The insidious hazard of hospitalisation: venous thromboembolism

Symptomatic venous thromboembolism (VTE) is a leading cause of death after admission to hospital. Recognition of when to act before and after patients are admitted to hospital with VTE will help prevent mortality and morbidity.

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Venous thromboembolism (VTE), comprising deep venous thrombosis (DVT) and pulmonary embolism, is a leading cause of death after admission to hospital, and more than 15,000 hospitalisations in Australia in 2008.[1] It is, however, a treatable and largely preventable disease. The long-term sequelae of VTE often seen in general practice are pernicious, with significant numbers of patients experiencing the post-thrombotic syndrome and many being debilitated with chronic venous ulceration. The financial burden of VTE on the Australian health care system is enormous and is estimated to be as much as $1.72 billion in 2008.[1]

There is currently no systematic approach to preventing VTE in many Australian hospitals. Assessment of patients who may be at risk of developing VTE is not uniformly undertaken by hospital staff.[2] Despite the availability of evidence-based guidelines for VTE prophylaxis,[3] many patients do not receive prophylaxis and are unknowingly at risk of developing VTE in hospital.

Patients remain at risk for some weeks after discharge from hospital when they have returned to the care of their GP. Processes to prevent this insidious hazard should be mandatory for all patients requiring hospital admission.

Identifying patients at risk of developing VTE

The risk of developing VTE is related to the presence of a number of predisposing factors in addition to the specific problem precipitating the patient's admission to hospital. Common

IN SUMMARY

- **Symptomatic venous thromboembolism (VTE) is estimated to be responsible for 7% of all hospital deaths and more than 15,000 hospitalisations in Australia annually.[1]**
- **Long-term sequelae of VTE often seen in general practice are pernicious, with significant numbers of patients experiencing the post-thrombotic syndrome and many being debilitated with chronic venous ulceration.**
- **In hospital, VTE risk assessment is often not undertaken and only 60% of patients receive appropriate VTE prophylaxis.**
- **Two main types of VTE prophylaxis have been shown to be effective: pharmaceutical agents and mechanical devices.**
- **VTE prophylaxis guidelines are available to assist with VTE risk assessment and to tailor appropriate treatment and duration of treatment to the patient's level of VTE risk.**
- **Knowledge of the current VTE guidelines will help GPs to facilitate community-based VTE prophylaxis and, for those with hospital-admitting rights, to care for their hospitalised patients.**

predisposing factors include:
- previous episodes of VTE
- malignancy
- immobility or paralysis
- obesity
- age over 40 years
- thrombophilias.

Hospitalised patients can be broadly subdivided into three groups of surgical, medical and obstetric patients, and the risk within each group can be identified by the presence of specific conditions.

Surgical patients

For patients undergoing surgery, the risk of developing VTE is dependent on the type of surgery performed. Procedures that put patients at a particularly high risk of developing VTE are:
- hip or knee replacement surgery
- hip fracture surgery
- surgery for active cancer
- major surgery in patients over the age of 40 years – for example, intra-abdominal surgery or surgery lasting more than 45 minutes.

The risk of developing VTE when undergoing day surgery or minor surgery is considered to be low; however, in some day surgery procedures, including laparoscopic or arthroscopic surgery, the intra-operative procedure can be relatively prolonged or the patient may already be at high risk of developing VTE. In either circumstance, full VTE prophylaxis should be considered.

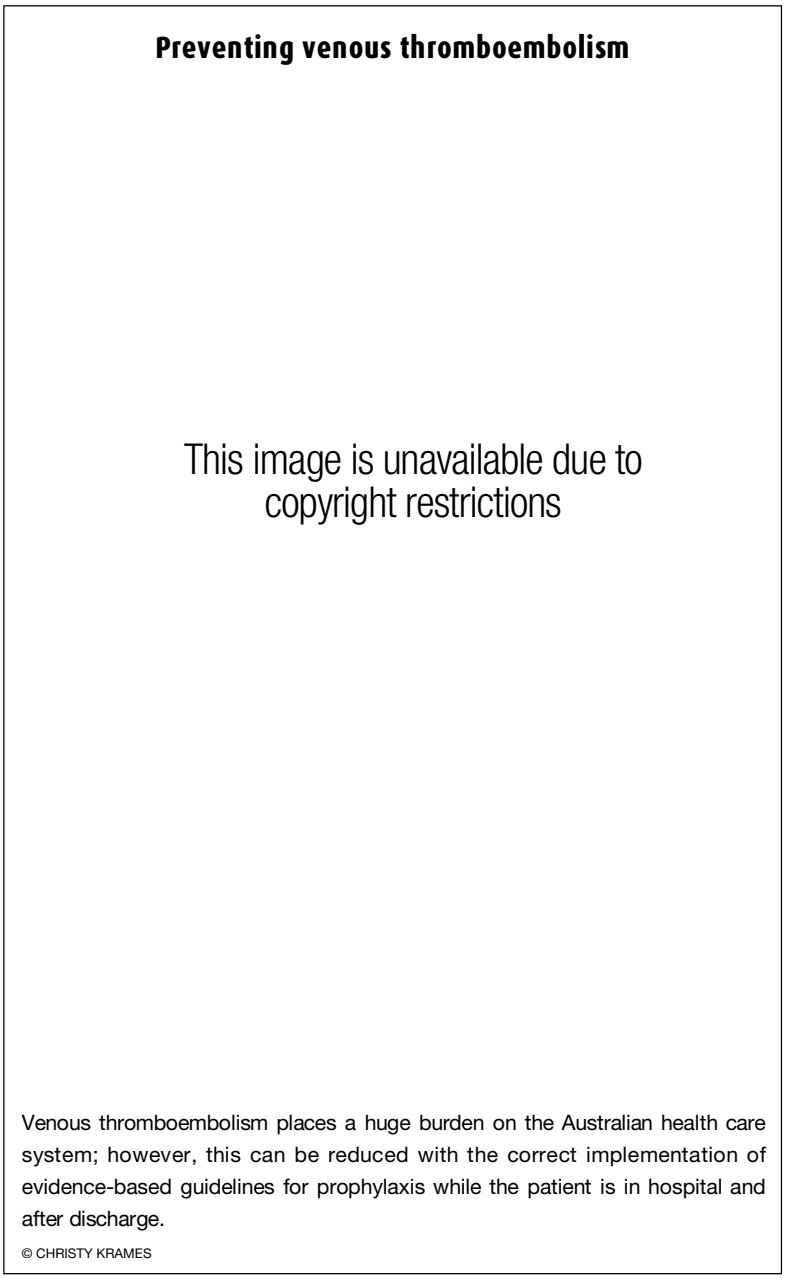
Medical patients

Up to 75% of pulmonary embolism resulting in death in general hospitals occurs in nonsurgical patients immobilised by medical illness, and the risk increases with age, particularly in those over the age of 60 years. Those at greatest risk of developing VTE are patients immobilised for more than three days of bed rest after hospital admission for the following medical conditions:
- acute stroke with lower limb paralysis
- active cancer
- decompensated cardiac failure
- acute-on-chronic lung disease
- acute inflammatory disease
- history of VTE.

Although patients over the age of 60 years are currently classified as being at high risk of developing DVT, those who are otherwise well and ambulant may not have an increased risk of developing VTE in the absence of other risk factors. This also applies to younger patients with acute-on-chronic lung disease (a group highlighted in a number of clinical studies as having a consistently high rate of VTE). This emphasises the requirement for individual VTE risk assessment.

Although smoking is considered by many GPs to be a factor predisposing to the development of

Preventing venous thromboembolism



Venous thromboembolism places a huge burden on the Australian health care system; however, this can be reduced with the correct implementation of evidence-based guidelines for prophylaxis while the patient is in hospital and after discharge.

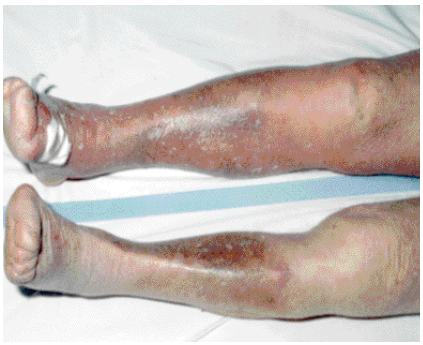


Figure. A patient with a right-sided swollen leg due to a DVT.

VTE, this has not been supported by published clinical evidence. Nevertheless, it is appropriate to take a history of smoking into consideration when assessing the patient.

Obstetric patients

Several factors may increase the risk of developing VTE during pregnancy, including obesity and advanced maternal age, and a women's risk is increased after a caesarean section. Specific conditions considered to place obstetric patients at high risk of developing VTE include:

- history of unprovoked or pregnancy-associated VTE
- presence of one or more high-risk thrombophilias – for example, antithrombin III deficiency or antiphospholipid syndrome.

Although VTE may occur during pregnancy, the daily risk is considerably higher during the four to six weeks after delivery than during the pregnancy itself.

Other considerations

Patients with a strong family history of VTE, recurrent VTE or documented unprovoked VTE before the age of 40 years are at increased risk of developing VTE during surgical procedures or if they have medical conditions requiring admission to hospital. Some of these patients may have blood thrombophilia factors, the presence of which could be useful in identifying those at higher risk of developing VTE before hospitalisation.

It is considered prudent for patients in the high risk surgical or medical categories outlined above to stop taking hormone replacement therapy (HRT) and the oral contraceptive pill preoperatively if possible. Ideally, the oral contraceptive pill should be ceased one menstrual cycle before planned surgery and other methods of nonhormonal contraception used. HRT should be ceased six weeks before planned surgery; however, if the patient continues to take HRT or the oral contraceptive pill, effective VTE prophylaxis given during the period of VTE risk substantially reduces the hormone-related risk of VTE.

Options available for VTE prophylaxis

For effective VTE prophylaxis of surgical, medical and obstetric patients, it is important to assess patients according to:

- their individual VTE risk
- their clinical condition
- their risk of bleeding
- the appropriateness of the prophylaxis for the individual patient.

The assessment for VTE prophylaxis should occur before or on admission to hospital and prophylaxis should be started without delay and re-assessed regularly to ensure the type of prophylaxis used remains appropriate. In patients with prolonged hospitalisation before surgery, prophylaxis should be commenced during the preoperative period. Continued encouragement of early mobilisation and adequate hydration are important principles in all patients regardless of risk category.

Two main categories of VTE prophylaxis have been shown to be effective: pharmaceutical agents and mechanical devices.

Pharmaceutical agents

The effectiveness of subcutaneous injections of low-dose unfractionated heparin, low molecular weight heparin (enoxaparin [Clexane], dalteparin [Fragmin]) and the pentasaccharide fondaparinux (Arixtra) for preventing VTE have been well established, reducing the risk of VTE by 60 to 80%. A number of new antithrombotics are expected to be available in the near future, extending the choice of prophylactic agents, particularly noninjectables. There is a requirement for VTE prophylaxis protocols and for doctors to select the appropriate dose, dosage interval, duration of therapy and brand of prophylactic agent for each individual patient having referred to full product information.

Aspirin may have, at best, only a weak protective effect against the development of DVT in some people and, therefore, is not generally recommended for this purpose. Adjusted-dose warfarin (Coumadin, Marevan) may play a role in some high-risk orthopaedic surgical patients but requires regular INR monitoring of its effect.

Mechanical devices

Two main types of mechanical devices are widely used for the prevention of VTE – graduated compression stockings and intermittent pneumatic compression.

Graduated compression stockings have been shown to reduce the incidence of DVT.[4] Although studies have generally investigated the use of full-length stockings, it is anticipated that below-the-knee stockings would also provide a degree of protection against DVT. To be effective, graduated compression stockings:

- should be measured and fitted for the individual patient
- should be worn continuously during the period of immobility and until walking freely
- should be worn as instructed, ensuring the stockings are not rolled down, because patient compliance is essential
- are contraindicated in patients with critical limb ischaemia.

Table 1. Recommended VTE prophylaxis for surgical patients

Risk category	Clinical features	Prophylaxis	Duration	Dosage
High	• Hip or knee arthroplasty • Major trauma	LMWH or fondaparinux* and IPC and/or GCS	28 to 35 days for hip arthroplasty, at least 10 days in other cases	Enoxaparin (Clexane) 40 mg/day or dalteparin (Fragmin) 5000 U/day or fondaparinux* (Arixtra) 2.5 mg/day
High	• Hip fracture surgery • Other surgery and previous VTE and/or active cancer	LMWH or LDUH or fondaparinux* and GCS and/or IPC	28 to 35 days for hip fracture surgery, 5 to 10 days in other cases	Enoxaparin 40 mg/day or dalteparin 5000 U/day or LDUH 5000 U tds or fondaparinux* 2.5 mg/day
High	• Major surgery† in those aged over 40 years	LMWH or LDUH and GCS and/or IPC	5 to 10 days	Enoxaparin 20 mg/day or dalteparin 2500 U/day or LDUH 5000 U bd or tds

*Fondaparinux for orthopaedic surgery only. †Major surgery: intra-abdominal surgery or surgery of more than 45 minutes' duration.
Abbreviations: bd = twice daily; GCS = graduated compression stockings; IPC = intermittent pneumatic compression; LDUH = low-dose unfractionated heparin; LMWH = low molecular weight heparin; tds = three times daily; VTE = venous thromboembolism.

In the hospital environment, it is the role of the nurse or physiotherapist to assist with the selection and fitting of graduated compression stockings. In the outpatient setting, this responsibility may rest with pharmacy staff.

Intermittent pneumatic compression also reduces the incidence of DVT and is more effective than graduated compression stockings in high-risk patients when used in combination with anticoagulants or when anticoagulants are contraindicated. Recommendations for the use of intermittent pneumatic compression devices for DVT prophylaxis are similar to those given for graduated compression stockings in that they should be used during the period of immobility until full ambulation has returned.

Recommended VTE prophylaxis

Recommendations for VTE prophylaxis are dependant on the assessed patient risk and the clinical condition.[3]

Surgical patients

Surgical patients at high risk of developing VTE are divided into three main groups dependent on the type and duration of the pharmacological prophylaxis as shown in Table 1.

It is important to note that the risk of patients who have undergone hip or knee arthroplasty, hip fracture surgery or major trauma developing VTE continues well after their operation and therefore prophylaxis needs to be prolonged. Many of these patients will be discharged from hospital before the risk abates, and their local GP or postdischarge community care service will be required to ensure their prophylaxis is continued and assess them for possible VTE and/or bleeding. Patients often seek advice from their GP about the length of time they should take VTE prophylaxis. Unfortunately, a specific recommendation regarding the duration of prophylaxis is frequently omitted from the discharge summary.

In hip fracture surgery and major nonorthopaedic surgery in patients over 40 years of age, the duration (more than 45 minutes) and type of operation (intra-abdominal or intrathoracic *v.* nonbody cavity surgery) are most important and constitute a substantial risk of developing VTE.

A previous history of VTE and/or active cancer are significant predictors for the development of VTE postoperatively with major or other types of surgery. The recommended prophylaxis for surgical patients is shown in Table 1.

The requirement for VTE prophylaxis for all other surgical patients is dependant on the presence of any additional VTE risk factors that the patient may have, including immobility, thrombophilia, oestrogen therapy, pregnancy or puerperium, active inflammation, a strong family history of VTE and obesity. These factors, if present, will require consideration of the patient for VTE prophylaxis. Otherwise, there are no specific recommendations for prophylaxis other than the option of using graduated compression stockings. Laparoscopic surgery is associated with a low risk of developing VTE and unless a number of other factors are present, the nonpharmacological methods are generally preferred.

Medical patients

Available data suggest that prophylaxis could prevent about two-thirds of cases of VTE in medical patients, a reduction rate similar to prophylaxis in surgical patients. The recommended prophylaxis for medical patients at high risk of developing VTE and who are likely to be

immobile for more than two to three days is shown in Table 2.

Obstetric patients

Although there are insufficient clinical research data on optimal timing and dosage, low-dose unfractionated heparin or low molecular weight heparin are often considered for use in pregnant women with a history of VTE, thrombophilia or other risk factors. VTE prophylaxis is also worthy of consideration after a caesarean section in patients with additional risk factors, such as older maternal age and obesity. In at-risk obstetric patients, thromboprophylaxis should be continued for at least four weeks postpartum (Table 3).

Contraindications to prophylaxis

There are contraindications to some prophylactic options for VTE and, therefore, the type of prophylaxis chosen must be specifically tailored to the individual patient.

Pharmaceutical prophylaxis

Bleeding is the major complication of anticoagulant prophylactic treatment and the relative risks of bleeding compared with the risk of developing a VTE must be considered before starting anticoagulation. The following conditions are relative contraindications:

- active bleeding
- high risk of bleeding – for example, haemophilia, thrombocytopenia (a platelet count <50 x 10^9/L)
- history of gastrointestinal bleeding
- severe hepatic disease (INR >1.3)
- adverse reaction to heparin
- concurrent anticoagulation therapy
- high risk of falls
- terminal phase of cancer
- palliative management
- renal impairment (creatinine clearance

Table 2. Recommended VTE prophylaxis for medical patients

Risk category	Clinical features	Prophylaxis	Duration	Dosage
High	• Ischaemic stroke* • History of VTE • Active cancer • Decompensated heart failure • Acute-on-chronic lung disease • Acute inflammatory disease • Age over 60 years	LMWH or LDUH	Until resolution of acute medical illness or until hospital discharge	Enoxaparin 40 mg/day or dalteparin 5000 U/day or LDUH 5000 U bd or tds

*Favour LMWH over LDUH. Abbreviations: bd = twice daily; LDUH = low-dose unfractionated heparin; LMWH = low molecular weight heparin; tds = three times daily; VTE = venous thromboembolism.

Table 3. Recommended VTE prophylaxis for obstetric patients

Risk category	Clinical features*	Prophylaxis	Duration	Dosage
High	• History of unprovoked or pregnancy-associated VTE • Previous thrombosis and any documented thrombophilia • High-risk thrombophilia – e.g. antithrombin III deficiency, antiphospholipid syndrome, multiple thrombophilias	LMWH	Consider throughout pregnancy and 4 to 6 weeks postpartum	Enoxaparin 40 mg/day or dalteparin 5000 IU daily
Lower	• History of provoked VTE with provoking factor no longer present	LMWH	4 to 6 weeks postpartum	Enoxaparin 40 mg/day or dalteparin 5000 IU daily

*Also consider the use of graduated compression stockings and/or intermittent pneumatic compression after a caesarean section or in high-risk women. Continue use until the patient is fully ambulant. Abbreviations: LMWH = low molecular weight heparin; VTE = venous thromboembolism.

<30 mL/min/m^2), which is a relative contraindication for low molecular weight heparin (see manufacturers' product information).

Drug interactions such as with aspirin or NSAIDs also need to be considered because they can contribute to the risk of bleeding.

Mechanical prophylaxis

The successful use of graduated compression stockings is dependant on correct fitting and their continuous use during the VTE risk period. Incorrect fitting can occur because of a limited range of available stocking sizes or poor limb measurement for sizing of the stockings. Incorrectly fitting stockings invariably do not provide the graduated compression required for VTE prophylaxis. Reported complications with graduated compression stockings and intermittent pneumatic compression are rare but include lower-limb compartment syndrome, skin ulceration and common peroneal nerve palsy. Most importantly, these devices should not be used in patients with severe or critical ischaemia of the limbs.

Role of the GP

Knowledge of the guidelines presented in this article should be helpful to those GPs who continue to care for patients in the hospital setting who meet the criteria to receive VTE prophylaxis. Other GPs with no hospital patients will still see a number of patients whose need for VTE prophylaxis will overlap with their community-based care. This may be particularly evident in patients managed through a 'hospital in the home' system or even those with acute medical diagnoses in whom hospital admission has been delayed.

All patients should have their risk of developing VTE assessed as part of their hospital admission. Unfortunately, recent studies show that this is only occurring in about 60% of hospitalised patients who are at risk of VTE development. Of those who are assessed to be at risk of developing VTE, just over half actually receive appropriate prophylaxis. This is clearly not optimal patient care.

In patients being referred for consideration of hospital admission, the GP can assist in improving VTE prevention by providing them with information about VTE risk and ensuring that they discuss the appropriateness of VTE prophylaxis with their specialist. When a GP organises hospital admission of a patient who fits the criteria of being at high-risk of developing VTE, the referral letter from the GP should prompt the resident medical staff to assess the VTE risk and could

continued

General practice tips on VTE prevention

- Include information in your referral letter to facilitate VTE risk assessment for patients being admitted to hospital because hospital staff may not have sufficient medical history for an adequate VTE risk assessment.
- GPs with hospital-admitting rights must consider VTE risk assessment and prophylaxis in all their hospitalised patients.
- Be aware that postoperative patients may require VTE prophylaxis after discharge from hospital. The GP will be called on to facilitate this process.
- Consider VTE prophylaxis for 'hospital in the home' patients.
- Develop protocols for low molecular weight heparin injections and assessment for the possibility of developing VTE and/or bleeding within your practice communities.

Case study: VTE prophylaxis after hip replacement surgery

Joe Smith is a 75-year-old man who is well known to your general practice. He returns to see you after having spent a total of 18 days in hospital and rehabilitation for elective total hip replacement surgery. He lives alone and requests repeat prescriptions for his medications, including the new medications that have been started since his admission. He asks you if he needs to keep going with his 'stomach injections' and says he does not want to inject himself.

What are the options for Joe?

Comment

Joe remains at high risk of developing VTE, with the current guidelines stating that he should remain on VTE prophylaxis for 28 to 35 days after surgery – that is, another two to three weeks of low molecular weight heparin. As his GP, you may need to issue a prescription for low molecular weight heparin if the hospital has not already done so.

The issue of the administration of the low molecular weight heparin injections remains. Joe could be educated to inject himself, but he has stated he is not happy to do this. The other options include him attending your surgery daily or you co-opting the community district nursing service to assist.

even suggest a management plan. Such a proactive approach is strongly encouraged.

Furthermore, many patients will be discharged before the risk of developing VTE has fully abated, particularly if their mobility has not fully recovered. Ongoing prophylaxis may be necessary in these patients for some time after their discharge from hospital. Review of patients recently discharged from hospital should include awareness and assessment of the presence of DVT or pulmonary embolism and prompt investigations for diagnosis and treatment. General practice tips on VTE prophylaxis and a case study are provided in the boxes above.

Conclusion

While this article has focused on VTE prophylaxis within a hospital setting, which is usually not the domain of the typical GP, the risk does not stop in the hospital. The GP must be alert to the risk of patients developing VTE after hospital discharge and take appropriate preventive action. MT

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