Venous thromboembolism is a major cause of death and morbidity among hospitalized patients. In this setting, it has been estimated that pulmonary embolism (PE) causes death in more than 100,000 patients each year in the United States and contributes to the death of another 100,000.1,2 These estimates have been substantiated in a community-wide study conducted in 16 short-stay hospitals in metropolitan Worcester, Mass, where the annual incidence of verified PE was 23/100,000 central Massachusetts residents with an in-hospital case fatality rate of 12%.3 Extrapolation of these data suggests that approximately 260,000 cases of clinically recognized venous thromboembolism occur each year in patients hospitalized in acute-care hospitals in the United States. The disease, however, is most often clinically silent with PE being unsuspected in 70 to 80% of patients whose conditions are diagnosed at autopsy.5,6 Because of the low rate of autopsy in the United States and the failure of the Worcester study to include nonacute-care facilities such as rehabilitation hospitals and nursing homes where the incidence of PE may be higher, the actual incidence of venous thromboembolism is much greater. Such considerations led to the conclusion that fatal PE may be the most common preventable cause of hospital death.6 PE and deep venous thrombosis (DVT) are particularly common in the elderly, both increase with age with no special predilection for sex and race.7

The rationale for prophylaxis of venous thromboembolism is based on the clinically silent nature of the disease. Both DVT and PE manifest few specific symptoms, and the clinical diagnosis is insensitive and unreliable.8 To rely on the diagnosis and treatment of established venous thromboembolism may expose susceptible patients to unacceptable risks. The first manifestation of the disease may be fatal PE. Although anticoagulant therapy is highly effective in treating venous thromboembolism, most patients who die of PE do so within 30 min of the acute event, too soon for anticoagulation to be effective.9 Unrecognized and untreated DVT may also lead to long-term morbidity from the postthrombotic syndrome and predispose patients to future episodes of recurrent venous thromboembolism. An alternative to prophylaxis would be to use serial surveillance tests such as impedance plethysmography or duplex ultrasonography in high-risk patients.10,11 Although attractive, this approach is expensive and can be applied to only limited numbers of patients at risk. In addition, impedance plethysmography and duplex ultrasonography have been shown to have only moderate sensitivity and positive predictive value when used in asymptomatic, high-risk patients such as those undergoing major orthopedic surgery.12-14 Most experts believe that broad application of effective methods of prevention is more cost-effective than selective, intensive surveillance.15-20

Despite overwhelming evidence of the efficacy of a wide variety of prophylactic agents, surveys conducted in the United States,21-22 England,23 Sweden,24,25 Switzerland,26 Spain,27 and Australia28 document wide practice variations among physicians with 28 to 100% of respondents indicating that they routinely used prophylaxis. In the most recent survey in the United States, 90% of randomly selected fellows of the American College of Surgeons favored use of prophylaxis.21 However, because of limited response rate and the possibility of sampling bias, these findings may not be representative of current practice standards among all physicians caring for patients at risk. A 1986 study of more than 2,000 patients with multiple risk factors hospitalized at 16 acute-care hospitals showed that only one third of these patients received prophylaxis.29 Use of prophylaxis was higher in teaching than nonteaching hospitals, and patients undergoing vascular, abdominal, and orthopedic operations were the most likely to receive prophylaxis. Risk factors for venous thromboembolism were highly prevalent in this population of hospitalized patients; 78% of all patients had one or more risk factors, 48% had two or more, and 19% had three or more. The authors concluded that despite widespread recognition of the problem and the effectiveness of multiple preventive strategies, prophylaxis is underutilized at present.29

Why do physicians fail to use prophylaxis more widely? Many believe that the overall incidence of venous thromboembolism among hospitalized and postoperative patients has decreased over the past decades to the point where the incidence is too low to consider prophylaxis. These physicians frequently cite informal, retrospective surveys of their own clinical services and the rare occurrence of fatal PE diagnosed by autopsy at their hospital to bolster this argument. In fact, the incidence of venous thromboembolism has declined in recent years,30,31 and this probably reflects the success of prophylactic strategies.32,33 Even so, the incidence remains too high for a condition that is preventable, and the current estimates of the incidence of fatal PE based on hospital discharge data suggest the need for even wider application of prophylaxis.34 Furthermore, the difficulties in establishing the antemortem diagnosis of PE have been alluded to as well as the low rate of autopsy in the United States, especially in elderly patients with chronic conditions. Data from countries where autopsy is common indicate that PE remains a significant problem.32,34,35 In addition, contemporary data from the central Massachusetts study show that clinically recognized PE is surprisingly common.3

Another reason for failure to use prophylaxis, especially in surgical patients, is the concern about bleeding complications from anticoagulants. Countering this argument are the abundant data from meta-analyses and placebo-controlled, double-blind randomized trials that demonstrate no significant increase in major bleeding with the use of low-dose unfractionated heparin (LDUH) and low molecular weight heparin (LMWH).36-40 The incidence of wound hematomas is increased with these agents,36,38 and this can be an important problem resulting in wound infection, dehiscence, and infection of a prosthetic device placed at the time of operation. The magnitude of the problem of hematoma occurrence, unfortunately, has been downplayed or ignored by many advocates of prophylaxis who are not surgeons. However, alternative, mechanical methods of effective prophylaxis...
laxis that carry no bleeding risk are available for such patients.36 Heparin-induced thrombocytopenia has also been raised as a concern with widespread use of heparin preparations. Critical review of this problem, though, suggests that the rate of thrombocytopenia with this route of heparin administration is about 3%; the incidence of vascular thrombosis associated with heparin-induced thrombocytopenia is uncommon.41 In addition, the costs of prophylaxis have also been used as an argument against its wider use; however, as argued above, every study addressing this issue has concluded that broad application of prophylaxis is highly cost-effective.15-20,42

The final reason for not using prophylaxis has to do with subjective perceptions of the magnitude of the problem and the effects of prophylaxis in individual practices. Because venous thromboembolism is most often clinically silent, the occurrence of overt venous thromboembolism among an individual physician’s patients is perceived to be rare.43 For example, extrapolation of data from meta-analyses suggests that fatal PE occurs in 0.5 to 0.8% of unprotected patients older than 40 years undergoing major abdominal surgery, and in many of these, the diagnosis and cause of death would not be known.17,36,37 Similarly, proximal or above-knee DVT is present in 6 to 7% of general surgical patients, and less than 50% of these DVTs would be clinically overt and detected. Therefore, an average busy surgeon whose practice consists of a high volume of major abdominal surgery may not perceive venous thromboembolism to be a significant problem. More importantly, this physician may have little appreciation of the effectiveness of, for example, LDH in reducing the incidence of fatal PE in the individual practice from 0.7 to 0.2%, as would be expected by extrapolation of data from meta-analyses dealing with large numbers of patients.36,37 Thus, from an individual practice perspective, it is difficult to appreciate the effectiveness of prophylaxis, whereas failures (patients developing clinically overt venous thromboembolism who receive prophylaxis) are readily apparent. Additionally, bleeding complications are highly visible, not easily forgotten, and frequently blamed on prophylaxis.

Educational programs are important in countering misperceptions about prophylaxis. A recent prospective study documented a nearly twofold increase in prophylaxis from 29 to 52% among hospitalized patients at risk with the inception of educational strategies designed to increase awareness of the problem of venous thromboembolism.44 Use of prophylaxis was significantly greater in hospitals whose physicians participated in formal continuing medical education programs. A key factor that motivated clinicians to change practices was the provision of hospital-specific data demonstrating compelling need for improvement.

Risk Factors

Application of effective prophylaxis depends on knowledge of specific clinical risk factors in individual patients. Clinical risk factors include advanced age (that clinically becomes important by 40 years and increases with further aging); prolonged immobility or paralysis; prior venous thromboembolism; cancer; major surgery (particularly operations involving the abdomen, pelvic, and lower extremities); obesity; varicose veins; congestive heart failure; myocardial infarction; stroke; fractures of the pelvis, hip, or leg; and, possibly, high-dose estrogen use.45-47 In addition, congenital and acquired aberrations in hemostatic mechanisms (hypercoagulable states) that ordinarily predispose to venous thromboembolism assume even greater risk when afflicted patients are hospitalized and undergo surgical procedures. Hemostatic abnormalities include activated protein C resistance (factor V mutation); antithrombin III deficiency; protein C deficiency; protein S deficiency; dysfibrinogeneration; disorders of plasminogen and plasminogen activation; antiphospholipid antibodies and lupus anticoagulant; heparin-induced thrombocytopenia; myeloproliferative disorders such as polycythemia vera; and hyperviscosity syndromes.38-51

In many patients, multiple risk factors may be present, and the risks are cumulative.52 For example, elderly patients with hip fractures undergoing major orthopedic operations who remain immobile in bed after operation are among the most susceptible to fatal PE. Awareness of the risk of venous thromboembolism in general categories and in clinical settings in which the risk has been defined by epidemiologic studies is also important in successful application of prophylaxis.53 For example, the overall incidence of venous thromboembolism is higher on orthopedic services and in ICUs than on general medical services.

The sections that follow are based on disease states and hospital services to which patients are admitted. In each patient category, the overall risks of venous thromboembolism and effective methods of prophylaxis are detailed. Although the order of presentation reflects the relative completeness with which each category has been studied, most patient groups have been studied sufficiently so that firm recommendations (grade A) can be made with regard to the benefits and risks of pharmacologic and physical methods to prevent venous thromboembolism. This area of medicine has been subjected to numerous randomized clinical trials, and level I data are abundant. Because of the completeness of data, general agreement among studies, and the large number of trials, data will be pooled when appropriate.

General Surgery

The overall incidence of thromboembolic end points in general surgical patients was calculated by pooling data in control patients in published English-language trials of prophylactic methods (Table 1). In most trials, the bulk of these patients had elective GI surgery. However, some of the patient populations were more heterogeneous and included individuals undergoing gynecologic, thoracic, urologic, and vascular operations. Almost all patients were older than 40 years. The overall incidence of DVT as assessed by the labeled fibrinogen uptake test (FUT) was 25% in control subjects. In trials in which the FUT was confirmed by plethysmography, the incidence was 19%. In surgical patients with malignant disease, the incidence of DVT was 29%. Interestingly, in pooled data from North American trials, the incidence was about one half that of European trials. It is unknown whether this represents higher-risk patients in European trials, true regional differences in the incidence of venous thromboembolism, or differences in standards of care. The presence of proximal or above-knee DVT was 6 to
The overall incidence of clinically recognized PE (fatal and nonfatal) was 1.6% and the incidence of fatal PE was 0.8%. The incidences of these more serious end points among control patients probably underestimate what would be expected generally among surgical patients in whom prophylaxis is withheld because most patients in the trials received anticoagulant therapy when serial FUT scans became abnormal.

In Table 2, the effect of commonly used prophylactic regimens is tabulated. Among antithrombotic drugs, LDUH and LMWH are the most effective in reducing the incidence of DVT as assessed with FUT. They have been the most completely studied and have been the subject of numerous overview meta-analyses in general surgical patients.\textsuperscript{36-40,54} Because of the large number of randomized trials comparing LDUH with placebo or other antithrombotic drugs, end points such as proximal DVT and PE can also be assessed. Most of these trials are level I (some are level II) and grade A recommendations can be made.

In 29 trials in which more than 8,000 general surgical patients were randomized to LDUH or control groups, the regimen of subcutaneous heparin (5,000 U) started 2 h before operation and continued every 8 or 12 h after surgery for 7 days (or when patients were fully ambulatory or discharged from the hospital) was studied.\textsuperscript{55-83} Low-dose heparin therapy was consistent in reducing the incidence of DVT assessed by FUT alone or FUT confirmed by phlebography. The overall incidence of leg DVT was reduced from 25 to 8%. Although there were no randomized trials comparing the every-12-h regimen with the every-8-h regimen, one meta-analysis showed that LDUH given every 8 h was more effective.\textsuperscript{36} The beneficial effect was also observed in trials in which patients with malignant disease were studied. Pooled data from meta-analyses show that LDUH also reduced the more serious end points of proximal DVT, clinically diagnosed PE, and fatal PE diagnosed at autopsy.\textsuperscript{36,37} These studies showed a 50% reduction in fatal PE with LDUH prophylaxis. Three large studies were designed to test the efficacy of LDUH in preventing fatal PE and all three of these studies showed a significant beneficial effect.\textsuperscript{35,84,85}

LMWH appears to be only slightly better than LDUH in preventing venous thromboembolism (Table 2) and may be associated with slightly fewer bleeding complications.\textsuperscript{36-96} Recent data indicate that LMWH causes fewer wound hematomas than does LDUH.\textsuperscript{38} A critical meta-analysis comparing LMWH with LDUH determined that both agents were equivalent in prophylaxis of venous thromboembolism in general surgical patients.\textsuperscript{38} Both strategies are highly successful in high-risk patients, and the marginal advantages of LMWH may be offset by its higher expense. At present, LMWH costs about tenfold to 20-fold more per dose than LDUH (in Europe, it is only three times the cost). Because LMWH has a prolonged half-life and can be given once daily, it has been promoted as being more convenient than bid or tid LDUH. Low-dose heparin combined with dipyridamole is also effective,\textsuperscript{73,97-105} but has been withdrawn from the market in the United States.

Intermittent pneumatic compression (IPC) is an attractive method of prophylaxis because there is no risk of hemorrhagic complications. These devices provide rhythmic external compression (ideally, one compression lasts about 10 s/min with inflation pressures of 35 to 40 mm Hg to the legs or thighs). IPC has not been as well studied as other agents used for general surgical patients. However, it is effective in reducing leg DVT in most general surgical patients and in high-risk surgical patients with malignant disease.\textsuperscript{38} It is also moderately effective in patients undergoing major
orthopedic surgery. In trials comparing IPC with LDUH, both agents were equivalent in reducing leg DVT. It is not proven that IPC prevents PE in general surgical patients, but if leg DVT is a valid marker for PE, this would be the case.

Graded compression elastic stockings (ES) reduce the incidence of leg DVT (Table 2), but too few data are available to assess their protective effect on proximal DVT and PE. Patients with malignant disease and other high-risk general surgical conditions have not been evaluated in sufficient numbers to allow firm conclusions with regard to the efficacy of ES in these clinical settings. In some of the randomized trials, high-risk patients were specifically excluded. Further clinical trials are needed to assess the effectiveness of ES in such patients. Another limitation is that 15 to 20% of patients cannot effectively wear ES because of unusual limb size or shape. Because the ES are relatively cheap and free of side effects, it would be important to know their efficacy in comparison with other prophylactic methods. To our knowledge, there are no studies in general surgical patients comparing ES with LDUH or other agents. Combining ES with other prophylactic agents, such as LDUH, may give better protection against venous thromboembolism than either approach alone.

The ES counteract venous stasis and augment venous return during abdominal insufflation for laparoscopic procedures; however, it is not known if this is adequate protection against venous thromboembolism.

Dextran, a branched polysaccharide of 40,000 or 70,000 d, is not as efficacious in preventing leg DVT as are LDUH and LMWH (Table 2). However, in randomized trials, dextran has been shown to reduce the incidence of PE and in a single randomized double-blind trial, dextran significantly lowered the incidence of autopsy-verified fatal PE. Furthermore, in comparison trials, dextran and LDUH were equivalent in protecting against PE. Although dextran does not prevent leg vein DVT as well as LDUH, it appears effective in halting growth and extension of thrombi so that PE is prevented. Dextran has not been a popular antithrombotic agent because it is relatively expensive and must be administered by IV. It has also been associated with rare anaphylactic responses and is contraindicated in patients with renal insufficiency and limited cardiac reserve. Although both dextran and LDUH may interfere with hemostasis, wound hematomas appear to be less common with dextran prophylaxis. This advantage might offset the expense and cumbersome aspects of dextran treatment in selected patients prone to wound hematomas with LDUH and in whom hematomas would be particularly undesirable.

Aspirin generally has been found to be ineffective in preventing venous thromboembolism in general surgical patients and has not been recommended as an appropriate strategy. This view has been challenged by a recently published meta-analysis of the Antiplatelet Trialists’ Collaboration, which concluded that perioperative antiplatelet treatment reduced the incidence of DVT in general surgical patients by 37% and PE by 71% in comparison to untreated controls. These reductions were highly significant and similar effects were reported in patients undergoing orthopedic and other operations. Because of its low expense, ease of administration, and lack of side effects, aspirin would appear to be an ideal antithrombotic agent to prevent venous thromboembolism. However, a closer scrutiny of the Antiplatelet Trialists’ Collaboration group’s method leads to many questions. They analyzed collectively more than 30 antiplatelet trials of variable scientific design. Such an inclusive approach may allow subtle biases present in some trials to be magnified when subjected to meta-analysis. Another recent meta-analysis, which included only rigorous, scientific trials, concluded against the efficacy of aspirin. In this analysis, trial eligibility criteria included proper randomization of patients to aspirin or control groups.

Table 2—Prevention of DVT After General Surgery (Pooled Data From Trials Based on FUT)

<table>
<thead>
<tr>
<th>Regimen (References)</th>
<th>No. of Trials</th>
<th>No. of Patients</th>
<th>No. of Patients With DVT</th>
<th>Incidence, %</th>
<th>95% Limits</th>
<th>Reduction of Relative Risk, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreated controls</td>
<td>54</td>
<td>4,310</td>
<td>1,084</td>
<td>25</td>
<td>24-26</td>
<td>—</td>
</tr>
<tr>
<td>Low-dose heparin</td>
<td>50</td>
<td>7,716</td>
<td>646</td>
<td>8</td>
<td>7-9</td>
<td>68</td>
</tr>
<tr>
<td>LMWH</td>
<td>12</td>
<td>4,386</td>
<td>226</td>
<td>5</td>
<td>4-6</td>
<td>80</td>
</tr>
<tr>
<td>Low-dose heparin/DHE</td>
<td>10</td>
<td>1,082</td>
<td>93</td>
<td>9</td>
<td>7-11</td>
<td>64</td>
</tr>
<tr>
<td>Warfarin</td>
<td>2</td>
<td>67</td>
<td>7</td>
<td>10</td>
<td>3-18</td>
<td>60</td>
</tr>
<tr>
<td>Dextran</td>
<td>10</td>
<td>738</td>
<td>115</td>
<td>16</td>
<td>13-18</td>
<td>36</td>
</tr>
<tr>
<td>Aspirin</td>
<td>5</td>
<td>372</td>
<td>76</td>
<td>20</td>
<td>16-24</td>
<td>19</td>
</tr>
<tr>
<td>IPC</td>
<td>5</td>
<td>313</td>
<td>31</td>
<td>10</td>
<td>7-13</td>
<td>60</td>
</tr>
<tr>
<td>ES</td>
<td>4</td>
<td>300</td>
<td>28</td>
<td>9</td>
<td>6-13</td>
<td>64</td>
</tr>
</tbody>
</table>

*DHE=dihydroergotamine.
Table 3—Classification of Level of Risk (Based on Published Data)*

<table>
<thead>
<tr>
<th>Thromboembolism Event</th>
<th>Low Risk</th>
<th>Moderate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Uncomplicated Minor Surgery in Patients Younger Than 40 yr With No Clinical Risk Factors)</td>
<td>(Major Surgery in Patients Older Than 40 yr With No Other Clinical Risk Factors)</td>
<td>(Major Surgery in Patients Older Than 40 yr Who Have Additional Risk Factors or MI)</td>
</tr>
<tr>
<td>Calf vein thrombosis, %</td>
<td>2</td>
<td>10-20</td>
<td>20-40</td>
</tr>
<tr>
<td>Proximal vein thrombosis, %</td>
<td>0.4</td>
<td>2-4</td>
<td>4-8</td>
</tr>
<tr>
<td>Clinical PE, %</td>
<td>0.2</td>
<td>1-2</td>
<td>2-4</td>
</tr>
<tr>
<td>Fatal PE, %</td>
<td>0.002</td>
<td>0.1-0.4</td>
<td>0.4-1.0</td>
</tr>
<tr>
<td>Successful preventive strategies</td>
<td>No specific measures</td>
<td>ES, LDUH (q12h), and IPC</td>
<td>LDUH (q8h), LMWH, and IPC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LMWH, oral anticoagulants, IPC (+ LDUH or LMWH), and ADH†</td>
<td></td>
</tr>
</tbody>
</table>

*Modified from Salzman and Hirsh.112
†ADH=adjusted-dose heparin.

appropriate diagnostic tests (FUT confirmed by venography, or venography in all patients), and interpretation of tests without knowledge of treatment. Only six trials in general surgical patients fulfilled these criteria, and aspirin-treated patients and controls had similar incidences of DVT. The authors concluded that aspirin is of no benefit in preventing venous thromboembolism in general surgical patients. In orthopedic patients, there was a modest and significant benefit, but much less than other forms of prophylaxis.

Warfarin, given either as a fixed low dose (2 mg/d)123 or adjusted dose to mildly prolong the prothrombin time (low-intensity warfarin)120 appears effective in preventing leg DVT. However, the method is cumbersome, requires monitoring, probably requires preoperative treatment, and may be subject to bleeding complications if drug effects are not closely monitored. Because of these shortcomings and the ready availability of other effective agents, there is little rationale to use warfarin in most general surgical patients. Warfarin may be an appropriate choice in selected, very high-risk general surgical patients, but data are scant.

An appropriate preventive strategy in individual general surgical patients takes into account the risk of venous thromboembolism, the potential benefits of the various agents, and the expense and possible complications incurred by their use.52,124 Levels of risk are defined in Table 3. In low-risk patients undergoing minor or relatively short operations, who are younger than 40 years of age and have no clinical risk factors, no specific prophylaxis other than early ambulation is necessary. In moderate-risk patients who are older than 40 years of age and are undergoing major operations, but who have no additional clinical risk factors, ES or LDUH given every 12 h would be sufficient. IPC would be a good alternative to these agents. In patients older than 40 years undergoing major surgery with additional risk factors and who are at higher risk of venous thromboembolism, several effective prophylactic methods are available. Low-dose heparin therapy given every 8 to 12 h and LMWH are effective. Dextran or IPC would also be good choices in higher-risk patients, particularly if they are prone to wound problems. Adding ES to any of these methods may give additional protection. In very-high-risk general surgical patients with multiple risk factors, combining the most effective pharmacologic methods with IPC offers excellent protection. In selected high-risk patients, perioperative warfarin therapy, as prescribed for high-risk orthopedic patients, may be an appropriate choice.

Surgery for Elective Hip or Knee Replacement or Hip Fracture

Patients undergoing major orthopedic surgery of the lower limb continue to be at high risk for postoperative venous thromboembolism despite modern surgical techniques and early patient mobilization (Table 4).125-147 Although many perioperative DVTs in these patients are asymptomatic and confined to the calf veins, recent intraoperative transesophageal echocardiography studies suggest that they may have clinical significance.138,149 These studies demonstrate a high rate of intraoperative PE with a coincident increase in pulmonary artery pressure and decrease in mixed venous oxygen saturation. These data coupled with epidemiologic data demonstrating a substantial risk of postoperative PE50-150 make some form of primary prophylaxis warranted in all patients. Withholding primary prophylaxis in favor of noninvasive studies such as postoperative impedance plethysmography or duplex ultrasonography is inadequate because noninvasive tests are not sufficiently sensitive to be an effective screening method in these high-risk patients.12-14,154-156 This has been confirmed in a recent meta-analysis evaluating the accuracy of duplex ultrasound screening for DVT in patients after orthopedic surgery, which found a 62% sensitivity for the detection of proximal thrombi.13

This review of orthopedic surgery patients is confined to published English-language prospective clinical trials that required mandatory postoperative venography for determination of efficacy. In order for efficacy results to be pooled and compared, studies of total hip replacement, total knee
replacement, and hip fracture surgery were analyzed separately due to operation-specific differences in the efficacy of available methods of prophylaxis. Total DVT prevalence rates are reported and only results from single-modality prophylaxis regimens (excluding graded elastic compression stockings) are included.

It is important to note that most clinical trials excluded patients with a history of either venous thromboembolism or clinically significant bleeding. Therefore, published results of efficacy and safety from these trials may not apply to patients judged as at especially high risk for either postoperative venous thromboembolism or bleeding. Physicians should tailor their prophylaxis regimens accordingly for these patients.

**General Prophylaxis Measures**

Several nonpharmacologic prophylaxis methods have been studied, including ES,\textsuperscript{157-159} IPC,\textsuperscript{127,160-166} and early ambulation.\textsuperscript{167} All are of some benefit, with DVT risk reductions of 25 to 82%. In addition, spinal or epidural anesthesia may be associated with a significantly reduced incidence of DVT when compared with general anesthesia.\textsuperscript{169} A recent review found a statistically significantly lower incidence of postoperative DVT with regional anesthesia among patients undergoing elective hip replacement or hip fracture surgery who received no other primary prophylaxis.\textsuperscript{169a} However, the venous thromboembolism prevalence after regional anesthesia remains substantial and warrants additional primary prophylaxis. Inferior vena cava filter placement is a prophylaxis option for patients at extremely high risk for both postoperative venous thromboembolism and bleeding.\textsuperscript{169-171} Insufficient data are available to recommend noncemented over cemented prostheses, continuous passive motion devices for knee replacement patients, or external pneumatic plantar compression.

**Elective Total Hip Replacement Surgery**

Several anticoagulant-based prophylaxis regimens for total hip replacement surgery have been studied (Table 5). Although meta-analysis has shown LDUH\textsuperscript{132} or aspirin\textsuperscript{118} to be more effective than placebo, both are inadequate when compared with other prophylaxis regimens. Preoperative LDUH with postoperative dose adjustment to maintain the activated partial thromboplastin time in the upper range of normal (adjusted-dose heparin) is very effective and should be considered for patients at extremely high risk of postoperative venous thromboembolism due to concomitant risk factors.\textsuperscript{172-174} However, most surgeons consider adjusted-dose heparin prophylaxis to be impractical for routine use.

Low-intensity oral anticoagulation is safe, effective prophylaxis and has been adopted by most orthopedic surgeons in North America.\textsuperscript{130,136,161,175-178} Oral anticoagulants should be administered at a dose sufficient to prolong the international normalized ratio (INR), 2.0 to 3.0. There is controversy as to the timing of the initial dose. One regimen begins very-low-dose warfarin prophylaxis 14 days prior to surgery in an attempt to prolong the preoperative prothrombin time only 1 to 2 s over baseline. Postoperatively, the dose is increased to prolong the INR (2.0 to 3.0).\textsuperscript{162,179} Although this “two-step warfarin” prophylaxis method appears to be safe and effective, it has not been widely adopted. Based on available evidence, the initial oral anticoagulant dose should be administered the evening prior to surgery. Low-intensity oral anticoagulation has the additional advantage of allowing continued prophylaxis after hospital dismissal.

LMWH or heparinoids have been studied extensively and are safe and effective venous thromboembolism prophylaxis.\textsuperscript{125,126,128,174,177,178,180-188} LMWH is more effective than LDUH based on meta-analysis,\textsuperscript{38} and equally effective\textsuperscript{180} or superior\textsuperscript{174} when compared with adjusted-dose unfractionated heparin. Two published trials have compared LMWH with low-intensity warfarin prophylaxis (Table 6).\textsuperscript{177,178} Both trials found no difference in either total DVT or proximal DVT prevalence or bleeding between LMWH and warfarin. Two recent meta-analyses of multiple different prophylaxis regimens concluded that LMWH was most effective, although the differences were small, compared with either low-intensity warfarin or adjusted-dose unfractionated heparin prophylaxis.\textsuperscript{180,189} Therefore, the choice among LMWH, low-intensity oral anticoagulant, or adjusted-dose heparin prophylaxis depends on cost and convenience. One analysis found LMWH to be cost-effective compared with unfractionated heparin when the LMWH cost was no more than 3.7 times the unfractionated heparin cost.\textsuperscript{191} A recent decision analysis based on health-care charges in Canada suggested LMWH to be cost-effective compared with warfarin.\textsuperscript{192} While only one LMWH is currently approved by the Food and Drug Administration for this indication, approval for several other LMWHs or heparinoids is anticipated. Subsequent competition may reduce LMWH cost and improve cost-effectiveness. Several caveats regarding LMWH prophylaxis should be mentioned. Most North American trials commenced LMWH prophylaxis postoperatively in hopes of preventing anticoagulant-associated bleeding complications. A recent literature review to determine the relative efficacy of preoperatively and postoperatively initiated prophylaxis suggested that any difference in efficacy was likely to be small.\textsuperscript{192a} However, additional randomized trials.
are required to resolve this issue. Laboratory monitoring is not required with LMWH prophylaxis. In North America, LMWH is administered subcutaneously twice daily,\textsuperscript{177,183,193} but in Europe only once daily.

**Elective Total Knee Replacement Surgery**

Recent studies have demonstrated that venous thromboembolism following total knee replacement is especially recalcitrant to prophylaxis.\textsuperscript{177,178,194} Four studies have demonstrated IPC to be effective prophylaxis (Table 7).\textsuperscript{163-166} These devices must be applied either intraoperatively or as soon as is feasible postoperatively and worn continuously except during ambulation. The utility of IPC devices is limited by nonuse during physical therapy and patient intolerance. IPC may provide significant benefit as an adjunct to anticoagulant-based prophylaxis regimens. Low-dose heparin\textsuperscript{194} and aspirin\textsuperscript{185} prophylaxis provides marginal efficacy.

Several recent studies have demonstrated fixed-dose unmonitored subcutaneous LMWH initiated postoperatively to be safe and effective.\textsuperscript{177,178,192,194} Five studies compared LMWH with low-intensity warfarin prophylaxis\textsuperscript{177,178c} (Table 8). All trials demonstrated low-intensity warfarin therapy to be relatively ineffective prophylaxis. In addition, the incidence of proximal DVT was significant and similar to that of total hip replacement surgery. All studies demonstrated LMWH efficacy to be superior to low-intensity warfarin therapy, although the venous thromboembolism prevalence in the LMWH groups was still substantial. Although there was no significant difference in major bleeding complications between LMWH, two studies each found a significant

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### Table 5—DVT Prophylaxis Following Total Hip Replacement*

<table>
<thead>
<tr>
<th>Regimen (References)</th>
<th>No. of Trials</th>
<th>No. of Patients</th>
<th>No. of Patients With DVT</th>
<th>Incidence, %</th>
<th>95% CI</th>
<th>Risk Reduction, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control/placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(125-128, 142, 157, 158, 160, 280-284)</td>
<td>13</td>
<td>655</td>
<td>332</td>
<td>51</td>
<td>47-55</td>
<td>—</td>
</tr>
<tr>
<td>Low-dose heparin</td>
<td>6</td>
<td>257</td>
<td>88</td>
<td>34</td>
<td>29-40</td>
<td>32</td>
</tr>
<tr>
<td>(126, 142, 172, 285-287)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted-dose heparin</td>
<td>(172-174)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LMWH</td>
<td>16</td>
<td>2,571</td>
<td>382</td>
<td>15</td>
<td>14-16</td>
<td>71</td>
</tr>
<tr>
<td>(125, 126, 128, 173, 174, 177, 178, 164-188)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-intensity oral</td>
<td>4</td>
<td>637</td>
<td>127</td>
<td>20</td>
<td>17-23</td>
<td>61</td>
</tr>
<tr>
<td>anticoagulant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(161, 177, 178, 285)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two-step warfarin</td>
<td>2</td>
<td>156</td>
<td>43</td>
<td>28</td>
<td>21-35</td>
<td>45</td>
</tr>
<tr>
<td>(162, 179)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>6</td>
<td>357</td>
<td>200</td>
<td>56</td>
<td>51-61</td>
<td>—</td>
</tr>
<tr>
<td>(195, 281, 282, 285, 288, 289)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dextran 70</td>
<td>5</td>
<td>229</td>
<td>68</td>
<td>30</td>
<td>24-36</td>
<td>41</td>
</tr>
<tr>
<td>(179, 252, 284, 285, 290)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPC</td>
<td>4</td>
<td>359</td>
<td>80</td>
<td>22</td>
<td>18-27</td>
<td>57</td>
</tr>
<tr>
<td>(127, 160-162)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graduated compression</td>
<td>2</td>
<td>137</td>
<td>52</td>
<td>38</td>
<td>30-46</td>
<td>25</td>
</tr>
<tr>
<td>stockings (157, 158)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Pooled data from trials requiring mandatory postoperative venography.

\(^{1}\)CI=Confidence interval.

### Table 6—DVT Prophylaxis After Total Hip Replacement: LMWH vs Warfarin

<table>
<thead>
<tr>
<th>Author (Reference)</th>
<th>Drug</th>
<th>Dose, Anti-Xa U</th>
<th>Bilateral Venogram, No.</th>
<th>Total DVT, No. (%)</th>
<th>Proximal DVT, No. (%)</th>
<th>Bleeding, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hull et al* (177)</td>
<td>Heparinoid (Logiparin)</td>
<td>75 U/kg qd</td>
<td>332</td>
<td>69 (21)</td>
<td>16 (5)</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Warfarin</td>
<td>INR</td>
<td>340</td>
<td>79 (23)</td>
<td>13 (4)</td>
<td>4</td>
</tr>
<tr>
<td>RD Heparin</td>
<td>LMWH (Ardeparin)</td>
<td>50 U/kg bid</td>
<td>178(^{1})</td>
<td>12 (7)</td>
<td>5 (3)</td>
<td>7</td>
</tr>
<tr>
<td>Arthroplasty Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(178)</td>
<td>LMWH (Ardeparin)</td>
<td>90 U/kg qd</td>
<td>171(^{1})</td>
<td>22 (13)</td>
<td>12 (7)</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Warfarin</td>
<td>PT(^{1}) ratio</td>
<td>174(^{1})</td>
<td>20 (12)</td>
<td>11 (6)</td>
<td>5</td>
</tr>
</tbody>
</table>

*Double blind.

\(^{1}\)PT=prothrombin time.

\(^{1}\)Unilateral venogram of operated-on leg only.
increase in the overall incidence of hemorrhage, blood loss, or transfusion requirement with LMWH compared with warfarin prophylaxis. Based on the strength of the data, LMWH is the most effective anticoagulant-based prophylaxis for this indication. While the pooled risk reduction estimate is greatest for IPC (Table 7), the number of patients enrolled in IPC prophylaxis trials is substantially less than the number enrolled in LMWH trials and to our knowledge, no trial has directly compared LMWH with IPC prophylaxis. The risk reductions provided by LMWH and IPC are probably comparable and one cannot recommend one prophylaxis modality over the other. For patients with other concomitant risk factors for postoperative venous thromboembolism, combined LMWH and external pneumatic compression prophylaxis should be considered.

There is controversy regarding the optimal duration of postoperative prophylaxis following either elective hip or knee replacement surgery. Virtually all reported trials provided prophylaxis for at least 7 to 10 days postoperatively. Currently, the duration of postoperative hospitalization is often 5 days or less, which may provide an inadequate duration of venous thromboembolism prophylaxis. Several studies suggest that a significant risk of DVT may persist for at least 2 months after elective total hip replacement surgery.

Available data suggest that the duration of postoperative prophylaxis should be at least 7 to 10 days regardless of hospital length of stay. There are several ongoing clinical trials addressing posthospital (home) prophylaxis and these should provide data for more definitive future recommendations.

### Hip Fracture Surgery

Prophylaxis of hip fracture surgery remains a major challenge due to the risk of bleeding in these typically elderly patients with recent trauma. Surprisingly, to our knowledge, there are no adequate studies of such nonpharmacologic approaches. However, data on the postoperative use of LMWH are available. Table 8 presents a comparison of LMWH and warfarin for prophylaxis following total knee replacement surgery, according to Hull et al.

**Table 7—DVT Prophylaxis Following Total Knee Replacement**

<table>
<thead>
<tr>
<th>Regimen (References)</th>
<th>No. of Trials</th>
<th>No. of Patients</th>
<th>No. of Patients With DVT</th>
<th>Incidence, %</th>
<th>95% CI</th>
<th>Relative Risk Reduction, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (163-165, 192)</td>
<td>4</td>
<td>116</td>
<td>71</td>
<td>61</td>
<td>52-70</td>
<td>—</td>
</tr>
<tr>
<td>Low-dose heparin (194)</td>
<td>1</td>
<td>225</td>
<td>77</td>
<td>34</td>
<td>25-40</td>
<td>44</td>
</tr>
<tr>
<td>LMWH (177, 178, 192, 194, 178a-178c)</td>
<td>7</td>
<td>1,354</td>
<td>399</td>
<td>30</td>
<td>28-32</td>
<td>51</td>
</tr>
<tr>
<td>Low-intensity warfarin (177, 178, 178a-178c)</td>
<td>5</td>
<td>1,033</td>
<td>486</td>
<td>47</td>
<td>44-50</td>
<td>23</td>
</tr>
<tr>
<td>Aspirin (195)</td>
<td>1</td>
<td>27</td>
<td>21</td>
<td>79</td>
<td>64-94</td>
<td>—</td>
</tr>
<tr>
<td>IPC (163-166)</td>
<td>4</td>
<td>366</td>
<td>41</td>
<td>11</td>
<td>9-14</td>
<td>82</td>
</tr>
</tbody>
</table>

*Pooled data from trials requiring mandatory postoperative venography.

1*CI-confidence interval.

**Table 8—DVT Prophylaxis After Total Knee Replacement: LMWH vs Warfarin**

<table>
<thead>
<tr>
<th>Author (References)</th>
<th>Drug</th>
<th>Dose, Anti-Xa U</th>
<th>Bilateral Venogram, No.</th>
<th>Total DVT, No. (%)</th>
<th>Proximal DVT, No. (%)</th>
<th>Bleeding, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hull et al* (177)</td>
<td>Logiparin</td>
<td>75 U/kg qd</td>
<td>258</td>
<td>116 (45)</td>
<td>20 (7.8)</td>
<td>4.4</td>
</tr>
<tr>
<td>Ardeparin Group (178)</td>
<td>Ardeparin</td>
<td>90 U/kg qd</td>
<td>149</td>
<td>41 (28)</td>
<td>7 (5)</td>
<td>6</td>
</tr>
<tr>
<td>Leclerc et al* (178a)</td>
<td>Enoxaparin</td>
<td>30 mg bid</td>
<td>206</td>
<td>76 (37)</td>
<td>25 (12)</td>
<td>2.1</td>
</tr>
<tr>
<td>Spiro et al (178b)</td>
<td>Enoxaparin</td>
<td>30 mg bid</td>
<td>211</td>
<td>109 (52)</td>
<td>22 (10)</td>
<td>1.8</td>
</tr>
<tr>
<td>Heit et al* (178c)</td>
<td>Ardeparin</td>
<td>50 U/kg bid</td>
<td>231</td>
<td>62 (27)</td>
<td>15 (6.5)</td>
<td>9</td>
</tr>
</tbody>
</table>

*Double blind.

1PT-prothrombin time.

Unilateral venogram of operated-on leg only.

1*<0.05

Heparinoid (Logiparin); LMWH (Ardeparin and Enoxaparin).
Untreated controls
(202, 293-298)

7
406
98
24
20-28
—

IPC
(293-298)

6
362
24
7
4-9
71

ES
(298)

1
80
7
9
2-15
63

Low-dose heparin
(202)

1
50
3
6
0-13
75

*CI = confidence interval.

prophylaxis measures as IPC. A recent meta-analysis suggested that antplatelet therapy was effective in preventing postoperative DVT and PE; however, the reduction in relative risk with aspirin prophylaxis is inadequate compared with other prophylaxis methods (Table 9). Two studies of LDUH suggested a substantial reduction in relative risk, although the sample size was small with accordingly broad confidence intervals. Five studies each of LMWH and low-intensity oral anticoagulant prophylaxis involving large numbers of patients show similar and substantial reductions in relative risk. To our knowledge, however, there are no studies directly comparing LMWH with low-intensity oral anticoagulant prophylaxis. Furthermore, because of differences in the reporting of bleeding complications, it is impossible to make definitive recommendations regarding their comparative safety. Two trials found no significant difference in bleeding with LMWH prophylaxis compared with either placebo or LDUH; however, the sample size of both trials was relatively small, such that a significant difference could have been missed (type II error). Reported bleeding rates for low-intensity oral anticoagulants range from 2 to 47%, although again, the sample size was small. At the present time, either LMWH or low-intensity oral anticoagulants are preferable and treatment should be initiated preoperatively as soon as the patient is judged to be in a clinically stable condition. Although IPC prophylaxis is likely to be effective, there are insufficient data on which to base firm recommendations.

ELECTIVE NEUROSURGERY

Patients undergoing elective intracranial neurosurgery are generally conceded to be at high risk of postoperative DVT and PE. There have been seven randomized, placebo-controlled studies of prophylaxis of venous thromboembolism in such patients (Table 10). In these studies, the average incidence of DVT in the control population was 24%. The diagnostic standard in all studies was FUT, supplemented in some studies by venography or impedance plethysmography. Most thrombi were confined to the calf veins.

Physical methods of prophylaxis in neurosurgical patients have been preferred to anticoagulant therapy because of concern about intracranial bleeding. The largest experience is with IPC, with and without ES. However, recent studies have also demonstrated the safety and efficacy of prophylaxis with LDUH in elective neurosurgical patients. In addition, a single, small study has demonstrated a strikingly low incidence (0%) of DVT in neurosurgical patients who received both IPC and LDUH. There was no increase in bleeding compared with patients receiving IPC alone, who had a 3.2% incidence of DVT. Intermittent pneumatic compression (with or without ES) can be recommended for prophylaxis of venous thromboembolism in patients undergoing elective neurosurgery, but LDUH is an acceptable alternative. IPC and LDUH may be more effective in combination than individually, particularly in high-risk patients.

ACUTE SPINAL CORD INJURY

In patients with acute spinal cord injury, the venographic incidence of DVT has been reported as 18 to 100%, with an average incidence of 40% (Table 11). In a multicenter review of 1,419 patients with acute spinal cord injury, Waring and Karunar reported a 14.5% and 4.6% incidence of clinically recognized DVT and PE, respectively. The period of great-

### Table 9—DVT Prophylaxis Following Hip Fracture Surgery

<table>
<thead>
<tr>
<th>Regimen</th>
<th>No. of Studies</th>
<th>No. of Patients</th>
<th>No. of Patients With DVT</th>
<th>Incidence, %</th>
<th>95% CI*</th>
<th>Relative Risk Reduction, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control/placebo</td>
<td>(137-145)</td>
<td>9</td>
<td>381</td>
<td>181</td>
<td>48</td>
<td>43-53</td>
</tr>
<tr>
<td>Low-dose heparin</td>
<td>(151, 153)</td>
<td>2</td>
<td>59</td>
<td>16</td>
<td>27</td>
<td>17-38</td>
</tr>
<tr>
<td>LMWH</td>
<td>(145, 198, 291, 292, 292a)</td>
<td>5</td>
<td>437</td>
<td>119</td>
<td>27</td>
<td>23-31</td>
</tr>
<tr>
<td>Low-intensity oral anticoagulant</td>
<td>(137, 141, 144, 199, 200)</td>
<td>5</td>
<td>239</td>
<td>58</td>
<td>24</td>
<td>19-29</td>
</tr>
<tr>
<td>Aspirin</td>
<td>(143, 144, 292a)</td>
<td>3</td>
<td>171</td>
<td>58</td>
<td>34</td>
<td>27-44</td>
</tr>
</tbody>
</table>

Table 10—Prevention of DVT After Elective Neurosurgical Operations

<table>
<thead>
<tr>
<th>Regimen (References)</th>
<th>No. of Trials</th>
<th>No. of Patients</th>
<th>No. of Patients With DVT</th>
<th>Incidence, %</th>
<th>95% Limits</th>
<th>Relative Risk Reduction, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreated controls</td>
<td>(202, 293-298)</td>
<td>7</td>
<td>406</td>
<td>98</td>
<td>24</td>
<td>20-28</td>
</tr>
<tr>
<td>IPC</td>
<td>(293-298)</td>
<td>6</td>
<td>362</td>
<td>24</td>
<td>7</td>
<td>4-9</td>
</tr>
<tr>
<td>ES</td>
<td>(298)</td>
<td>1</td>
<td>80</td>
<td>7</td>
<td>9</td>
<td>2-15</td>
</tr>
<tr>
<td>Low-dose heparin</td>
<td>(202)</td>
<td>1</td>
<td>50</td>
<td>3</td>
<td>6</td>
<td>0-13</td>
</tr>
</tbody>
</table>
Table 11—Incidence of Objectively Diagnosed DVT in Patients With Acute Spinal Cord Injury

<table>
<thead>
<tr>
<th>Source, yr (Reference)</th>
<th>No. of Patients</th>
<th>No. of Patients With DVT</th>
<th>Incidence, %</th>
<th>End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bors et al, 1954 (299)</td>
<td>99</td>
<td>58</td>
<td>59</td>
<td>Venography</td>
</tr>
<tr>
<td>Silver, 1974 (300)</td>
<td>100</td>
<td>18</td>
<td>18</td>
<td>FUT*</td>
</tr>
<tr>
<td>Brach et al, 1977 (301)</td>
<td>10</td>
<td>9</td>
<td>90</td>
<td>FUT/IPG*1</td>
</tr>
<tr>
<td>Rossi et al, 1980 (302)</td>
<td>18</td>
<td>13</td>
<td>72</td>
<td>FUT*</td>
</tr>
<tr>
<td>Myllynen et al, 1985 (303)</td>
<td>9</td>
<td>9</td>
<td>100</td>
<td>FUT*</td>
</tr>
<tr>
<td>Merli et al, 1988 (304)</td>
<td>17</td>
<td>8</td>
<td>47</td>
<td>FUT*</td>
</tr>
<tr>
<td>Petaja et al, 1989 (305)</td>
<td>9</td>
<td>7</td>
<td>78</td>
<td>FUT*</td>
</tr>
<tr>
<td>Gunduz et al, 1993 (306)</td>
<td>30</td>
<td>16</td>
<td>53</td>
<td>Venography</td>
</tr>
<tr>
<td>Yelnik et al, 1991 (307)</td>
<td>127</td>
<td>29</td>
<td>23</td>
<td>Venography</td>
</tr>
<tr>
<td>Overall incidence</td>
<td>419</td>
<td>167</td>
<td>40</td>
<td></td>
</tr>
</tbody>
</table>

*Confirmed by venography where positive

1IPG=impedance plethysmography.

Table 12—Prevention of DVT After Acute Spinal Cord Injury*

<table>
<thead>
<tr>
<th>Agent, Author, yr (Reference)</th>
<th>Untreated Controls (%)</th>
<th>Treated (%)</th>
<th>End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low-dose heparin:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frisbie and Sasahara, 1981 (208)</td>
<td>1/17 (6)</td>
<td>1/15 (7)</td>
<td>IPG</td>
</tr>
<tr>
<td>Green et al, 1988 (209)</td>
<td>None</td>
<td>9/29 (31)</td>
<td>IPG</td>
</tr>
<tr>
<td>Green et al, 1990 (210)</td>
<td>None</td>
<td>5/21 (24)</td>
<td>IPG</td>
</tr>
<tr>
<td><strong>IPC</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Green et al, 1982 (211)</td>
<td>None</td>
<td>6/15 (40)</td>
<td>FUT, IPG</td>
</tr>
<tr>
<td><strong>Adjusted-dose heparin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Green et al, 1988 (209)</td>
<td>None</td>
<td>2/29 (7)</td>
<td>IPG</td>
</tr>
<tr>
<td><strong>LMWH</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Green et al, 1990 (210)</td>
<td>None</td>
<td>0/20 (0)</td>
<td>IPG</td>
</tr>
<tr>
<td>Green, 1994 (212)</td>
<td>None</td>
<td>5/60 (8)</td>
<td>IPG, DU, VEN</td>
</tr>
<tr>
<td><strong>Combined prophylaxis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Green et al, 1982 (211)</td>
<td>None</td>
<td>4/12 (25)</td>
<td>FUT, IPG</td>
</tr>
<tr>
<td>IPC, ASA, DPI</td>
<td>None</td>
<td>4/12 (25)</td>
<td>FUT, IPG</td>
</tr>
<tr>
<td>Merli et al, 1992 (213)</td>
<td>6/17 (35)</td>
<td>1/19 (5)</td>
<td>FUT</td>
</tr>
</tbody>
</table>

*DPD=dipyridamole; DU=duplex ultrasound; ASA=aspirin; IPG=impedance plethysmography; VEN=venography.

...est risk appears to be during the first 2 weeks following injury. Death due to PE is rare 3 months or more after injury.304-306 Based on these data, it has been recommended that DVT prophylaxis be continued for a minimum of 3 months in patients recovering from acute spinal cord injury who are unable to ambulate.307

To our knowledge, there are no large, prospective, controlled studies of DVT prophylaxis in patients with acute spinal cord injury. However, several small (level II) trials have been published and are shown in Table 12. Three randomized studies compared LDUH with untreated controls,306 adjusted-dose subcutaneous heparin,309 or LMWH (Table 12).310 Impedance plethysmography was used as the diagnostic standard and presumably detected primarily...
proximal vein thrombi. In the first study, the overall rate of DVT was surprisingly low and was not significantly different between untreated control patients208 and those treated with LDUH. In the other two studies, there was no untreated control group and patients were randomized to treatment with LDUH vs adjusted-dose heparin209 or LMWH.210 The incidence of DVT was unacceptably high in patients who received LDH: 24% in one study209 and 31% in the second.210 Only one small, uncontrolled trial has been conducted of IPC prophylaxis in spinal cord injury. The incidence of DVT was 40%.211 Thus, there is no evidence that LDH or IPC alone provide adequate protection from DVT in acute spinal cord injury patients.

Using adjusted-dose heparin, the incidence of DVT in acute spinal cord injury patients was 7% (Table 12).209 Two additional studies using LMWH prophylaxis found an incidence of DVT of 0% and 8%, respectively.210,212 Thus, there is limited evidence to support the use of either adjusted-dose heparin or LMWH therapy in patients with acute spinal cord injury in whom other medical conditions do not contraindicate their use. Prophylaxis with warfarin has not been studied. Two additional trials have been performed using combined methods of prophylaxis. The first trial studied the combination of IPC, ES, and LDUH. The incidence of DVT detected by FUT was 5% in the treatment group compared with 35% in an untreated control group.213 Thus, the combination of IPC, ES, and LDUH appears to be effective prophylaxis against DVT in spinal cord injury patients, although the data are limited. The second trial combined IPC, aspirin, and dipyridamole.211 The incidence of DVT was 25%. There was no control group, but the combination of IPC and antiplatelet agents does not appear to provide adequate protection in acute spinal cord injury patients.

Although to our knowledge, there are no large, well-controlled studies of DVT prophylaxis following acute spinal cord injury, currently available studies suggest that there is a significant clinical benefit of prophylaxis in spinal cord injury patients. LMWH looks particularly promising, but additional randomized trials are needed. Low-dose heparin therapy, IPC, or ES provide inadequate protection when used alone, but appear to be of benefit when used in combination.

**MULTIPLE TRAUMA**

The high incidence of DVT in patients with hip and lower extremity fractures is well established. The incidence of DVT following other types of trauma is less clearly defined. The literature is difficult to interpret because trauma patients are inherently dissimilar in nature, unlike other patient groups in whom the incidence of DVT has been studied, and because of the large proportion of patients in published studies who have hip or lower-extremity fractures. The inclusion of lower-extremity trauma in the overall group of trauma patients undoubtedly gives a falsely high impression of the true incidence of DVT when extrapolated to other types of injury (Table 13). While one review suggests that trauma patients with no additional risk factors are at low risk,214 a recent large study using venography has demonstrated that major trauma patients (injury severity score >9) have an extremely high risk of venous thromboembolism with an incidence of 58% (201 of 349 patients).215 While the expected high rate of DVT was seen in trauma patients with lower-extremity fractures (69%) and spinal cord injury (62%), this study also documented a 50% incidence of DVT in trauma patients whose only major injury involved the face, chest, or abdomen. Most of these patients suffered blunt trauma, and the incidence of venous thromboembolism among patients with penetrating trauma is virtually unknown.

To our knowledge, no randomized controlled studies have been carried out to evaluate the role of prophylaxis in multiple trauma patients. Such patients often have associated injuries that contraindicate anticoagulant prophylaxis, particularly head injury. Roughly one in seven trauma patients cannot receive anticoagulants because of associated injuries that pose a high risk of bleeding.214 It is generally accepted that LDUH prophylaxis is inadequate in hip surgery. Thus, it is not surprising that a recent nonrandomized study suggests an inadequate prophylactic effect in multiple trauma as well.216 IPC has been the most commonly employed prophylactic regimen in trauma patients but cannot be applied to one third of trauma patients owing to lower extremity fractures, casts, or bandages. Recent studies in orthopedic surgery patients using intermittent foot compression, rather than calf compression, are promising and may offer an alternative to IPC in trauma patients with lower-extremity casts. In patients with extensive trauma who have multiple risk factors but who cannot receive other forms of prophylaxis, inferior vena cava filter insertion has been employed,217-219 but to our knowledge, there are currently no randomized controlled studies to verify its efficacy.

It is now well established that multiple trauma patients are at high risk for DVT. Older patients are at particularly high risk of DVT and PE following major trauma. While randomized controlled trials are not available to define the optimum prophylaxis in trauma patients, the weight of evidence from nonrandomized trials suggests that prophylaxis should be considered for all major trauma patients. One study randomly assigned 281 trauma patients to receive either LDUH or IPC. Only 2.9% of these patients had DVT by duplex ultrasound compared with an 8.8% incidence of DVT in trauma patients who received no prophylaxis.209 A smaller study found equivalent incidences of duplex-detected DVT among patients receiving LDUH (5%) and IPC (12%).221 However, a nonrandomized study showed no benefit for LDUH prophylaxis in trauma patients.216 A third nonrandomized trial demonstrated a reduction from 1 to 0.25% in the incidence of PE in a trial period, in which a subgroup of very-high-risk trauma patients received an inferior vena cava filter, which was compared with a control period before this policy was instituted.216 More clinical trials of DVT prophylaxis in trauma patients are urgently needed.

In selected trauma patients with well-established risk factors, including lower-extremity fractures, spinal cord injury, or an indwelling femoral venous catheter, it may be appropriate to add screening strategies to DVT prophylaxis due to the high failure rate of prophylaxis in these very high-risk patients.222-224 Until additional trials are available, selection of a specific prophylactic strategy in major trauma patients appears best determined on a case-by-case basis. As in well-defined high-risk groups, such as hip fracture and spinal cord injury, a combination of prophylactic methods
may be more beneficial than any single method.

**BURNS**

There is little evidence to suggest that DVT and PE are frequent complications in burn patients. A recent study based solely on clinical observation suggests that the incidence of clinically recognized PE in burn patients is only 0.4%, 235 Sevitt and Gallagher 236 recommended oral anticoagulant prophylaxis in patients with burns of less than 15% of body surface but not in larger burns due to the risk of GI bleeding from stress ulceration; however, there is no evidence to justify the broad use of DVT prophylaxis in burn patients. Burn patients with additional risk factors for venous thrombosis may warrant prophylaxis.

**MEDICAL CONDITIONS**

In contrast to surgical patients, prevention of venous thromboembolism is less well studied in hospitalized medical patients. The trials are, in general, limited in number and smaller in size. Among medical conditions, myocardial infarction (MI) and ischemic stroke are the most completely studied.

**Myocardial Infarction**

Prophylactic antithrombotic therapy in patients with MI can be used to prevent venous thromboembolism, mural thrombosis, and systemic arterial embolism. In this section, the prevention of venous thromboembolism in patients with MI will be considered. Both heparin and oral anticoagulants have been evaluated in clinical trials in such patients. Heparin has been used either in low doses by subcutaneous injection, in high doses parenterally, or in combination with oral anticoagulants.

The overall incidence of leg DVT is about 24% among MI patients not treated with antithrombotic therapy (Table 14). Four trials evaluated LDUH in varying regimens (5,000 U bid or tid to 7,500 U bid) 227-229 and three of these found a significant reduction in calf DVT. 228-230 Two trials evaluated high-dose IV heparin (40,000 U/d) and also found a beneficial effect in reducing leg DVT with no increase in bleeding complications. 231,232 Several older randomized trials have addressed full anticoagulation with heparin and oral anticoagulation in patients after MI. These trialsanted widespread application of objective radiologic tests to diagnose venous thromboembolism and end points consist of clinical diagnoses of DVT and PE in patients with overt signs and symptoms. Because of the lack of confirmatory tests and the open nature of most of these trials, these data should be interpreted cautiously.

In the Medical Research Council trial, 1,427 patients with MI were randomized to either high-dose anticoagulant therapy or low-dose treatment. 233 The high-dose group received heparin, 15,000 U IV, followed by heparin, 10,000 U IV, every 6 h for five doses. In addition, patients received concurrent phenindione (vitamin K antagonist) to maintain a targeted thrombotest of 10 to 20%. The low-dose treatment group received 1 mg daily of phenindione. Treatment in both groups continued for 4 weeks. The primary outcome measure in this study was mortality at 4 weeks. No difference in mortality was detected between groups. Eleven high-dose patients experienced DVT compared with 30 low-dose patients. Similarly, 16 high-dose patients experienced PE compared with 40 low-dose patients. Thirty-six of the high-dose patients experienced bleeding compared with only 9 low-dose patients. There were no fatal bleeding events.

In the Bronx Municipal Hospital trial, 1,136 patients with MI were randomized to either anticoagulants or placebo. 234 The anticoagulant group received 200 mg of phenindione and 5,000 U of heparin IV initially. Then heparin, 10,000 U every 8 h subcutaneously, was administered for 5 doses followed by phenindione for 4 weeks to maintain the prothrombin time between 2 and 2.5 times control (INR, 2 to 2.5). The control group received an identical placebo. PE occurred in 6.1% of patients in the control group compared with 3.8% in those treated with anticoagulants. This difference was not statistically significant. The rate of bleeding was 12.8% in the anticoagulant group compared with 5.3% in the control group. This difference was statistically significant, but none of the hemorrhagic complications were fatal.

In the Veterans Administration trial, 999 patients with MI were randomized to heparin, 10,000 U subcutaneously, and concurrent warfarin or no antithrombotic treatment. 235 Warfarin therapy was adjusted to a targeted INR of 2 to 2.5, and the heparin therapy was discontinued when the INR reached therapeutic levels. Clinical PE occurred in 2.6% of patients in the control group and in 0.2% of the anticoagulant group. This difference was statistically significant. The rate of bleeding was 2.6% in the oral anticoagulant group compared with 1.2% in the control group.

Wright et al 236 conducted a prospective study in which 368 patients admitted to the hospital on even days received no oral anticoagulants and 432 patients admitted to the hospital on odd days received dicumarol at a targeted prothrombin time of 30 s. The rate of DVT was 2% in the anticoagulant group compared with 5% in the control group, and the rates of PE were 5.2% and 9.4%, respectively. The rate of bleeding was 6% in the oral anticoagulant group compared with 12.4% in the control group.

In a recent trial, 80 patients with acute MI wore graduated compression stockings on one leg with the other leg

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**Table 13—Incidence of Venous Thromboembolism in Trauma Patients**

<table>
<thead>
<tr>
<th>Author, yr (Reference)</th>
<th>Fractures* (%)</th>
<th>DVT (%)</th>
<th>End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sevitt and Gallagher, 1961 (226)</td>
<td>58 (46)</td>
<td>81/125 (65)</td>
<td>Autopsy</td>
</tr>
<tr>
<td>Frearke et al, 1967 (308)</td>
<td>84 (68)</td>
<td>44/124 (35)</td>
<td>Venography</td>
</tr>
<tr>
<td>Nylander and Semb, 1972 (309)</td>
<td>15 (100)</td>
<td>7/15 (47)</td>
<td>Venography</td>
</tr>
<tr>
<td>Wilen et al, 1982 (310)</td>
<td>38 (100)</td>
<td>8/38 (21)</td>
<td>Venography</td>
</tr>
<tr>
<td>Kudsk et al, 1989 (311)</td>
<td>12 (32)</td>
<td>24/38 (63)</td>
<td>Venography</td>
</tr>
<tr>
<td>Geerts et al, 1994 (215)</td>
<td>181 (52)</td>
<td>201/349 (58)</td>
<td>Venography</td>
</tr>
</tbody>
</table>

Mean incidence: 385 (56) 365/689 (53)

*Fractures of the pelvis or lower extremities.
serving as control. The FUT was used as an outcome measure. There were eight control legs with an abnormal scan compared with no abnormalities for legs on which stockings were worn (p=0.003).

From available data, LDUH and full anticoagulation reduce the incidence of venous thromboembolism in patients with MI. Because of this and because anticoagulants reduce other thromboembolic events in these patients without incurring a significant major bleeding risk, their liberal use is recommended. Presumably, mechanical methods of prophylaxis (ES, IPC) would also be useful in MI patients when bleeding risk is great and conventional antithrombotic agents are contraindicated. The effect that concurrent or antecedent lytic therapy might have on the development of DVT after MI is not known.

Ischemic Stroke

Stroke patients have a high risk of DVT in the parietic or paralyzed lower extremity. The overall incidence of leg DVT is 42% from the pooled data in Table 14. To date, there have been five randomized trials evaluating prophylactic methods in patients with ischemic stroke. Considering the high incidence of venous thromboembolism in this condition, this is surprising. Only LDUH and LMWH have been evaluated. In one small study, results with LDUH were better than with the control substance; in two other trials, LMWH yielded better results than placebo; in a different trial, LMWH was superior to LDUH for the prevention of DVT while in another trial, no difference was detected between LMWH administered once daily and placebo. The lack of efficacy of LMWH in this trial may have been due to an inadequate dose. Thus, both LDUH and LMWH can be recommended in patients with stroke. Because of the highly beneficial effect of IPC in neurosurgical patients, many of whom have hemiparesis, this method should also be beneficial in stroke patients. ES may also be of benefit. Unfortunately, however, these and other prophylactic methods have not received sufficient study in this condition.

Other Medical Conditions

There have been relatively few studies of venous thromboembolism prophylaxis in medical patients admitted to hospitals without MI or stroke. Rates of DVT in such patients have been determined in descriptive studies that used FUT as the outcome measure. These studies reported rates of DVT of approximately 20% and found that congestive heart failure and/or underlying chest infection predisposed patients to DVT.

Belch et al randomized 100 patients with heart failure or chest infection or both who were older than 40 years to either LDUH, 5,000 U every 8 h, or no prophylaxis. The rate of leg scan-detected DVT was reduced from 26% in the control group to 4% in the heparin group (p<0.01). The two cases of PE documented by lung scan occurred in the control patients. No bleeding complications occurred in either group.

Dahan et al randomized 262 medical patients older than 65 years to either LMWH once daily by subcutaneous injection or placebo. The rate of leg scan-detected DVT was 9.1% in the placebo-treated patients compared with 3.0% in the LMWH-treated patients (p=0.03). Two patients in the placebo group had PE at autopsy. There were three patients with bleeding in the placebo group compared with one in the LMWH group. In a trial reported by Harenberg et al medical patients were randomized to LDUH or LMWH. The rates of DVT detected by impedance plethysmography and duplex ultrasound were 5% and 4%, respectively.

In a trial reported by Cade, patients were stratified into two groups, critically ill in the ICU or within a medical ward, and they were randomized to either LDUH, 5,000 U subcutaneously twice daily, or placebo. Some of the patients in the ICU were postoperative. In the ICU patients, the incidence of leg DVT was 29% in control patients, which was reduced to 13% in patients receiving LDUH (p<0.05). The incidence among the medical ward patients was not significantly reduced by LDUH.

In a prospective study reported by Harvey and Finch in 1950, patients with congestive heart failure received dicumarol if admitted to the hospital on an even day and no treatment if admitted on an odd day. Venous thromboembolic events were documented using clinical and autopsy criteria. In the oral anticoagulant group, 1 patient had DVT

Table 14—Prevention of DVT in Patients With MI and Ischemic Stroke

<table>
<thead>
<tr>
<th>Condition</th>
<th>Regimen (References)</th>
<th>No. of Trials</th>
<th>No. of Patients</th>
<th>No. of Patients With DVT</th>
<th>Incidence, %</th>
<th>95% Limits</th>
<th>Reduction of Relative Risk, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>Untreated control</td>
<td>(227-230)</td>
<td>4</td>
<td>214</td>
<td>51</td>
<td>24</td>
<td>18-30</td>
</tr>
<tr>
<td></td>
<td>LDUH</td>
<td>(227-230)</td>
<td>4</td>
<td>165</td>
<td>11</td>
<td>7</td>
<td>3-11</td>
</tr>
<tr>
<td></td>
<td>High-dose heparin</td>
<td>(231, 232)</td>
<td>2</td>
<td>70</td>
<td>3</td>
<td>4</td>
<td>1-9</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>Untreated control</td>
<td>(237a, 239, 241)</td>
<td>4</td>
<td>125</td>
<td>52</td>
<td>42</td>
<td>33-51</td>
</tr>
<tr>
<td></td>
<td>LDUH</td>
<td>(237a, 240)</td>
<td>2</td>
<td>58</td>
<td>15</td>
<td>26</td>
<td>15-37</td>
</tr>
<tr>
<td></td>
<td>LMWH</td>
<td>(238-241)</td>
<td>4</td>
<td>163</td>
<td>27</td>
<td>17</td>
<td>11-23</td>
</tr>
</tbody>
</table>

*Pooled data based on FUT.

For the ACCP Consensus Conference on Antithrombotic Therapy
compared with 8 patients with DVT and 13 with PE in the control group. In another cohort study of similar design conducted by Halkin and colleagues, LDUH was administered if a patient had an even hospital identification number, and no prophylaxis if the number was odd. There was a statistically significant reduction in mortality in the heparin group; thromboembolic events were not reported.

Patients with malignant disease are at high risk for thromboembolic disease. Most of the studies reporting the incidence of thromboembolism in cancer patients have been conducted in patients with breast cancer. The risk of thromboembolism in women with stage II breast cancer receiving chemotherapy is approximately 5%. The antiestrogen, tamoxifen, increases the thrombotic risk of chemotherapy in stage II breast cancer patients. The risk of thromboembolism is even higher (approximately 15%) in patients with stage IV breast cancer. In a randomized trial of tamoxifen vs placebo in stage I breast cancer, the risk of thromboembolism was 0.9% in the tamoxifen group compared with 0.2% in the placebo patients. There are other advanced cancers that are likely to be associated with a high risk of thromboembolism, eg, brain tumors, rectal cancer, pancreatic cancer, and advanced GI cancers. However, precise estimates of thrombotic rates in these groups are not available. Finally, cancer patients with indwelling central catheters are at increased risk for thrombosis of the axillary/subclavian veins.

Although cancer patients receiving outpatient anticancer therapy are at high risk for thrombosis, at present there is only one trial of primary prophylaxis in such patients (to our knowledge). In addition, a number of prophylactic methods are not practical in this ambulatory patient group, eg, LDUH, IPC, and ES. Oral anticoagulant therapy requires careful laboratory monitoring and is associated with the potential risk of bleeding.

Levine et al randomized 311 women with metastatic breast cancer receiving chemotherapy to either very-low-dose warfarin or placebo. The warfarin dose was 1 mg for 6 weeks and then the dose was adjusted to maintain the INR between 1.3 and 1.9. The average INR was 1.5 and the average dose of warfarin to maintain the INR within the target range was 2.5 mg. There were seven thromboembolic events in the placebo group compared with one in the warfarin group (p=0.03). Major bleeding occurred in two placebo-treated patients and one warfarin-treated patient.

Bern et al have conducted a randomized trial in which patients with indwelling central vein catheters were randomized to either 1 mg of warfarin or no treatment. All patients underwent upper extremity venography at 90 days or sooner if they developed symptoms of upper extremity thrombosis. Patients who received warfarin had a 9.5% rate of venous thrombosis compared with 37.5% in the control patients. This difference was statistically significant. Based on these results, it would be reasonable to administer 1 mg of warfarin daily to cancer patients with indwelling central catheters. The approach of using prophylaxis with 1 mg of warfarin or another less intense warfarin regimen in the ambulatory cancer patient to prevent DVT or PE is promising but warrants further evaluation.

Other Patient Categories

For many patients, there are insufficient data in the literature to make firm recommendations about prophylaxis of venous thromboembolism. A reasonable but empiric approach would be to assess clinical risk factors and to assign a level of risk as outlined in Table 3. In this schema, the intensity of prophylaxis is linked to the presence and number of clinical risk factors. Because this rationale is based on extrapolation of results from other patient categories, it is a grade C recommendation.

Recommendations

1. In low-risk (levels of risk detailed in Table 3) general surgery patients who are undergoing minor operations, are younger than 40 years of age, and have no clinical risk factors, no specific prophylaxis other than early ambulation is recommended. This is a grade C recommendation based primarily on the low risk in such patients.

2. It is recommended that ES, LDUH (given 2 h before and every 12 h after operation), or IPC be used in moderate-risk general surgery patients who are older than 40 years of age and are undergoing major operations, but who have no additional clinical risk factors for venous thromboembolism. IPC and ES should be applied during operation, if possible, and throughout the postoperative period. These are grade A recommendations based on level I data.

3. It is recommended that LDUH (every 8 h) or LMWH be used in higher-risk general surgery patients who are older than 40 years, undergoing major operations, and have additional risk factors. These are grade A recommendations based on level I data.

4. In higher-risk general surgery patients (as profiled in recommendation 3) who are prone to wound complications such as hematomas and infection, IPC would be a good alternative choice for prophylaxis. This is a grade A recommendation based on level I data.

5. In very high-risk general surgery patients with multiple risk factors, it is recommended that effective pharmacologic methods (LDUH, LMWH, or dextran) be combined with IPC. This is a grade B recommendation based on level II data and on extrapolation of data from other patient groups. LDUH and LMWH therapy should be started preoperatively and dextran given intraoperatively. IPC should also be applied intraoperatively, if possible.

6. In selected very high-risk general surgery patients, perioperative warfarin (INR, 2.0 to 3.0) therapy may be used. This is a grade A recommendation based on level I data.

7. It is recommended that aspirin not be used for prophylaxis in general surgery patients because other measures (as recommended above) are more efficacious. This is a grade A recommendation based on level I data.

8. In patients undergoing total hip replacement surgery, postoperative subcutaneous twice-daily fixed-dose unmonitored LMWH, low-intensity (INR, 2.0 to 3.0) oral anticoagulation (started preoperatively or immediately after operation), or adjusted-dose unfractionated heparin (started preoperatively) are the most effective anticoagulant-based prophylaxis regimens and are recommended for routine use. These are grade A recommendations based on level I data. Adjuvant prophylaxis with ES or IPC may provide additional
efficacy. Although other agents such as LDUH, aspirin, dextran, and IPC reduce the overall incidence of venous thromboembolism, they are less effective and should not be used routinely.

9. In patients undergoing total knee replacement surgery, postoperative subcutaneous twice-daily fixed-dose unmonitored LMWH is the most effective anticoagulant-based prophylaxis regimen. IPC is the most effective nonpharmacologic prophylaxis regimen and provides a reduction in relative risk comparable to LMWH. Either LMWH or IPC is recommended for routine prophylaxis. This is a grade A recommendation based on level I data.

10. In patients undergoing hip fracture surgery, either preoperative subcutaneous fixed-dose unmonitored LMWH or oral anticoagulation (INR, 2.0 to 3.0) is the most effective prophylactic agent and is recommended for routine use. This is a grade A recommendation based on level I data. IPC combined with either of the recommended anticoagulant-based prophylaxis regimens may provide additional benefit.

11. Data are insufficient to recommend prophylactic inferior vena cava filter placement for orthopedic surgery patients. Prophylactic inferior vena cava filter placement should be limited to high-risk patients in whom other forms of anticoagulant-based prophylaxis are not feasible due to active bleeding. This is a grade C recommendation based on level IV and V data.

12. It is recommended that IPC with or without ES be used in patients undergoing intracranial neurosurgery. Low-dose heparin therapy may be an acceptable alternative. These are grade A recommendations based on level I data. IPC and LDUH may be more effective in combination than individually, and should be considered in high-risk patients.

13. In patients with acute spinal cord injury with paralysis, treatment with adjusted-dose heparin or LMWH is recommended for prophylaxis. These are grade B recommendations based on level II data. Warfarin prophylaxis may also be effective. This is a grade C recommendation based on extrapolation of results from other patient groups. LDUH, ES, and IPC when used alone appear ineffective and are not recommended. However, these methods may have benefit when used together. This is a grade B recommendation based on level II data.

14. In multiple trauma patients, it is recommended that IPC, warfarin, or LMWH be used when feasible. These are grade C recommendations based on extrapolation of data from other patient groups. Because of the high risk of venous thromboembolism, the inability to apply standard methods of prophylaxis in many trauma patients, and the uncertainty about the efficacy of preventive measures, serial surveillance with duplex ultrasonography may be a successful strategy. In selected very-high-risk patients, prophylactic caval filter placement may be used. These are grade C recommendations based on level III and IV data.

15. It is recommended that LDUH be used in patients with myocardial infarction. Full-dose anticoagulation is also effective. These are grade A recommendations based on level I data. IPC and possibly ES may be useful when heparin therapy is contraindicated. These are grade C recommendations based on extrapolation of data from other patient groups.

16. In patients with ischemic stroke and lower-extremity paralysis, LDUH and LMWH are effective. These are grade A recommendations based on level I data. IPC and ES are also probably effective. These are grade C recommendations based on extrapolation of data from other patient groups.

17. In general medical patients with clinical risk factors for venous thromboembolism, particularly those with congestive heart failure and/or chest infections, LDUH and LMWH are effective. These are grade A recommendations based on level I data.

18. It is recommended that warfarin, 1 mg daily, be used in patients with long-term indwelling central vein catheters to prevent axillary-subclavian venous thrombosis. This is a grade A recommendation based on level I data.

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