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Update

Risk Factors for Venous Thromboembolism

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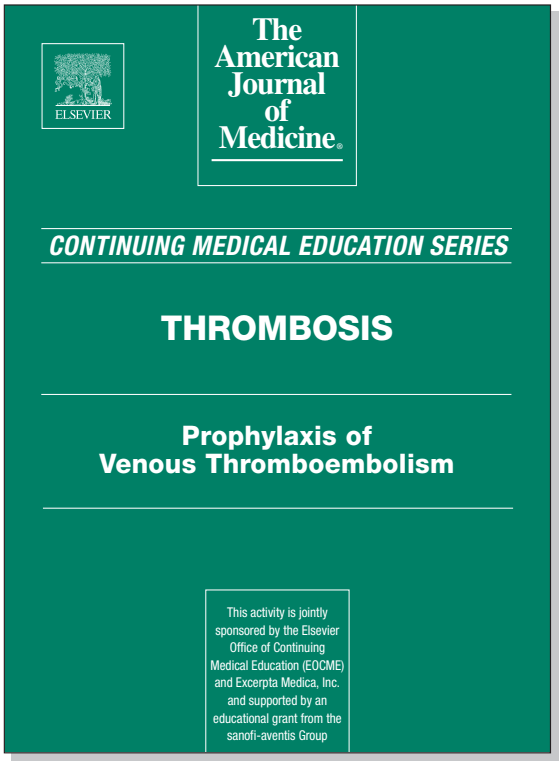

Risk factors for pulmonary embolism, and current strategies for risk management and pharmacologic therapy generated from a monograph to be published on the appropriate use of prophylaxis for venous thromboembolism.

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PROGRAM GOAL

There are >2 million cases of venous thromboembolism (VTE) reported in the United States each year. For the most part, it is a disease of hospitalized patients, with pulmonary embolism (PE) being one of the top preventable causes of mortality in these individuals. A variety of measures are available to reduce or eliminate the risk of VTE. These include careful risk assessment and the use of thromboprophylaxis. In view of the decreasing lengths of hospitalization and the long-term risk of a thromboembolic event, there is a need for extended prophylaxis in the outpatient setting to further reduce the incidence of VTE. This publication addresses these issues.

EDUCATIONAL OBJECTIVES

At the conclusion of this educational activity, participants will be able to:

- Discuss risk assessment models for VTE.
- Identify patients at risk for VTE and PE.
- Understand and implement the use of thromboprophylactic measures in patients at risk of an event.
- Compare efficacy and safety of low-molecular-weight heparin versus unfractionated heparin and list the appropriate clinical utilization of each.

CONTENT DEVELOPMENT

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Update on Risk Factors for Venous Thromboembolism

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INTRODUCTION

Venous thromboembolism (VTE) includes several manifestations of the same disease process: deep-vein thrombosis (DVT), ischemic stroke, and pulmonary embolism (PE).[1] Without thromboprophylaxis, the incidence of objectively documented DVT ranges from 16% to 55% in medical or general surgical patients and from 50% to 60% in patients who have undergone major orthopedic surgery.[1] Each year an estimated 700,000 people experience a new or recurrent stroke; of these, 88% are ischemic, 9% are intracerebral, and 35 are subarachnoid.[2]

VTE is the most serious complication many hospitalized patients encounter. A 5-year retrospective study of all autopsy records and associated hospital records for 2888 autopsies reported that at least 10% of in-hospital deaths are attributable to PE.[3] While the use of thromboprophylaxis strategies combined with improved patient care may have lowered the incidence of VTE over the years,[1,4] PE remains one of the most common preventable causes of in-hospital death in the United States.[5]

In 2001, the Agency for Healthcare Research and Quality (AHRQ) carried out a systematic review of 79 interventions that may favorably impact patients' safety. The appropriate use of thromboprophylaxis in patients at risk was ranked by the AHRQ as the most highly rated practice for patient safety.[6] This recommendation was based, in part, on a large number of clinical trials performed over the past 30 years that provide overwhelming evidence that thromboprophylaxis reduces the risk of DVT and, accordingly, nonfatal and fatal PE.[4] The Seventh American College of Chest Physicians (ACCP) Conference on Antithrombotic and Thrombolytic Therapy also bestowed its strongest recommendation (grade 1A–a clear benefit is observed derived from randomized, controlled trials without limitations[7]) on the pharmacologic prophylaxis of DVT in patients with risk factors for VTE.[4]

IDENTIFYING PATIENTS AT RISK FOR VTE AND PE

Hospitalized Patients Versus Community Residents

VTE is largely a disease of hospitalized patients. To estimate the incidence rates of VTE and PE in hospitalized patients and community residents, Heit et al[8] performed a retrospective review of medical records from a population-based cohort of patients residing in Olmsted County in Minnesota over a 15-year period. The average annual age- and sex-adjusted first episode of in-hospital VTE was 961 per 10,000 person-years (95% CI, 795–1126)—more than 100 times greater than the incidence among community residents (7.1 per 10,000 person-years; 95% CI, 6.5–7.6).

Virchow's Triad

Over 100 years ago, Rudolph Virchow[9] put forward a hypothesis that thrombosis was the result of the interaction of the following factors: stasis of blood flow, hypercoagulability of the blood, and damage to the vascular endothelium. It has become increasingly clear that one or more of Virchow's triad of pathophysiologic factors is usually a part of any risk associated with the development of DVT.

RISK FACTORS

Current ACCP guideline recommendations on the need for VTE prophylaxis in an individual patient focus on that patient's risk for developing VTE.[4] This assessment of a patient's risk is based on a number of risk factors that have been identified from epidemiologic studies. Some of the more defined risk factors are briefly summarized in the following discussion.

General Surgery

Surgical operations associated with a high risk of VTE include orthopedic and trauma procedures,[4] coronary artery bypass surgery,[10] surgery for abdominal or gynecologic cancer,[11] major urologic surgery,[12] and neurosurgery.[13] The decision to use thromboprophylactic measures should be based on the overall status of the patient and on the sum of the individual risks present in that patient, and not on the presence of 1 low-risk feature or 1 operative procedure thought to carry a low risk of VTE. Hence, the ACCP guidelines recommend no prophylaxis in low-risk general surgical patients <40 years of age undergoing minor procedures who have no additional risk factors.[4] Prophylactic measures are recommended in higher-

risk general surgical patients who are >40 years of age, in those undergoing major surgery, and in patients with additional risk factors.[4] Therefore, thrombosis prophylaxis is not solely procedure-specific but depends on the individual's level of risk based on careful risk assessment (**Table I**).[4]

Major Orthopedic Surgery

Major orthopedic surgery carried out on the lower extremities is associated with a higher risk of VTE, and a notable percentage of patients will develop a thrombosis if they are not given prophylaxis. This risk may reflect immobility of the lower limbs following such procedures. Patients with fractures of the hip, pelvis, or femur are at very high risk of VTE. In a study of patients who underwent total knee replacement, venographic evidence of DVT was found in 84% of patients who did not receive prophylaxis.[14] In a randomized, controlled, open-label trial of 76 patients undergoing elective hip surgery, venographic evidence of DVT was detected in 51% of patients not receiving prophylaxis.[15] In another series of 7959 total hip replacements, the incidence of PE was 15.2% and fatal PE was 2.3% in the 1174 patients who received no prophylaxis.[16] The most frequent time of onset of PE (75%) was in the second and third weeks after surgery, with ~10% of cases occurring within the first week.

Before the widespread use of prophylaxis in the 1960s and 1970s, an autopsy study showed that the incidence of fatal PE in patients undergoing hip fracture repair was 7.5%.[17] Since then, with improved anesthetic and surgical techniques and the use of thromboprophylaxis, the risk of fatal PE has fallen dramatically to <1%.[18]

Both the risk of VTE and the timing of events in patients with a hip fracture differ from those in patients undergoing elective hip or knee replacement. Patients with a hip fracture appear to be at higher risk of DVT than patients undergoing elective surgery, which may reflect their older age, the presence of more comorbidities, and the traumatic nature of their injuries. Hip fracture repair is an urgent procedure following trauma, but delays of > 48 hours are common and can lead to the preoperative development of DVT.[18] Insufficient data are available for a reliable estimation of the current risk in this group,[18] but it is clear that the risk of DVT following surgery for fracture of the hip extends well beyond the first few days in hospital. In a prospective study of 4840 patients, the mean time to symptoms of DVT following nailed hip fracture was 36 days and 27 days after total hip surgery, compared with symptoms of DVT that appeared, on average, 17 days after total knee replacement and 1 day after knee arthroscopy.[19] Furthermore, symptoms of DVT may be easier to suspect after those interventions where hardly any calf swelling is expected, whereas after major joint surgery postoperative swelling and pain may effectively mask the symptoms of DVT.[19]

For patients who survive VTE, the economic costs of DVT after major orthopedic surgery are approximately 2-fold higher than for patients who do not develop this complication

TABLE I. RISK OF VENOUS THROMBOEMBOLISM IN SURGICAL PATIENTS WITHOUT PROPHYLAXIS AND SUCCESSFUL PREVENTION STRATEGIES.

	DVT, %		PE, %		
Level of Risk	Calf	Proximal	Clinical	Fatal	Successful Prevention Strategies
Low risk Minor surgery inpatients <40 yr with no additional risk factors	2	0.4	0.2	<0.01	No specific prophylaxis; early and aggressive mobilization
Moderate risk Minor surgery in patients with additional risk factors Surgery in patients aged 40 to 60 yr with no additional risk factors	10–20	2–4	1–2	0.1–0.4	LDUH (q12h), LMWH (≤3400 U daily), GCS, or IPC
High risk Surgery in patients >60 yrs, or 40 to 60 yrs with additional risk factors	20–40	4–8	2–4	0.4–1.0	LDUH (q8h), LMWH (>3400 U daily), or IPC
Highest risk Surgery in patients with multiple risk factors Hip or knee arthroplasty, HFS Major trauma; spinal cord injury	40–80	10–20	4–10	0.2–5.0	LMWH (>3400 U daily), fondaparinux* oral VKAs (INR 2–3), or IPC/GCS + LDUH/LMWH

LDUH = low-dose unfractionated heparin; LMWH = low-molecular-weight heparin; GCS = graded compression stockings; IPC = intermittent pneumatic compression; VKAs = vitamin K antagonists, INR = international normalized ratio; HFS = hip fracture surgery.
*Note: Fondaparinux has a boxed warning for spinal/epidural hematomas: For full prescribing information, please go to http://us.gsk.com/products/assets/us_arixtra.pdf.
Adapted with permission.[4]

(US $17,114 vs US $9345, respectively), largely due to a near doubling of hospital length of stay. Thus, DVT places a heavy burden on both the health care system and the patient.[20]

Major Trauma

The risk of VTE in patients after a major trauma is very high. An autopsy study reported the presence of DVT in 65% of patients fatally injured in road traffic accidents, with PE being the cause of death in one fifth of patients.[21] In a prospective study of 716 patients with multiple trauma, the incidence of DVT was 47%. When analyzed by type of injury, 56% of patients with injuries to the pelvis or lower limbs developed a DVT, compared with 40% in those in whom the primary site of injury was the face, chest, or abdomen.[22] In the same study, Geerts et al[22] also reported that the incidence of DVT in multiple trauma victims with leg fractures was >70%. In another series of trauma patients, VTE was associated with obesity, age over 40 years, spinal fractures and fractures of the lower extremities, and immobilization.[23]

Spinal Cord Injury

Of all hospital admissions, patients with acute spinal cord injury are at the highest risk of DVT,[24] and PE has been shown to be the third most common cause of death in these individuals.[25] In a large multicenter study involving 1419 patients hospitalized with acute spinal cord injury, the incidence of symptomatic DVT was 15% and of clinically recognized PE was 5%.[25]

Acute Medical Illnesses

VTE has most commonly been associated with surgery or trauma. However, by far the greatest proportion (70%) of symptomatic cases of VTE occur in patients hospitalized for acute medical illnesses such as myocardial infarction (MI), malignancy, pneumonia, and congestive heart failure.[4,26,27]

Malignancy

According to data from a population-based, case-control study by Heit et al,[28] the risk of thrombosis for patients with malignant neoplasm compared with patients with no malignant neoplasm is increased 4-fold (odds ratio [OR], 4.05; 95% CI, 1.93–8.52). This risk is multiplied further (over 6-fold) when chemotherapy is given (OR, 6.53; 95% CI, 2.11–20.23).[28] Advanced cancer is associated with a high risk of VTE, especially breast cancer, lung cancer, brain tumors, gynecologic cancer, rectal cancer, pancreatic cancer, and advanced gastrointestinal cancers.[29,30]

Myocardial Infarction

MI offers a good example of the importance of regarding a patient as a whole and not as one or more risk factors. Although MI has not in itself been clearly shown to be a risk factor for DVT, the incidence of VTE in hospitalized patients with MI is ~20%.[31] This high frequency is likely to be related to the older age of the patients, immobility due to bed rest, congestive heart failure, and obesity leading to venous stasis in the lower limbs.

Congestive Heart Failure

Features that include increasing age, prolonged immobility, and cardiac or respiratory failure in patients with MI probably account for the well-documented association of VTE with congestive heart failure.[32] In a series of 451 patients, the incidence of thromboembolic events in patients with congestive heart failure or respiratory failure up to 12 days after admission ranged from 6% to 16%, even for thromboprophylaxis with either low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH).[33]

Ischemic Stroke

In a pooled analysis of data from 1047 patients in 10 clinical trials by Sandercock et al,[34] it was reported that the prevalence of DVT is 53% and PE is 6% in acute presumed or confirmed ischemic stroke patients not receiving prophylaxis.

History of VTE

A previous episode of VTE has been shown to be a strong risk factor for recurrence. In an epidemiologic study of 1272 medical outpatients in France (the Sirius study), of whom half presented with a DVT, prior VTE was shown to be the most important risk factor for a new VTE event.[35] Furthermore, in a report on risk factors in surgical patients, Flordal et al[36] demonstrated that previous VTE was also an independent risk factor for VTE in this population.

Age

Patients >40 years of age are at an increased risk of VTE compared with younger patients, with the risk approximately doubling with each decade thereafter.[26] Further evidence for the importance of age as a risk factor for VTE was reported by Oger[37] in a study of the incidence of VTE in a French community population. This study found that the incidence of VTE increased with age, reaching >1% in patients >75 years of age. This study reported that the incidence of PE as a percentage of total VTE also increased with age. A subanalysis of data from the prophylaxis of VTE in MEDical patients with ENOXaparin (MEDENOX) study confirmed that age >75 years is an independent risk factor for VTE in patients hospitalized with an acute medical illness.[38]

Immobility

In a post hoc analysis of data from the MEDENOX study, immobile patients (defined as an autonomous walking distance of less than 10 meters at the end of the treatment period) in the placebo group had a 20.3% (26 of 128 patients) incidence of VTE.[39] Similarly, the investigators of the SIRIUS study identified immobility (defined as total confinement to bed or bed and armchair) as a major risk factor for VTE (OR, 5.61; 95% CI, 2.30–13.67).[35]

Obesity

The association between obesity and VTE is under investigation. A relationship between obesity (often defined as body mass index [BMI] >30 kg/m^2) and VTE has been demonstrated in studies such as the SIRIUS study (>2-fold risk for DVT)[35] and the Nurses' Health Study (3-fold increase of primary PE).[40] Furthermore, in patients ≥65 years of age who had undergone total hip arthroplasty, a BMI of ≥25 has been shown to be associated with a 2.5-fold increase in rehospitalization for VTE (OR, 2.5; 95% CI, 1.8–3.4).[41] However, other studies have found that obesity is not an independent risk factor for VTE.[28,38]

Varicose Veins

The importance of varicose veins as an independent risk factor for VTE is currently unclear. Varicose veins were identified as an independent risk factor by Heit et al,[28] with the associated risk for VTE decreasing with age. On the basis of a subanalysis of data from the MEDENOX study, Alikhan et al[39] have reported a VTE rate of 21.3% (17 of 80 patients). However, it should be noted that these patients also exhibited numerous other risk factors for VTE.

Central Venous Catheters

Indwelling central venous catheters (CVCs) are associated with an increased risk of VTE. A small prospective study found that venographically confirmed thrombosis occurred in 38% of patients who did not receive thromboprophylaxis.[42] In a community-based analysis of independent risk factors for VTE, the presence, or history, of a CVC or transvenous pacemaker was associated with a >5-fold risk of VTE (OR, 5.5; 95% CI, 1.57–19.58).[28] Investigators of an epidemiologic study in patients with DVT reported risk factors for upper-extremity DVT.[43] In these patients, an indwelling CVC was associated with the highest risk of upper-extremity DVT.

Pregnancy

Pregnancy is rarely complicated by the development of VTE,[44] but when it does occur it can be fatal. PE is a leading cause of maternal death after childbirth, occurring in 1 in 100,000 births.[45,46] Together with amniotic fluid embolism and hemorrhage, PE is one of the main causes of death within 24 hours of delivery. Age and parity are highly important risk cofactors.[46]

Hormone Therapy

Second- and third-generation oral contraceptives increase the risk of VTE in otherwise healthy young women by 3- to 4-fold, respectively. The risk is primarily influenced by the duration of use, with ORs decreasing significantly over time. The risk of VTE also decreases significantly with decreasing estrogen dose.[47] In one large study in women receiving hormone replacement therapy (HRT), there was an increase in the risk of VTE of almost 4-fold in women without the factor V Leiden mutation (OR, 3.7; 95% CI, 1.4–9.4). In women with the factor V Leiden mutation treated with HRT, the incidence of VTE was 15 per 1000 per year compared with 2 per 1000 ($P < 0.01$) per year in women without the mutation who were not receiving HRT.[48]

Inflammatory Bowel Disease

In a population-based cohort study, inflammatory bowel disease (IBD) was associated with a 3-fold risk of DVT or PE when compared with patients without IBD.[49] However, neither the SIRIUS study[35] nor a further population-based study[28] was able to demonstrate that IBD is a risk factor for VTE.

Infectious Disease/Sepsis

In a subgroup analysis of data from the MEDENOX study, the VTE incidence rate for patients with an acute infectious disease who received placebo was 25.5% (24 of 155 patients).[39] Similarly, the investigators of the SIRIUS study identified infectious disease as a risk factor for VTE (OR, 1.95; 95% CI, 1.31–2.92).[35]

Thrombophilias

The risk of VTE associated with antiphospholipid antibody syndrome is not clear in otherwise healthy young women, but thromboembolic rates of 6% to 8% have been reported in healthy patients with lupus anticoagulant. The presence of these antibodies should be regarded as increasing the likelihood of the development of VTE.[50]

A number of inherited thrombophilias also predispose to the development of VTE. The first of these, antithrombin deficiency, was described in 1965.[51] Over the past 40 years there has been an enormous increase in the identification and understanding of a number of other inherited factors that play a role in the development of thrombosis. Among them are factor V Leiden mutation, prothrombin 20210A, and an elevation of

serum homocysteine. When constructing a risk profile for development of VTE in an individual patient, it is important to know the status of that patient with respect to these factors.

THE USE OF RISK FACTORS IN THE SELECTION OF PATIENTS FOR THROMBOPROPHYLAXIS

The ACCP guidelines highlight 2 approaches to decision-making with regard to thromboprophylaxis.[4] The first is to consider the risk of VTE in each patient based on their individual predisposing factors and the risk associated with their current illness or procedure, with the use of prophylaxis based on the composite risk estimate. A second approach, favored by the ACCP, is to implement group-specific prophylaxis for all patients who belong to one of several major target groups (eg, type of surgery, age, and presence of additional risk factors).

A simplified approach to estimating an individual patient's risk, based on the presence of both predisposing and exposing (in-hospital) risk factors, might provide a suitable way to ascertain a patient's risk of VTE. Such a system would allocate patients with a reasonable measure of certainty to low, moderate, or high-risk groups so that prophylaxis could be tailored to the element of risk that the patient is facing. This type of risk score, the Thrombosis in Myocardial Infarction (TIMI) risk score, has been developed for the assessment of patients with unstable angina or non–ST-segment elevation MI. The TIMI risk score is both simple to use and reliable for assessing outcome.[52]

Another useful risk-prediction tool is based on data from the Global Registry of Acute Coronary Events (GRACE), which is a multinational registry involving 94 hospitals in 14 countries.[53] The GRACE risk-prediction tool is used for bedside risk estimation of 6-month mortality in patients surviving admission for an acute coronary syndrome (ACS). This tool identifies 9 variables predictive of 6-month mortality: older age, history of MI, history of heart failure, increased pulse rate at presentation, lower systolic blood pressure at presentation, elevated initial serum creatinine level, elevated initial serum cardiac biomarker levels, ST-segment depression on presenting electrocardiogram, and not having a percutaneous coronary intervention performed in hospital.[53] Physicians may find this tool is simple to use and applicable to clinical practice.

In the absence of a published, validated, and widely accepted scoring system for VTE, the ACCP guidelines recommend that every hospital develop a formal strategy that addresses the prevention of thromboembolic complications. This strategy should be in the form of a written thromboprophylaxis policy, especially for high-risk patients.[4] One such example is a thrombosis risk-factor assessment (**Table II**)[54] that is currently in use in a large teaching hospital in the Midwest. This scoring system helps to identify patients at mild, moderate, high, and highest risk of VTE, and recommends that any patient who scores 3 or more points should receive thromboprophylaxis.[54] If a patient has contraindications for anticoagulation (active bleeding, history of heparin-induced thrombocytopenia, a platelet count <100,000, receiving oral anticoagulants or platelet inhibitors, or abnormal creatinine clearance rate), intermittent pneumatic compression should be considered.

It is important to note that this note scoring system for determining risk factors helps to identify all of the possible factors that can result in a VTE. Most individuals receive prophylaxis based on this screening tool. Those with very high point totals can also be counseled about the high risk of VTE even with prophylaxis. Thus, a frank discussion about the risk-benefit ratio surrounding an elective surgical operation can occur. A patient may decide that certain cosmetic and quality-of-life improvement operations may not be worth the high VTE risk.

ANTITHROMBOTIC PROPHYLAXIS

While a review of the thromboprophylactic regimens is beyond the scope of this article, 2 important points can be made. First, thromboprophylaxis should be continued after discharge in patients because episodes of VTE often develop up to several months later.[4] Second, there is a trend toward the use of LMWH over UFH for prophylaxis.[55] This is largely because of the better profile of LMWH over UFH. The anticoagulant effect of UFH is more variable than that for LMWH, and immune-mediated or type II heparin-induced thrombocytopenia, osteoporosis, and heparin resistance are more common in UFH-treated patients. Therefore, patients treated with UFH must undergo close monitoring. In contrast, LMWHs bind specifically to antithrombin III and have a better bioavailability at low doses; there is a reduced risk of heparin-induced thrombocytopenia and osteoporosis, obviating the requirement for coagulation monitoring. The half-life of LMWHs is longer than that for UFH, which translates into a once- or twice-daily injection schedule.[56] Finally, there is growing evidence that the use of LMWH may provide a slight survival benefit in selected cancer patients.[57]

CONCLUSIONS

VTE is generally a disorder of hospitalized patients, with PE being one of the top preventable killers in these individuals. A variety of measures are available to reduce or eliminate the risk of VTE. These include careful risk assessment of individual patients and the use of thromboprophylactic measures in patients at risk of an event. The introduction of a validated

TABLE II. RISK-ASSESSMENT SCORE FOR VENOUS THROMBOEMBOLISM. EACH RISK FACTOR REPRESENTS A SPECIFIED NUMBER OF POINTS.[54]

Factor = 5 points
- Elective major lower-extremity arthroplasty
- Hip, pelvis, or leg fracture (<1 month)
- Stroke (<1 month)
- Multiple trauma (<1 month)
- Acute spinal cord injury (paralysis) (<1 month)

Factor = 3 points
- Age >75 years
- History of deep-vein thrombosis or pulmonary embolism
- Family history of thrombosis
- Positive factor V Leiden
- Positive prothrombin 20210A
- Elevated serum homocysteine
- Positive lupus anticoagulant
- Elevated anticardiolipin antibodies
- Heparin-induced thrombocytopenia
- Other congenital or acquired thrombophilia

Factor = 2 points
- Age 60–74 years
- Arthroscopic surgery
- Malignancy (present or previous)
- Major surgery (>45 minutes)
- Laparoscopic surgery (>45 minutes)
- Prolonged bed rest (>72 hours)
- Immobilizing plaster cast of the leg or foot (<1 month)
- Central venous access

Factor = 1 point
- Age 41–60 years
- Minor surgery planned
- History of major surgery (<1 month)
- Varicose veins
- History of inflammatory bowel disease
- Swollen legs (current)
- Obesity (body mass index >25)
- Acute myocardial infarction
- Congestive heart failure (<1 month)
- Sepsis (<1 month)
- Serious lung disease
- Abnormal pulmonary function
- Medical patient currently at bed rest

Factor = 1 point (women only)
- Oral contraceptives or hormone replacement therapy
- Pregnancy or postpartum (<1 month)
- Unexplained stillborn infant. Spontaneous abortion.
- Premature birth with toxemia or growth-restricted infant

simple bedside tool for estimating the risk of VTE in an individual patient could refine the decision-making process. In view of the decreasing lengths of hospitalization and the long-term risk of a thromboembolic event, there is a need for extended prophylaxis in the outpatient setting to further reduce the incidence of VTE.

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CME Test Questions

RISK FACTORS FOR VENOUS THROMBOEMBOLISM

1. After major orthopedic surgery without perioperative DVT prophylaxis, the incidence of DVT, objectively confirmed, is approximately ____.

a. 10% to 40%
b. 20% to 40%
c. 40% to 50%
d. 50% to 60%

2. The AHRQ ranks "the appropriate use of prophylaxis to prevent VTE in patients at risk" as the ____ strategy for increase in patient safety.

a. number one
b. second most important
c. the least effective

3. In patients undergoing elective hip surgery, DVT occurred in 51% of the patients assigned to placebo, and in a very large series of patients who had a total hip replacement, the incidence of PE was 15.2% and of fatal PE, 2.3%. The onset of PE occurred most frequently in the ____ week(s).

a. first
b. second
c. first and second
d. second and third

4. Patients with cancer who receive chemotherapy have a risk of thrombosis that is ____-fold higher than patients without cancer.

a. 2
b. 3
c. 4
d. 6

5. The incidence of VTE in hospitalized patients with MI is roughly ____.

a. 15%
b. 17%
c. 20%
d. 27%

6. The ACCP favors which of the following choices to assess when and to whom thromboprophylaxis should be given?

a. Consideration of an individual's predisposing factors and the risks associated with their current illness or procedure. Prophylaxis is given based on the composite risk estimate.
b. Implement group-specific prophylaxis for all patients belonging to one or more major target group (type of procedure, age, cancer, or additional factors).

7. Prophylaxis should not be continued in most patients after discharge from the hospital.

a. True
b. False

8. UFH is associated with all of the following except ____.

a. osteoporosis
b. thrombocytopenia
c. heparin resistance
d. less variable anticoagulant effect

CME Test Answer Sheet and Evaluation Form for

RISK FACTORS FOR VENOUS THROMBOEMBOLISM

Release Date of Activity: May 2005
Expiration Date: May 2007
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CME TEST

(*Please circle correct answers*)

1. a b c d	3. a b c d	5. a b c d	7. a b
2. a b c	4. a b c d	6. a b	8. a b c d

COURSE EVALUATION: *Please rate the overall course on a scale of 1 to 5, with 1 the lowest and 5 the highest.*

1. Did the material provide an adequate overview of the risk factors for venous thromboembolism? **1 2 3 4 5**

2. Did the material explain the importance of prophylaxis in the prevention of thromboembolic events? **1 2 3 4 5**

3. How well did the material explain the latest risk assessment models? **1 2 3 4 5**

4. How well did the material compare the efficacy and safety of pharmacotherapy for prophylaxis of VTE? **1 2 3 4 5**

5. Were the articles appropriate to the topic? ___ Yes ___ No
   Comments:
   _____
   _____

6. Did you find the information presented to be objective, fair, balanced, and free of commercial bias? ___ Yes ___ No
   Comments:_____
   _____
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7. Give at least one example of how the content of this publication will be of use in your practice.
   _____
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8. When you receive literature that is accredited for AMA/PRA CME versus literature that is not accredited for CME, which are you more likely to review?
   □ CME □ Non-CME □ Does not matter

9. If CME certification is important to you, where do you prefer it come from?
   □ Professional Society □ Medical School/Hospital □ Private CME provider □ Does not matter

10. Do you have any recommendations to improve this publication?
    _____
    _____
    _____

CME INSTRUCTIONS

This Update on Risk Factors for Venous Thromboembolism provides free Category 1 CME credits. To receive CME credit, forward the Test Answer Sheet and Evaluation Form to the address shown below. (Refer to p. 2 for CME Information.)

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CME Test Answers

RISK FACTORS FOR VENOUS THROMBOEMBOLISM

1. d.

When prophylaxis is not given, the incidence of DVT, objectively confirmed, is ~10% to 40% among medical or general surgical inpatients and 50% to 60% after major orthopedic surgery.

2. a.

PE is the most common preventable cause of in-hospital death. The AHRQ has carried out a systematic review of 79 interventions that may favorably impact patients' safety and ranks "the appropriate use of prophylaxis to prevent VTE in patients at risk" as the number one strategy to be pursued for increase in patient safety.

3. d.

In a randomized, controlled, open-label trial of patients undergoing elective hip surgery, DVT occurred in 51% of the patients assigned to placebo; in a very large series (n = 1174) of patients who had a total hip replacement, the incidence of PE was 15.2%, and of fatal PE, 2.3%. The onset of PE (75%) occurred most frequently in the second and third weeks with only 10% occurring in the first week.

4. d.

Patients with cancer have a risk of thrombosis that is about 4-fold higher than patients without cancer. This risk is multiplied further (about 6-fold) when chemotherapy is given.

5. c.

MI offers a good example of the importance of looking at the patient as a whole and not as 1 or 2 risk factors. Although MI has not in itself been clearly shown to be a risk factor for DVT per se, the incidence of VTE in hospitalized patients with MI is roughly 20% and this frequency most probably occurs because of the concurrence of a number of features in these patients: increased age, immobility due to bed rest, and/or congestive heart failure, and/or obesity leading to venous stasis in the lower limbs.

6. b.

The guidelines point out that there are 2 general approaches to making decisions about when and to whom thromboprophylaxis should be given. One approach would be to consider the risk of VTE in each patient based on their individual predisposing factors and the risks associated with their current illness or procedure. Prophylaxis would then be given based on the composite risk estimate. The ACCP considers this approach to be too cumbersome without the use of computer technology, which places it beyond the reach of most hospitals. Additionally, there is little understanding of how individual factors interact to determine the position of each patient along the spectrum of thromboembolic risk. The second approach, favored by ACCP, is to implement group-specific prophylaxis for all patients who belong to one of several major target groups (type of procedure, age, and the presence of additional factors such as cancer).

7. b.

False. Prophylaxis should be continued in many patients after discharge from the hospital because, as has been discussed, many of the episodes of VTE develop, in some cases, as long as 3 months after discharge.

8. d.

There is a trend toward the use of LMWH over UFH for prophylaxis. This is largely because of the better profile of LMWH over UFH. The anticoagulant effect of UFH is more variable than that of LMWH, and immune-mediated or type II heparin-induced thrombocytopenia, osteoporosis, and heparin resistance are more common in UFH-treated patients. Therefore, patients treated with UFH must undergo close monitoring. In contrast, LMWHs bind specifically to antithrombin III and have a better bioavailability at low doses; there is a reduced risk of heparin-induced thrombocytopenia and osteoporosis, obviating the requirement for coagulation monitoring. The half-life of LMWHs is longer than that of UFH, which translates into a once- or twice-daily injection schedule.

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