.2 percent) of the patients managed with enoxaparin and in eight (0.5 percent) of the patients managed with warfarin. A analysis of adverse bleeding events revealed that fourteen of eighteen patients managed with enoxaparin who had a notable bleeding episode had either received the initial dose of enoxaparin within twelve hours after the operation or had had twice-daily administration of the drug rather than daily administration. Similarly, in a case-control study of 152 patients who were managed with either enoxaparin or pneumatic compression as prophylaxis against venous thromboembolism, Watson et al. demonstrated that an increased rate of bleeding episodes was associated with the use of enoxaparin\(^{123} \). The postoperative drop in the hematocrit was significantly greater in the group managed with enoxaparin, and major bleeding events occurred in 3.3 percent of the patients managed with enoxaparin compared with 1.3 percent of the patients managed with pneumatic compression. As in the study by Colwell et al., in the study by Watson et al. the patients who received the initial dose of enoxaparin at least ten hours postoperatively had significantly fewer complications than those who received the drug within ten hours after the operation \( (p = 0.05) \).

The published literature, therefore, presents a clear dose-response relationship between increasing doses of fractionated heparin and decreasing prevalences of deep venous thrombosis, but fractionated heparin is associated with increasing hemorrhagic complications. This point was well illustrated by Spiro et al., who conducted a dose-response study of 568 patients with a hip replacement who were managed with three different regimens of enoxaparin (ten milligrams daily, forty milligrams daily, or thirty milligrams every twelve hours) for prophylaxis against deep venous thrombosis\(^{123} \). The prevalence of deep venous thrombosis in these groups was reduced to 25, 14, and 11 percent, respectively, as the dose of enoxaparin increased. These reductions were associated with significant increases in the overall rate of hemorrhagic events of 5, 11, and 13 percent, respectively \( (p < 0.05) \). It has become increasingly evident that bleeding complications (especially those related to the operative wound) associated with the use of fractionated heparins at a dose sufficient to substantially reduce the prevalence of deep venous thrombosis occur at considerably greater rates than those observed with a regimen of low-dose warfarin. Considering the many years necessary for surgeons to accept routine use of warfarin as prophylaxis against thromboembolic disease and its attendant rate of bleeding complications of 1 to 2 percent, it is difficult to endorse a regimen of fractionated heparin, which is associated with a substantially greater rate of bleeding episodes during hospitalization. A doption of fractionated heparin as the standard for prophylaxis against thromboembolic disease after total hip replacement does not appear to be justified at this time.

**Pneumatic Compression Devices**

Intermittent pneumatic compression devices provide intermittent inflation of air-filled cuffs, which increase the velocity of venous blood flow to overcome
venous stasis. Intermittent pneumatic compression devices offer many advantages over pharmaceutical methods: patients have a high tolerance for these devices, there is no associated risk of bleeding, and laboratory monitoring is not required. The pumping mechanism of the sleeve and boots appears to stimulate endogenous fibrinolytic activity; when applied to the arm, intermittent pneumatic compression devices have been shown to decrease the development of deep venous thrombosis in the lower extremities. These devices should not be used on patients who have acute deep venous thrombosis; they also cannot be applied to patients who have a fracture of the lower extremity. Recently, pulsatile foot pumps have been reported to be effective in preventing venous thromboembolic disease after total hip replacement.

In patients who are at high risk for deep venous thrombosis, intermittent pneumatic compression has been shown to decrease the prevalence of deep venous thrombosis. Clinical studies combining elastic stockings and intermittent pneumatic compression have shown a decrease in the prevalence of venous thromboembolism. However, Keith et al. were unable to show that use of a combination of graduated compression elastic stockings and intermittent pneumatic compression had an additive effect on peak velocity of venous blood flow in the superficial femoral vein. Studies comparing the effectiveness of these two methods when used alone for the prevention of deep venous thrombosis are lacking. A number of investigations have demonstrated that mechanical devices designed to reduce venous stasis are effective in reducing the overall rate of deep venous thrombosis after total joint replacement and traumatic injury. In at least three studies specifically concerning total hip replacement, the overall rate of deep venous thrombosis in patients managed with pneumatic compression sleeves was not found to be significantly different from that in patients managed with warfarin. Interestingly, some of those studies demonstrated a complementary decrease in distal deep venous thrombosis and a worrisome increase in proximal deep venous thrombosis after total hip arthroplasty, suggesting relative inefficacy of thigh-high pneumatic compression sleeves in the prevention of proximal thrombosis compared with warfarin prophylaxis.

Paiement et al. compared the effect of intermittent pneumatic compression in sixty-six patients with that of warfarin in seventy-two patients after total hip replacement. The overall prevalence of deep venous thrombosis in the groups was not found to be significantly different (p = 0.05); however, the location of the thrombi, as determined by radiographic phlebography, was 31 percent for the patients managed with warfarin and 27 percent for those managed with pneumatic compression sleeves. Intermittent pneumatic compression offered better protection against thrombi in the calf, and warfarin offered better protection against thrombi in the thigh. Francis et al. reported similar results in a series of 201 patients who had had a total hip replacement; the overall prevalence of deep venous thrombosis, as determined by screening with contrast venography, was 27 percent for those who received warfarin and 21 percent for those managed with warfarin (p = 0.021). Conversely, warfarin resulted in a significant decrease in the prevalence of proximal deep venous thrombosis (3 percent) compared with that observed with pneumatic compression (12 percent) (p = 0.012). The proximal thrombi in this trial were typically located within fifteen centimeters of the femoral head and were segmental and not continuous with thrombi in the deep veins of the calf.

In a study of intermittent pneumatic compression after total hip replacement, Wille-Jørgensen et al.

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**Table II**

*RATES OF DEEP VENOUS THROMBOSIS ASSOCIATED WITH USE OF INTERMITTENT PNEUMATIC COMPRESSION AS REPORTED IN THE LITERATURE*

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients Managed with Intermittent Pneumatic Compression</th>
<th>Overall Rate of Deep Venous Thrombosis (percent)</th>
<th>Rate of Proximal Deep Venous Thrombosis* (percent)</th>
<th>Rate of Pulmonary Embolism* (percent)</th>
<th>Additional Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradley et al., 1993</td>
<td>30</td>
<td>7</td>
<td>3</td>
<td>NA</td>
<td>Heparin</td>
</tr>
<tr>
<td>Francis et al., 1992</td>
<td>201</td>
<td>27</td>
<td>12</td>
<td>NA</td>
<td>Heparin</td>
</tr>
<tr>
<td>Grady-Benson et al., 1994</td>
<td>110</td>
<td>18</td>
<td>9</td>
<td>1</td>
<td>NA</td>
</tr>
<tr>
<td>Hooker et al., 1999</td>
<td>502</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>Heparin</td>
</tr>
<tr>
<td>Kaempfle et al., 1991</td>
<td>48</td>
<td>16</td>
<td>12</td>
<td>NA</td>
<td>Aspirin</td>
</tr>
<tr>
<td>Lieberman et al., 1994</td>
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<td>6</td>
<td>0</td>
<td>1</td>
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<tr>
<td>Paiement et al., 1987</td>
<td>66</td>
<td>17</td>
<td>14</td>
<td>0</td>
<td>Aspirin</td>
</tr>
<tr>
<td>Paiement et al., 1992</td>
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<td>20</td>
<td>17</td>
<td>17</td>
<td>Aspirin</td>
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<td>Woolson et al., 1996</td>
<td>322</td>
<td>6</td>
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</tbody>
</table>

*NA = not available.
noted a reduction in thromboembolism in patients managed with epidural anesthesia compared with those managed with general anesthesia. The prevalence of deep venous thrombosis was determined by plasmapheresis with technetium-99m, and the prevalence of pulmonary embolism was assessed by pulmonary perfusion scans and ventilation scintigraphy. The prevalence of deep venous thrombosis was reduced from 31 to 9 percent, whereas the prevalence of pulmonary embolism decreased from 9 to 3 percent. Similarly, Woolson, in a study of the efficacy of intermittent pneumatic compression after 289 primary or revision total hip replacements, reported an overall prevalence of deep venous thrombosis, as determined by venous ultrasonography, of 6 percent; the prevalence of proximal thrombi was 4 percent for the patients who had regional anesthesia compared with 11 percent for the patients managed with general anesthesia (p = 0.02). Bradley et al. compared the combination of intermittent plantar venous compression, thigh-high antiembolism stockings, and pharmacological prophylaxis (a combination of heparin and hydroxychloroquine) in 31 to 9 percent, whereas the prevalence of pulmonary embolism decreased from 9 to 3 percent. The prevalence of deep venous thrombosis was determined by bilateral ascending venography, was 7 percent in the former group and 27 percent in the latter (p = 0.025).

Although the optimum characteristics of these pumps for the reduction of the rate of deep venous thrombosis and pulmonary embolism are not yet known, it has been proposed that intermittent pneumatic compression is effective by means of two mechanisms. The primary mechanism is the ability to decrease venous stasis or to accelerate venous emptying, and a secondary mechanism is the ability to increase fibrinolysis. Sequential compression of the calf may offer advantages over single-chamber compression; sequential gradient thigh-high compression produces a 240 percent increase in the peak velocity of femoral blood flow compared with a single-chamber device, which produces a 180 percent increase in peak velocity. Sequential gradient thigh-high compression clears venographic contrast medium from the thigh eight times more quickly than single-chamber compression of the calf does. Nonetheless, in some studies these devices have been associated with increased rates of proximal thrombosis and reduced rates of distal thrombosis when compared with the use of warfarin. The available devices differ in a number of ways, including the length and location of the sleeve and the bladder, the frequency and duration of activation, the rate at which the pressure increases and the maximum pressure that is achieved, and whether the compression is simultaneous or sequential. Interest in this area has appropriately refocused attention on physiological exercises performed in bed; unassisted active movement of the ankle increases femoral venous flow by more than 75 percent compared with baseline resting values.

Intermittent pneumatic compression offers both theoretical and practical advantages over pharmacological prophylaxis against venous thromboembolism — namely, safety, absence of bleeding complications, and efficacy in reducing calf thrombosis. Notably, in some studies, proximal deep venous thrombosis after total hip replacement has been rather refractory to calf-thigh compression alone as a means of prophylaxis.

Screening Tests for Deep Venous Thrombosis

Despite negative findings for deep venous thrombosis on contrast venography and ultrasonography after total hip replacement, a small percentage of patients nonetheless sustain a pulmonary embolism. It has been postulated that the occult source of these emboli may be within the deep veins of the pelvis.

Traditional screening techniques for the detection of deep venous thrombosis include contrast venography and color Doppler ultrasound. Conventional contrast venography of the lower extremity, performed by means of cannulation of a dorsal vein in the foot, is limited with regard to the assessment of pelvic thrombosis. In addition, the potential risk of allergy to the contrast medium is well documented, as are the risks of local soft-tissue damage created by extravasation of contrast medium at the site of puncture and postvenographic thrombosis. Direct femoral venipuncture affords superior visualization of the external iliac and common iliac veins of the pelvis; however, visualization of the internal iliac veins is impaired because of the fact that contrast medium injected distally must reflux against the flow in the venous direction. In addition, direct femoral venipuncture over a site of a recent hip replacement raises concerns about local hematoma formation and the potential for infection.

Color Doppler ultrasound has been very effective in the detection of symptomatic deep venous thrombosis. A similar to the use of this modality as a screening tool for the identification of nonocclusive asymptomatic thrombosis in the postoperative setting provides a greater challenge. Thrombi in the thigh have been successfully identified in several centers; however, identification of thrombi in the calf is highly variable, with sensitivities as low as 12 percent compared with venography. Similarly, visualization of pelvic veins is limited by the ileus in association with the administration of narcotic analgesic agents, which cause air reflection of the ultrasound beam as well as noncompressibility of the deep veins of the pelvis. In one large series in which contrast venography was compared with color Doppler ultrasound in 2000 patients who had had an orthopaedic operation, the sensitivity of ultrasound in the detection of asymptomatic proximal deep venous thrombosis was found to be only 62 percent compared with venog-
raphy. A multicenter study including 385 patients who had had unilateral hip or knee replacement also demonstrated that color Doppler ultrasound had poor sensitivity (38 percent) in the detection of proximal venous thrombosis. The advantages of color Doppler ultrasound include its noninvasive nature, relatively low cost, and portability, which allows procedures to be performed at the bedside. It is, however, highly operator-dependent, with accuracy varying widely depending on the expertise and the experience of the technician.

Given these limitations of both contrast venography and color Doppler ultrasound in the detection of both proximal and pelvic thrombosis, additional methods of diagnostic assessment are necessary. Magnetic resonance venography is an imaging technique providing venographic detection on the basis of the magnetic properties of soft tissue. Conventional magnetic resonance venography has successfully identified occult deep venous thrombosis following acetabular and pelvic trauma, in the initial study by Montgomery et al., contrast venography failed to detect 58 percent of the thrombi detected by magnetic resonance venography, most of which were localized in the pelvis. However, a high association between the findings of conventional contrast venography and those of magnetic resonance venography has been documented in preliminary studies of patients without acetabular or pelvic trauma. Conventional magnetic resonance venographic techniques use a noninvasive imaging sequence, which provides increased signal based on flow characteristics, allowing for bilateral evaluation of the veins in the thigh and the pelvis with no contrast agent (Fig. 2). Differential venographic or arteriographic techniques are afforded by use of a saturation pulse, which selectively eliminates flow in either the venous or the arterial direction. High signal intensity of fully magnetized protons in flowing blood is contrasted with the low signal intensity of the stationary saturated background tissue. Individual axial images are so-called stacked by a computer algorithm into a projected image that simulates a conventional angiogram. Careful study of these individual axial sections is essential to discern diminished signal secondary to turbulent flow related to the cardiac cycle or at areas of bifurcation of vessels from fixed intraluminal saturation that is indicative of deep venous thrombosis (Fig. 3). This technique also helps to distinguish extrinsic compression, which can simulate venous occlusion on a reformatted image, from true intraluminal thrombosis.

Contraindications to the use of magnetic resonance venography include the presence of a pacemaker, certain otological and penile implants, and most cerebral aneurysm clips. It is generally recommended that patients who have indwelling vascular stents and inferior vena cava filters wait six weeks before magnetic resonance imaging. In addition, claustrophobic patients may not tolerate magnetic resonance imaging and morbidly obese patients may not fit into the center of the imaging bore. The presence of orthopaedic instrumentation, including hip-replacement components, does not preclude these techniques. In a report on an early experience with magnetic resonance venography after hip replacement, occult thrombi in the pelvic veins that had not been documented on contrast venography or Doppler ultrasound were identified in three of fifteen patients. Nonetheless, variable segments of signal loss adjacent to the acetabular component have been observed, whereas depiction of the profunda femoris vein and the superficial femoral veins adjacent to the femoral component has been superior to that with conventional contrast venography and ultrasound. The orientation of acetabular screws, particularly in patients who had a revision, is divergent from the long axis of the magnetic field and
creates greater focal disturbance and image artifact. Alterations in technique, use of fast spin-echo sequences, and use of gadolinium compounds as contrast agents have helped to improve the visualization of the pelvic veins adjacent to the acetabulum.

Magnetic resonance venography is an evolving technique that is superior to either conventional contrast venography or color Doppler ultrasound in detecting occult thrombi in the pelvis.

**Discussion**

With improved operative and anesthetic techniques that afford accelerated rehabilitation, the prevalence of fatal pulmonary embolism after total hip arthroplasty has declined in recent years independent of routine anticoagulant prophylaxis. Additionally, predeposit of autologous blood is associated with a reduction in the overall prevalence of venous thromboembolic disease. Notwithstanding, venous thromboembolism remains the single greatest threat to the life of a patient during the extended postoperative period after total hip arthroplasty. Although several advances in anesthetic and perioperative management have had a favorable impact on the prevalence of venous thromboembolism, controversy continues with respect to the issues of appropriateness and type of routine prophylaxis.

It has been conclusively shown that spinal anesthesia and epidural anesthesia reduce blood loss and the development of thromboembolism compared with general anesthesia. The benefit is even more substantial if hypotension is added; its safety in older adults has been documented in a prospective, randomized trial. A surgeon who operates on a bloodless field can proceed expeditiously, without the delay caused by persistent bleeding and repeated attempts at hemostasis and with perfect visualization of the anatomical structures. The importance of an effective and expeditious operation cannot be overemphasized, as there is a direct association between the duration of the operation (particularly the duration of femoral vein occlusion), the amount of blood loss, and the prevalence of postoperative thromboembolic disease. Patients who are managed with spinal or epidural anesthesia do not recover active motion of the lower extremities for a few hours after the operation, which further compromises the venous return. The prompt application of mechanical devices immediately after the operation increases venous flow, preventing or minimizing the formation and propagation of clots. Once motor function has been recovered, active dorsiflexion of the foot and ankle increases femoral venous flow and such motion should be strongly encouraged. Intermittent pneumatic compression devices mimic this effect on the augmentation of venous return and exert a beneficial effect in reducing deep venous thrombosis in the calf. Use of intermittent pneumatic compression devices alone for prophylaxis against venous thromboembolism after total hip replacement, however, has been associated with an increase in the

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**FIG. 3**

Individual axial source time-of-flight magnetic resonance image of a patient made after a recent right total hip arthroplasty, demonstrating a subtle focus of diminished signal intensity (arrow) within the external iliac vein adjacent to the acetabular component (asterisk), indicating an acute thrombosis. 
prevalence of proximal thrombi in two prospective, randomized clinical trials.

Selective heparin anticoagulation administered a few minutes before the intense activation of the clotting cascade, which occurs during femoral preparation, has been shown to reduce or obliterate the thrombogenic stimulus. The response is dose-related. Likewise, limiting the time that the lower extremity is maintained in a position that causes extreme torsion of the femoral vein reduces venous stasis and endothelial injury. Preheating of the femoral stem or the cement, or both, can reduce the time of polymerization, without an adverse effect on their biomechanical properties.

Beyond these intraoperative maneuvers, the issue of routine chemical prophylaxis against venous thromboembolism remains controversial and has been challenged recently by the British orthopaedic community. The suggestion of Murray et al. that the effectiveness of thromboprophylaxis should be assessed on the basis of overall rates of mortality is plausible, but the concept of Dunsmuir et al. of so-called accelerated mortality caused by an operation with no absolute effect on overall mortality is less intuitive. Although historical death rates attributable to pulmonary embolism have ranged from 2.2 to 3.4 percent, a meta-analysis from the United Kingdom of more recent studies has suggested that the rate of fatal pulmonary embolism even in the absence of chemical prophylaxis is 0.1 to 0.2 percent. The cumulative experience of five single-center series of 1079, 1099, 1492, 2592, and 3000 patients in North America demonstrated an average rate of fatal pulmonary embolism of 0.09 percent (range, 0.2 percent. The cumulative experience of five single-center series of 1079, 1099, 1492, 2592, and 3000 patients in North America demonstrated an average rate of fatal pulmonary embolism of 0.09 percent (range, 0.2 to 0.18 percent) or less with either warfarin or aspirin.

The suggestion of Murray et al. that the effectiveness of routine anticoagulation as prophylaxis against venous thromboembolic disease has been demonstrated in association with epidural and spinal anesthesia in patients who do not have additional risk factors for venous thromboembolic disease.

A review of the North American experience with low-molecular-weight heparins reveals that the risk of serious bleeding, especially that related to the operative wound, is significantly higher (p = 0.034 for wound-related bleeding complications) for patients managed with heparin than for those managed with warfarin.

Imperfect as it is, warfarin has demonstrated efficacy for prophylaxis against venous thromboembolism after hip replacement, especially for patients with other risk factors for venous thromboembolic disease. Use of warfarin may begin the day before the operation. As the thrombogenic stimulus occurs during the operation, the effectiveness of such delayed anticoagulation would be decreased in the interest of safety. In view of this increased risk of bleeding complications, the popularity of fractionated heparins appears to be declining.

The most popular techniques for the assessment of deep venous thrombosis after total hip replacement have included venography (considered the so-called gold standard) and ultrasound. Ultrasound is insensitive in the identification of thrombi in the calf and variable in its ability to identify proximal thrombi; therefore, it is a poor surveillance tool for the identification of asymptomatic deep venous thrombosis in most institutions. Neither ultrasound nor conventional venography routinely visualize intrapelvic clots. Advances in magnetic resonance imaging of the venous system permit noninvasive identification of clots in both lower extremities, including the iliac veins. The early experience with this technique has demonstrated clots in the external iliac veins, even in patients who had negative findings on venograms and ultrasound studies. This finding may explain the occurrence of pulmonary embolism in patients who had negative findings on venography or ultrasound. The implications of clots in the iliac veins need to be defined, as the potential threat and morbidity associated with venous clots increase as the location becomes more proximal. A noninvasive and reliable method of sur-
veilance for deep venous thrombosis might allow for a strategy of selective anticoagulant therapy after discharge from the hospital and for better secondary prevention of fatal embolic events, without unnecessary exposure of a larger group of patients to the risks of outpatient anticoagulation.

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