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Prevention of venous thrombosis in hospitalised medical patients

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ABSTRACT Venous thromboembolism (VTE), mainly deep vein thrombosis and pulmonary embolism, is a significant cause of morbidity and mortality in the Western world. It has been estimated that there are 300,000 new cases of first lifetime VTE in the US each year, and there are 60,000 deaths annually from VTE in the UK. Parallels have been drawn with other clinical conditions that have received more attention, and it has been estimated that the mortality rate for VTE in the UK is five times greater than the combined total number of deaths from breast cancer, AIDS and road traffic accidents and more than ten times greater than from methicillin-resistant *Staphylococcus aureus* infection.

KEYWORDS Deep vein thrombosis, pulmonary embolism, thromboprophylaxis, venous thromboembolism

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EDUCATION

Hospitalised patients are particularly vulnerable to venous thromboembolism (VTE) and may account for half the total number of deaths from this condition. Autopsy data have shown that in up to 10% of deaths in hospital, VTE is a significant contributing factor. In addition to the clinical situation necessitating hospitalisation, many patients have other pre-existing risk factors such as advanced age, obesity and immobility. The absolute risk of deep vein thrombosis (DVT) in patients not receiving thromboprophylaxis is 10–20% for medical patients, 14–40% for general surgery patients and 40–60% for high-risk orthopaedic procedures.

The risk of venous thromboembolism after surgical procedures has been the subject of much study, and there have been many publications highlighting the risks and the efficacy of thromboprophylaxis. This has contributed to the widespread uptake of thromboprophylaxis in surgical patients. The risk of VTE in general medical patients has, until relatively recently, received far less attention, despite the fact that around 75% of hospital-associated VTE occurs in acutely ill non-surgical admissions. Patients admitted to hospital with acute medical illness have an eight-fold increased relative risk of VTE, and this group accounts for almost 25% of the total number of cases of this condition.

Adopting specific measures to reduce the risk of VTE in hospitalised patients is good clinical practice and makes economic sense. The prevalence of VTE in this group is high, DVT and pulmonary embolism (PE) may be clinically silent and treating established VTE with high doses of anticoagulants may be dangerous. The early mortality rate can be as high as 3.8% in patients with DVT and 38.9% in those with PE. Patients who develop DVT may develop post-thrombotic syndrome, which is associated with a reduction in quality of life comparable to chronic heart, lung or arthritic disease. Furthermore, the investigation for and treatment of VTE may delay discharge from hospital and may necessitate readmission after discharge.

Risk factors for VTE in medical patients

Hospitalisation itself may increase the risk of thrombosis, but a growing body of published studies and meta-analyses has identified specific risk factors for venous thromboembolism in medical patients (Table 1).

In the absence of antithrombotic drugs, asymptomatic DVT has been found in 24% and clinical PE in up to 9.4% of patients with myocardial infarction. Asymptomatic DVT has been found in up to 50% of individuals with acute hemiplegic stroke and symptomatic DVT in 5% of this group. Autopsy studies have demonstrated PE in a large proportion of patients with stroke, and this may contribute to a significant number of early deaths.

Older age, prior history of VTE, active cancer, exacerbations of chronic obstructive pulmonary disease (COPD), heart failure and acute infection have been identified as independent risk factors. Other risk factors include inflammatory disease, obesity, neurological disease with lower limb weakness, long bone fracture, chronic renal disease and prolonged immobilisation, including nursing home stay. In addition, medical interventions such as anticancer therapy, intensive care unit care, central vein lines and respiratory assistance may increase the risk of VTE.

Assessment for these risk factors should allow the identification of medical patients at higher risk of VTE

TABLE 1 Risk factors for venous thromboembolism (VTE)

Age	Exponential increase with age: <40 annual risk 1:10,000 60–69 annual risk 1:1,000 >80 annual risk 1:100
Obesity	Body mass index (BMI) >30 kg/m^2
Previous VTE	Recurrence rate: 10% per annum unprovoked 3% per annum transient risk factors (medical) 1% per annum post-surgical
Cancer	x 7 but varies with tumour and treatment
Heart failure	
Recent myocardial infarction/cerebro-vascular accident	
Severe infection	
Chronic obstructive pulmonary disease	
Varicose veins	
Inflammatory bowel disease	
Collagen vascular disorders	
Thrombophilias	
Hormone therapy	x 3 risk. Combined oral contraceptive, HRT, raloxifine, tamoxifen x 6 risk. High-dose progestogens
Pregnancy	x 10 risk
Nursing home confinement	
Acute trauma	
Intensive care stay	

and permit targeting of thromboprophylaxis. It has therefore been recommended in all major guidelines that all patients admitted with general medical conditions should undergo systematic assessment for risk factors for VTE.

Studies of such risk-scoring suggest that more than 80% of hospitalised patients have at least three recognised VTE risk factors.

The Department of Health in England, through its independent expert working group, has recommended that each trust should have a risk assessment that is formally documented and incorporated into the trust's system for the Clinical Negligence Scheme. It was also recommended that the core standards should be set nationally to ensure maximum compliance with risk assessment for thromboprophylaxis.

TABLE 2 Incidence of proximal deep vein thrombosis or symptomatic venous thromboembolism at days 14–21

MEDENOX	PREVENT	ARTEMIS
Enoxaparin 2.1%	Dalteparin 2.6%	Fondaparinux 1.5%
Placebo 6.6%	Placebo 5.0%	Placebo 3.4%
P=0.037	*P*=0.002	*P*=0.085

THROMBOPROPHYLAXIS IN MEDICAL PATIENTS

Anticoagulant drugs

Venous thromboembolism in hospitalised medical patients has been less extensively studied than in surgical patients. However, solid data from several randomised trials comparing low molecular weight heparin (LMWH) or unfractionated heparin (UFH) against placebo in a broad range of medical conditions demonstrate that these drugs reduce the risk of asymptomatic and symptomatic VTE. Three studies carried out in more controlled conditions, MEDENOX (enoxaparin vs. placebo), PREVENT (dalteparin vs. placebo) and ARTEMIS (fondaparinux vs. placebo), were consistent in their results of an approximately 50% reduction of VTE. In these trials, thromboprophylaxis was administered for 14 days, but the effect persisted for up to three months (see Table 2). There was a non-significant excess of major bleeding (<1%).

Meta-analysis of studies comparing UFH and LMWH demonstrated a trend in favour of LMWH for reducing DVT and PE with less bleeding. Once-daily administration of LMWH may be preferable compared with three times daily dosing with UFH, and LMWHs are associated with less risk of heparin-induced thrombocytopenia.

Mechanical methods

There have been few studies of the efficacy of mechanical methods in preventing VTE in medical patients. One small study of patients with acute stroke suggested that rates of VTE were lowered by the use of graded compression stockings, but this was not statistically significant. The American College of Chest Physicians concluded that there was insufficient evidence to recommend the use of graded compression stockings in medical patients except where the use of anticoagulants was contraindicated.

RECOMMENDATIONS

The key recommendation for most guidelines that address thromboprophylaxis in medical patients is that all patients admitted to hospital with acute medical illness and who are confined to bed, particularly those with cardiac or respiratory failure or those that have one or more additional risk factors (see Table 1), should receive thromboprophylaxis with low-dose LMWH or UFH.

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Special considerations

Renal function should be assessed before starting thromboprophylaxis. Low molecular weight heparin may accumulate with marked renal impairment (creatinine clearance <30 ml/min) and a dose reduction may be appropriate.

The clinical trials described above used a regimen of 14 days' treatment. The optimal duration of thromboprophylaxis in medical patients is not yet determined.

Implementation of recommendations

Although there is clear evidence of benefit for thromboprophylaxis in at-risk patients hospitalised for medical conditions, there is difficulty in implementing recommendations for the assessment and treatment of such patients. Data from the International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) show that only 41% of acutely ill medical patients receive thromboprophylaxis, and another study in a US tertiary care hospital demonstrated that 75% of medical patients warranted thromboprophylaxis but only 43% actually received it. In the UK, the House of Commons Health Select Committee has estimated that only 20% of eligible patients receive thromboprophylaxis.

Possible causes include a lack of awareness of the problem in medical patients and the heterogeneity of medical patients, making risk assessment more difficult.

CONCLUSIONS

In the US and UK, government agencies have identified the prevention of VTE in adult patients in hospital as the main challenge to patient safety. Despite clear evidence of benefit for thromboprophylaxis in high-risk medical patients and several guidelines from expert groups, there is evidence that a formal risk stratification of medical patients at admission does not take place as rigorously as it should and many patients remain unprotected from VTE. It has been estimated that failure to prescribe thromboprophylaxis for all hospitalised patients accounts for 25,000 preventable deaths each year.

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KEY POINTS

- Hospitalised patients are at risk of deep vein thrombosis and pulmonary embolism. This group represents a substantial proportion of the total numbers of individuals developing venous thromboembolism each year.
- Much attention has been focused on surgical patients, but the number of medical patients at risk of and developing venous thromboembolism is much higher.
- There is clear evidence of benefit for thromboprophylaxis in hospitalised medical patients.
- On current evidence, low molecular weight heparin is the treatment of choice in patients stratified at higher risk for venous thromboembolism.
- Health trusts will need to demonstrate a clear strategy for identifying patients at risk of venous thromboembolism and demonstrate appropriate clinical practice.

FURTHER READING

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