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Venous Thromboembolism Prevention Strategies In Hospitalized Patients

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Abstract

- **Objective:** To provide an overview of venous thromboembolism (VTE) prevention strategies, including a review of current quality initiatives.
- **Methods:** A review of relevant journal articles and web sites related to VTE prevention and risk assessment was conducted.
- **Results:** VTE is a major source of morbidity and mortality world-wide and considered to be the most common preventable cause of hospital death. Evidence-based consensus guidelines on thromboembolic prophylaxis have been available internationally for decades, yet VTE prophylaxis is often underutilized or inappropriately used. Recommendations for VTE prophylaxis include early ambulation or education for low-risk patients and pharmacologic prophylaxis using anticoagulants for moderate- or high-risk patients. Mechanical prophylaxis measures are recommended for patients at high risk of bleeding as they are not eligible for pharmacologic prophylaxis. Systems approaches to improving VTE prophylaxis have been developed, and agencies have established quality measures to improve care of this condition.
- **Conclusion:** Health care organizations should ensure that all hospitalized patients receive VTE risk assessment upon admission and after a major event and that appropriate interventions for VTE prevention are taken. An evaluation of processes used in the assessment and prevention of VTE and subsequent clinical outcomes should be integrated with quality improvement and patient safety measures.

Venous thromboembolism (VTE), manifesting as deep vein thrombosis (DVT) and pulmonary embolism (PE), is the third most common cardiovascular disease after myocardial infarction and stroke [1]. It affects 350,000 to 600,000 Americans annually and causes at least

100,000 deaths [2]. Over half of affected individuals develop VTE in the hospital or within 30 days of hospital discharge [3]. The total annual health care costs attributable to VTE in the United States are \$2 to \$10 billion [4]. Many VTE events are preventable, and evidence-based guidelines for prevention have been published. However, despite the availability of guidelines, VTE prophylaxis is underutilized. The current paper provides an overview of strategies for VTE prophylaxis including systems-supported strategies for improving VTE care in health care settings.

• What are risk factors for VTE?

In 1884, Rudolf Virchow first described the pathophysiology of VTE [5]. Virchow identified 3 main etiologic factors for VTE: venous stasis, endothelial damage, and hypercoagulability (Virchow's triad). Other important findings described by Virchow and others during this era were that thrombi commonly occur within the lower extremity deep veins and less commonly in the vena cava or upper extremity deep veins [5]. During the next century, many risk factors for VTE were identified. The most common inherited (genetic) risk factors for VTE are factor V Leiden and the prothrombin gene mutation [6]. The most common acquired (nongenetic) risk factor for VTE is anticardiolipin syndrome [6]. A list of the risk factors for VTE is presented in **Table 1** [7].

Risk Assessment

All hospitalized adult patients, particularly elderly patients, patients with cancer, and patients undergoing major surgery, should be assessed for VTE risk. Patients should be

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Table 1. Risk Factors for Venous Thromboembolism

Surgery
Trauma (major trauma or lower-extremity injury)
Immobility, lower-extremity paresis
Cancer (active or occult)
Cancer therapy (hormonal, chemotherapy, angiogenesis inhibitors, radiotherapy)
Venous compression (tumor, hematoma, arterial abnormality)
Previous venous thromboembolism
Increasing age
Pregnancy and the postpartum period
Estrogen-containing oral contraceptives or hormone replacement therapy
Selective estrogen receptor modulators
Erythropoiesis-stimulating agents
Acute medical illness
Inflammatory bowel disease
Nephrotic syndrome
Myeloproliferative disorders
Paroxysmal nocturnal hemoglobinuria
Obesity
Central venous catheterization
Inherited or acquired thrombophilia

Adapted from reference 7.

assessed upon admission and continuously throughout hospitalization. Assessment should also occur at the time of hospital discharge, as approximately three-quarters of VTE events occur after patients leave the hospital [6].

A variety of VTE risk assessment models are used. There are 2 main approaches: an individualized approach or a group approach. The 8th American College of Chest Physicians (ACCP) guidelines support using group-specific thromboprophylaxis due to the lack of evidence supporting individualizing prophylaxis [7,8]. Furthermore, individualizing prophylaxis is logistically complex and can be associated with suboptimal compliance [7,8].

A prospectively validated VTE risk assessment model for hospitalized patients was introduced by the Agency for Healthcare Research and Quality (AHRQ) in 2008 [9]. Developed by Maynard et al, this group approach has been shown to have ease of use, good interobserver agreement, and to be effective in reducing VTE incidence [10]. **Table 2** presents the model, with VTE risk assessment levels and appropriate preventive measures for each level of risk (high, moderate, or low).

Other VTE risk assessment models have been developed [11–13]. Some of these models include a list of exposing and predisposing risk factors and use scoring to assign a patient to 1 of 3 or 4 risk levels. Recently, Bahl et al

validated a retrospective VTE risk scoring method based on the Caprini [11] risk assessment model for hospitalized medical and surgical patients and measured compliance with University of Michigan Health System prophylaxis guidelines [14]. Their risk scoring method supports use of individual patient assessment of risk for VTE within 30 days after surgery [14].

• What are the signs and symptoms of DVT and PE?

The diagnosis of VTE (DVT and/or PE) is challenging since classic signs and symptoms are often absent or mimic other disease processes. In a recent multicenter prospective cohort study, the most common signs/symptoms in patients with DVT were extremity edema (80%), leg pain (75%), and erythema (26%); dyspnea (85%), chest pain (40%), tachypnea (30%), and tachycardia (23%) were common signs/symptoms in patients with PE [15]. The clinical presentations of DVT and PE are closely related; when thinking about one, it is important to assess for the other as well. Approximately 40% of patients with symptomatic DVT have asymptomatic PE, and a lower extremity DVT can be found in approxi-

Table 2. A Venous Thromboembolism Risk Assessment Model and Prophylaxis

Risk Level	Low Risk	Moderate Risk	High Risk
Patients	Ambulatory patient without VTE risk factors Ambulatory patient with expected LOS ≤ 2 days; same day surgery or minor surgery	All other patients (not in low-risk or high-risk category); most medical/surgical patients; respiratory insufficiency, heart failure, acute infectious or inflammatory disease Pace up sitting times	Lower extremity arthroplasty Hip, pelvic, or severe lower extremity fractures Acute spinal code injury with paresis Multiple major trauma Abdominal or pelvic surgery for cancer
Prevention measures	Early ambulation	LMWH q day; OR UFH 5000 units SC q8 hours or q 12 hours (if weight < 50 kg or age >75) AND suggest adding IPC	LMWH (UFH if ESRD); OR fondaparinux 2.5 mg SC daily; OR warfarin, INR 2–3; AND IPC (unless not feasible)

Note: IPC indicated for patients with contraindications to pharmacologic prophylaxis. ESRD = end-stage renal disease; INR = international normalized ratio; IPC = intermittent pneumatic compression devices; LMWH = low-molecular-weight heparin; LOS = length of stay; SC = subcutaneously; UFH = unfractionated heparin. (Adapted from reference 10.)

mately 70% of patients with symptomatic PE [15]. Since the signs and symptoms of VTE often overlap with other clinical conditions, clinical prediction rules have been developed. Wells' scoring strategies for DVT and PE are the most commonly used and validated in various patient populations for the assessment of pre-test probability of VTE [16].

• What options are available for VTE prevention in hospitalized patients?

The main interventions for VTE prevention are nonpharmacologic measures (early and frequent ambulation or mobilization), mechanical prophylaxis, and pharmacologic prophylaxis [7]. Almost all hospitalized patients need pharmacologic prophylaxis unless their VTE risk level is low or they have contraindications to anticoagulants. Pharmacologic prophylaxis options available for hospitalized patients at risk for VTE are unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), fondaparinux, or warfarin (Table 2). The use of aspirin as a thromboprophylaxis is no longer recommended for any patient population [7]. Contraindications to pharmacologic prophylaxis or other conditions to consider with pharmacologic prophylaxis are described in Table 3.

Mechanical approaches for thromboprophylaxis include intermittent pneumatic compression (IPC), venous foot pump, or graduated compression stockings [7]. Mechanical methods of thromboprophylaxis should be used primarily in patients who are at high risk for bleeding. Mechanical

prophylaxis can also be used as an adjunct to anticoagulant-based thromboprophylaxis in patients in the highest risk category for VTE who are on anticoagulants and need additional preventive measures. Since patient compliance with mechanical methods is relatively low [17], health care providers, particularly bedside nurses, should pay careful attention to ensuring the proper use and optimal adherence in patients receiving mechanical prophylaxis.

Special Populations

Renal function should be considered when making decisions about dosing anticoagulants for VTE prevention, particularly in elderly patients or patients with diabetes mellitus. Prophylaxis options depend on individual patient's clinical circumstance. Recommended options are (1) no use of an anticoagulant, (2) use of a lower dose of anticoagulant, or (3) monitoring the drug level. Another special group for VTE prophylaxis is patients who receive neuraxial anesthesia/analgesia or peripheral nerve blocks. Caution is needed when considering the use of anticoagulant thromboprophylaxis in these patients because of the risks for bleeding [18].

Obesity (body mass index [BMI] > 30 kg/m² [19]) is an independent risk factor for VTE [7]. Clinical trials reported fixed-dose enoxaparin (40 mg once daily) reduces the risk of VTE in medically ill patients [20–23]. However, weight-based dosing with LMWH (eg, enoxaparin) for VTE prophylaxis in morbidly obese patients (BMI ≥ 35 kg/m²) should be considered because obesity affects drug distribution and pharmacokinetics [24].

Patients who are fully anticoagulated for existing clinical

Table 3. Contraindications and Other Conditions to Consider With Pharmacologic VTE

Absolute	Relative	Other Conditions
Active hemorrhage	Intracranial hemorrhage within last year	Heparin-induced thrombocytopenia
Severe trauma to head or spinal cord with hemorrhage in the last 4 weeks	Craniotomy within 2 weeks	Epidural analgesia with spinal catheter
	Intraocular surgery within 2 weeks	
	Gastrointestinal or gastrourinary hemorrhage within the last month	
	Thrombocytopenia (< 50K) or coagulopathy (prothrombin time > 18 sec)	
	End-stage liver disease	
	Active intracranial lesions/neoplasms	
	Hypertensive crisis	
	Postoperative bleeding concerns*	

Adapted from reference 9.

*Postoperative bleeding concerns are (1) scheduled return to operation room within the next 24 hours, (2) major orthopedic surgery (24 hours leeway), (3) spinal cord or orthopedic spine surgery (7 days leeway), and (4) general surgery, status post transplant, status post trauma admission (48 hours leeway).

conditions such as atrial fibrillation, valve diseases, or stroke do not need additional pharmacologic prophylaxis, but mechanical prophylaxis should be considered to prevent VTE during their hospitalization.

• How often is prophylactic treatment utilized?

Despite evidence-based VTE prevention guidelines, significant underuse or inappropriate use of VTE prophylaxis measures have been reported in the literature [25–29]. A multinational cross-sectional study, Epidemiologic International Day for the Evaluation of Patients at Risk of Venous Thromboembolism in the Acute Hospital Care Setting (ENDORSE), reported that approximately 59% of surgical patients and 40% of medical patients received ACCP-recommended VTE prophylaxis [26]. Another multinational observational study, International Medical Prevention Registry on Venous Thromboembolism (IMPROVE), showed that only half of medical patients from 52 hospitals in 12 countries including the United States received pharmacologic and/or mechanical VTE prophylaxis and that practices of VTE prophylaxis markedly varied. For instance, IPC was the most commonly used approach in medical patients in the United States while it was rarely used in other countries (22% vs 0.2%, respectively) [28]. In a larger study looking at VTE prevention in 390,024 discharges, of which 51.6% were medical and 48.4% surgical patients, the overall rate of any prophylaxis was 71.6%,

with the rate being lower for medical patients (65.9%) compared with surgical patients (77.7%). Only 14.5% of all patients received appropriate prophylaxis, meeting the recommendations of the 7th ACCP guidelines [30]. Medical patients at risk for VTE were less likely than surgical patients to receive appropriate prophylaxis [26,31].

• What systems approaches can improve VTE prophylaxis practices?

Strategies to improve VTE prophylaxis practices include provider education, reminder systems, electronic alerts, decision support systems, audits, and feedback [3,32]. A multifaceted quality improvement strategy using several strategies has been shown to be effective in most VTE prophylaxis improvement studies [32].

The 8th ACCP guidelines emphasized that every hospital should develop thromboprophylaxis policies and use computer decision support systems, preprinted orders, and periodic audit and feedback to increase thromboprophylaxis adherence by physicians. Passive methods including educational materials or educational programs were not recommended as effective strategies to increase adherence in the use of thromboprophylaxis [7].

In a systematic review to assess strategies to improve prophylaxis, the most effective strategies incorporated a system for reminding clinicians to assess patients for VTE risk, either electronic decision-support systems or

paper-based reminders, and used audit and feedback to facilitate the iterative refinement of the intervention [33]. Other studies have shown the effectiveness of computer-based reminder systems in improving rates of prophylaxis [13,34].

- **What regulatory and quality initiatives have been instituted to improve VTE prevention?**

Performance measures aimed at improving quality of care and reducing unnecessary health care costs associated with VTE have been derived from the work of public and private organizations, including the National Quality Forum (NQF), the Joint Commission, and the Leapfrog Group (Table 4) [3]. The NQF, the Joint Commission, the Centers for Medicare and Medicaid Services (CMS), and the Agency for Healthcare Research and Quality have made VTE prophylaxis a patient safety priority. VTE quality improvement initiatives are rapidly developing in recognition of this important need.

One initiative sponsored by the CMS in collaboration with national partners is the Surgical Care Improvement Project (SCIP), which has developed measures for reporting VTE prophylaxis in surgery patients [35]. The SCIP VTE measures are among the core measures used by the Hospital Quality Alliance [36] and are part of the Joint Commission accreditation requirements [37].

Financial incentives ("pay for performance) and disincentives have been instituted as a mechanism to improve the use and reporting of VTE prophylaxis. The CMS Physician Quality Reporting Initiative offers physician incentive payments for reporting on performance measures. Further, the CMS has ruled that it will not reimburse hospitals for care of VTE after hip and knee replacement [38,39], as they have classified it as a hospital-acquired condition. There is an added incentive for hospitals to ensure VTE risk assessment and adequate prophylaxis in high-risk patients.

Currently, the Joint Commission requires hospitals to ensure that all patients receive appropriate VTE prophylaxis within 24 hours of hospital admission or transfer to critical care setting [37]. If VTE prophylaxis is not initiated, a justification for not using prophylaxis, such as contraindications to anticoagulation, must be documented.

Conclusion

VTE is an important public health problem. Hospitals and providers are encouraged to adopt hospital-wide protocols to ensure that patients are assessed for VTE risk and appropriate prophylaxis is provided. A multifaceted approach and continuous monitoring for appropriate pro-

phylaxis for hospitalized patients is a requirement that must be seriously addressed by all hospitals and medical-surgical centers.

CASE REVIEW QUESTIONS

Case 1.

A 47-year-old woman with amyotrophic lateral sclerosis who is wheelchair-bound is admitted for tracheostomy and feeding tube placement. Testing reveals hematocrit 34%, platelets 180,000/ μ L, INR 1.0, creatinine 1.1 mg/dL. What is the most appropriate VTE prevention strategy?

Answer: Pharmacologic prophylaxis is appropriate VTE prevention option. This patient's risk factors for VTE include age > 40, immobility, and upcoming surgery. She requires VTE prophylaxis and there are no contraindications to pharmacologic prophylaxis. Therapeutic options include unfractionated heparin 5000 units SQ q8h or enoxaparin 40 mg SQ once daily.

Case 2.

A 48-year-old woman with a right frontal glioblastoma is admitted for tumor resection on the day of admission. Testing reveals hematocrit 46%, platelets 219,000/ μ L, INR 0.9, creatinine 0.7 mg/dL. What is the most appropriate VTE prevention strategy?

Answer: Mechanical prophylaxis is the appropriate VTE prevention option. This patient's risk factors for VTE include age > 40 and scheduled neurosurgery. She requires VTE prophylaxis, but pharmacologic prophylaxis is contraindicated due to the potential intracranial bleeding risk associated with neurosurgery. Therefore, mechanical prophylaxis is indicated at this time. The patient should be switched to pharmacologic prophylaxis as soon as it is safe to do so after surgery.

Case 3.

A 78-year-old man with a history of coronary artery disease, hypertension and hyperlipidemia is admitted with acute chest pain and ST segment elevation on electrocardiogram. He will be started on intravenous heparin (70 U/kg bolus, 15 U/kg/hr infusion) and sent to the cardiac catheterization laboratory as soon as possible. Testing reveals hematocrit 39%, platelets 284,000/ μ L, INR 1.2, creatinine 1.4 mg/dL. What is the most appropriate VTE prevention strategy?

Answer: This patient has no need for prophylaxis, as he will be fully anticoagulated with heparin for acute coronary syndrome. This therapy is adequate prophylaxis.

Table 4. Quality Initiatives for Venous Thromboembolism Prevention

Organization	Initiative	Web Address	Description
AHRQ	Preventing hospital-acquired VTE: A guide for effective quality improvement	www.ahrq.gov/qual/vtguide/	Based on quality improvement initiatives undertaken at the University of California, San Diego Medical Center and Emory University Hospitals, this guide offers a framework to help the QI practitioner. Includes talking points to attract administration support, sample protocols, and chart audit form
CMS	Physician Quality Reporting Initiative (PQRI)	www.cms.gov/PQRI/	Offers incentive payment equal to 2% of physician's total estimated Medicare Part B Physician Fee Schedule
The Joint Commission	VTE measures	www.jointcommission.org/venous_thromboembolism/	See National Quality Forum below
NQF	National Consensus Standards for Prevention and Care of VTE	www.qualityforum.org/Projects/s-z/VTE_Phase_II_(2008)/VTE_Phase_II.aspx	Six VTE measures were endorsed by the NQF in May 2008 and aligned with the CMS. The VTE measure set was approved as a core measure set for use in the Joint Commission's ORYX program, and available for selection by hospitals to meet their 4 core measure set accreditation requirement
Leapfrog Group	Leapfrog Hospital Survey	www.leapfroghospitalsurvey.org	The Survey, Leapfrog's hallmark public reporting initiative, was launched in 2001 and is now in its 5th version. It assesses hospital performance based on 4 quality and safety practices that are proven to reduce preventable medical mistakes and are endorsed by the National Quality Forum
Coalition to Prevent DVT		www.preventdvt.org	Includes 70 member organizations engaged in education and spreading awareness
US Surgeon General	The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism 2008	www.surgeongeneral.gov/topics/deepvein/calltoaction/call-to-action-on-dvt-2008.pdf	

AHRQ = Agency for Healthcare Research and Quality; CMS = Centers for Medicare & Medicaid Services. (Adapted and updated from reference 3.)

Case 4.

A 42-year-old man with diabetes and chronic renal failure with a creatinine clearance of 20 mL/min is admitted with pneumonia. Testing reveals hematocrit 28%, platelets 160,000/ μ L, INR 1.4, creatinine 2.8 mg/dL. What is the most appropriate VTE prevention strategy?

Answer: Pharmacologic prophylaxis is the appropriate VTE prevention option. This patient's risk factors for VTE include age > 40 and hospital admission for an acute medical illness. He requires VTE prophylaxis and there are no contraindications

to pharmacologic prophylaxis. Therapeutic options for prophylaxis include unfractionated heparin 5000 units SQ q12h or enoxaparin 30 mg SQ once daily. Enoxaparin is decreased to approximately 50% to 60% of normal dosage (30 mg once daily) in patients with a creatinine clearance of 10 to 30 mL/min.

Case 5.

A 60-year-old man is admitted for lower anterior resection of his colon. The plan is to insert an epidural catheter for post-operative pain relief. Testing reveals hematocrit 34%, platelets

112,000/ μ L, INR 1.0, creatinine 1.0 mg/dL. Pharmacologic VTE prophylaxis with enoxaparin 40 mg SQ once daily is selected. What is the most appropriate time for administration of this dose after the placement of the epidural catheter?

- A. Give the first dose 2 hours after the epidural catheter has been placed
- B. Give the first dose 8 hours after the epidural catheter has been placed
- C. Enoxaparin 40 mg SQ once daily is contraindicated while the epidural catheter is in place

Answer: B. When enoxaparin 40 mg SQ once daily is used for VTE prophylaxis after an epidural catheter has been placed, a delay of at least 8 hours must occur before the first dose can be safely given.

Case 6.

A 39-year-old morbidly obese woman (BMI 56) is admitted for bariatric surgery. Testing reveals hematocrit 36%, platelets 315,000/ μ L, INR 0.9, creatinine 0.9 mg/dL. Pharmacologic VTE prophylaxis is indicated. What is the most appropriate drug therapy choice?

- A. Enoxaparin 40 mg SQ q12h
- B. Enoxaparin 40 mg SQ once daily
- C. Unfractionated heparin 5000 units SQ q8h

Answer: A. Morbidly obese patients with BMI > 50 require twice daily dosing of enoxaparin instead of the usual 40 mg once daily.

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