Prevention of Deep Vein Thrombosis and Pulmonary Embolism in High-Risk Medical Patients

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KEYWORDS

• Venous thromboembolism • Deep vein thrombosis • Pulmonary embolism • Prevention and control

KEY POINTS

- Venous thromboembolism (VTE) occurs in approximately 3% to 16% of hospitalized patients on wards and 10% to 40% of those in medical intensive care units.
- American College of Chest Physician guidelines along with a growing body of literature implore the use of pharmacologic prophylaxis in high-risk patients and mechanical prophylaxis when anticoagulants are contraindicated.
- There is consistent evidence that unfractionated heparin, low-molecular-weight heparin, and fondaparinux reduce VTE events by approximately 50% to 75% in high-risk groups, with a trend toward superiority of low-molecular-weight heparin.
- The risk of major bleeding with pharmacologic prophylaxis is low and large meta-analyses show that low-molecular-weight heparin may have slightly decreased bleeding risk compared with unfractionated heparin.
- Mechanical prophylaxis with intermittent pneumatic compression devices decrease VTE in acutely ill medical adults but with lesser efficacy compared with pharmacologic prophylaxis.

INTRODUCTION

Incident venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), accounts for $7 billion to $10 billion of United States health care expenditures each year.[1] Approximately 10% of inpatient deaths are attributable to VTE, 60% of which occur in nonsurgical patients based on necroscopy examination.[2,3] Pharmacologic and mechanical modalities can decrease the rate of VTE by 50–75%, yet the rate of appropriate VTE prophylaxis in acutely ill medical patients has been reported as low as 40% in the recent past.[4] In the United States, the Joint Commission and the Centers for Medicaid & Medicare Services consider VTE prophylaxis in high-risk patients a core quality measure.[5] Features that confer higher risk are either inherited or acquired. The most common acquired risks are age, acute congestive heart failure, respiratory failure, rheumatologic disease, inflammatory bowel disease, malignancy,

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trauma, prolonged immobility, and postsurgical status.[6,7] The studies that guide VTE prophylaxis date back to the 1970s and extend through present day. Prophylaxis options range from a variety of injectable heparins to direct oral anticoagulants among medical therapies and from graduated compression stockings (GCS) to intermittent pneumatic compression (IPC) devices among mechanical ones (Table 1).

American College of Chest Physicians (ACCP) guidelines suggest that any form of prophylaxis can lead to reduction in VTE by 0 to 1 fewer per 1000 persons in low-risk patients and by 34 fewer per 1000 in high-risk patients.[8] In medical patients,

Table 1
Types of venous thromboembolism prophylaxis

Prophylaxis Method	Mechanism of Action	Advantages	Disadvantages	Indications for Primary Venous Thromboembolism Prophylaxis
UFH	Nonspecifically binds to ATIII to inactivate thrombin	Low cost Reversal agent	Frequent dosing Unpredictable dose response Causes HIT Nonspecific binding to plasma proteins	Hospitalized medical patients Critically ill adults
LMWH Enoxaparin Dalteparin	Specifically inactivates factor Xa via ATIII	Once-daily dosing Trend toward improved efficacy over UFH	Increased cost compared with unfractionated heparin Protamine reverses 60% of activity Causes HIT Enoxaparin requires dose adjustment in renal impairment whereas dalteparin does not	Hospitalized medical patients Critically ill adults Enoxaparin approved for extended-duration VTE prophylaxis in those with active malignancy
Pentasaccharide Fondaparinux	Specifically inactivates factor Xa via ATIII	Once-daily dosing	Increased cost compared with UFH but similar to LMWH No reversal agent	Hospitalized medical patients Critically ill adults Active malignancy
Betrixiban	Direct and selective inhibition of factor Xa	Oral agent	High cost No reversal agent Used with caution in renal impairment	Extended-duration prophylaxis in hospitalized medical patients Not endorsed by guidelines yet
GCS	Increases blood flow, decreases venous stasis	Low cost Does not increase bleeding risk	Not effective for VTE prophylaxis Skin breakdown	Not considered first line
IPC	Increases blood flow leading to release of tPA, prostacyclin, and NO	Does not increase bleeding risk	Poor efficacy when not battery powered or when low compliance Not as effective as pharmacologic prophylaxis	Immobilization due to stroke Medical patients in whom pharmacologic prophylaxis is contraindicated

Abbreviations: ATIII, antithrombin III; GCS, graduated compression stockings; HIT, heparin induced thrombocyopenia; IPC, intermittent pneumatic compression device; LMWH, low molecular weight heparin; NO, nitric oxide; tPA, tissue plasminogen activator; UFH, unfractionated heparin; VTE, venous thromboembolism.