

PREVENTION OF

Venous Thromboembolism



The Australia & New Zealand Working Party
on the Management and Prevention
of Venous Thromboembolism.

Best Practice Guidelines for
Australia & New Zealand

3rd Edition

The Australia & New Zealand Working Party on the Management and Prevention of Venous Thromboembolism is proud to be affiliated with the International Union of Angiology and the Australasian Society for Thrombosis & Haemostasis.



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guidelines for practice in Australia and New Zealand.

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INTRODUCTION

The Australian & New Zealand Working Party on the Prevention of Venous Thromboembolism consists of a group of experts dedicated to promoting best practice in the prevention, treatment and management of venous thromboembolism. They are:

Professor John Fletcher (Chairman)

Professor of Surgery,
Westmead Hospital,
University of Sydney

Assoc Prof Ross Baker

Consultant Haematologist
Royal Perth Hospital,
University of Western Australia

Professor Donald MacLellan

Area Performance Manager,
NSW Department of Health
North Sydney

Professor Beng Chong

Professor of Medicine,
University of NSW
St.George Hospital, Sydney

Dr Charles Fisher

Vascular Surgeon
Royal North Shore Hospital, Sydney

Professor Alex Gallus

Professor of Haematology,
Flinders Hospital, Adelaide

Assoc Prof Harry Gibbs

Vascular Physician
Princess Alexandra Hospital, Brisbane

Dr. Terry Hannan

Vascular Physician,
Tasmania

Dr. Geoff Matthews

Director of the Vascular Laboratory
Austin & Repatriation Med. Centre,
Melbourne

Professor Hatem Salem

Professor of Medicine,
Monash University,
Box Hill Hospital, Melbourne

Assoc Professor Michael Stacey

Associate Professor of Surgery,
University of Western Australia
Fremantle Hospital, Fremantle

Assoc Prof Stephen Gatt

Area Chair for Anaesthesia,
Prince of Wales Hospital
South Eastern Health, Sydney

Professor Andre Van Rij

Professor of Surgery
University of Otago Medical School,
Dunedin, New Zealand.

Dr. Damian Flanagan

General Practitioner,
Mornington Peninsula,
Victoria

These updated guidelines have been developed by the Australian and New Zealand Working Party to assist in the identification and treatment of patients at risk of developing venous thromboembolism (VTE). The recommendations are based on the International Union of Angiology (IUA) and American College of Chest Physicians (ACCP) consensus statements adapted to Australian and New Zealand conditions. The recommendations issue from evidence based practice using the highest level of evidence available.

The members of the Australian and New Zealand Working party hope that this booklet will encourage more appropriate and frequent VTE prophylaxis and treatment and in so doing reduce both patient suffering and health care costs. Further booklets in this series will specifically address the treatment of VTE and the management of chronic venous insufficiency (CVI).

Although there is extensive evidence to guide proper prophylaxis and treatment of VTE, several surveys show that the evidence is not always being followed. One reason for this is that current approaches tend to focus on the acute management of deep venous thrombosis (DVT), rather than on its prevention and chronic sequelae.

Symptomatic VTE is a major health problem with an annual incidence of 160 per 100,000 for DVT, 20 per 100,000 for symptomatic non-fatal pulmonary embolism (PE) and 50 per 100,000 for fatal autopsy detected PE. The need for prevention applies regardless of ethnicity.

One of the sequelae of VTE is CVI, a significant problem throughout the world. CVI decreases quality of life and increases health care costs by causing chronic oedema, cellulitis and recurrent venous ulceration. Venous ulcers develop in 300 per 100,000 population and the proportion due to deep vein thrombosis (DVT) is approximately 25%.

1**IMPORTANCE OF PREVENTION**

DVT occurs in over 50% of some categories of hospitalised patients if prophylaxis is not used (Table 1) although many are asymptomatic. It prolongs the length of hospital stay, increases drug and laboratory costs and causes potentially fatal PE. PE remains the commonest cause of preventable death; 1% of all hospital admissions will die from this. The long term sequelae of DVT may also be substantial, the most important being post-thrombotic CVI. Approximately 25% of all venous ulcers are due to DVT and may cost the Australian Health Care system over \$200 million annually.

Table 1. Incidence of DVT* without prophylaxis

Patient Group	
Stroke	56%
Elective hip replacement	51%
Multiple trauma	50%
Total knee replacement	47%
Hip fracture	45%
Spinal cord injury	35%
General surgery	25%
Myocardial infarction	22%
Neurosurgery	22%
Gynaecological surgery	14-22%
General medicine	17%

* DVT detected by screening – includes symptomatic & sub-clinical DVT.

2**VTE PROPHYLAXIS**

For effective VTE prophylaxis of surgical and medical patients, it is important to treat patients according to their individual VTE risk and associated clinical conditions.

The optimum length of VTE prophylaxis and treatment requires further research. Decisions regarding time of commencement and duration of prophylaxis should be made for each patient individually. However, in most studies, prophylaxis was used for at least 10 days in high-risk patients, 10 days or more in patients with knee replacement and 4-6 weeks in patients with hip replacement.

In hospital patients with a prolonged stay prior to surgery, prophylaxis during the pre-operative period should be considered. In higher risk surgical patients, if prophylaxis is not commenced before surgery then it should be used intra-operatively and/or post-operatively.

Continued encouragement of ambulation and adequate hydration are important principles in all patients regardless of risk category.

2.1 Duration of Prophylaxis

The duration of prophylaxis is important. In high-risk patients, the duration of prophylaxis is recommended to be a minimum of 10 days. In patients undergoing knee replacement surgery, prophylaxis should continue for 10 days or more and for 4-6 weeks in patients having hip replacement surgery.

2.2 Day Surgery & Minor Surgery

The risk of developing VTE when undergoing day surgery or minor surgery is considered to be generally low. However, in some day surgery including laparoscopic and arthroscopic surgery, the operative procedures can be relatively prolonged or the patient is already at moderate or high risk. In either circumstance, full VTE prophylaxis should be considered.

The following sections include information on common methods of prophylaxis. Section 6 provides recommendations for DVT prophylaxis in a wide variety of clinical situations.

3 PHARMACOLOGICAL AGENTS

Studies have confirmed the effectiveness of subcutaneous low-dose unfractionated heparin (LDUH), low molecular weight heparin (LMWH) and the pentasaccharide fondaparinux for preventing VTE. Dosage recommendations have not been included in this booklet, as it is up to each hospital and doctor to select the dose, dosage interval and brand of prophylactic agents having referred to full product information.

Aspirin may have at best a weak protective effect against DVT in some people and therefore is not first-line therapy for prophylaxis. Adjusted dose warfarin has a role in some high risk surgical patients but requires

regular monitoring of its effect. Newer agents, e.g. oral thrombin or Factor Xa inhibitors, may have a role in prophylaxis in the future.

3.1 Out of Hospital & Extended Prophylaxis

Many trials are based on inpatients remaining in hospital for 7-10 days. Increasingly, fewer patients stay as long as 10 days and after discharge may spend a considerable amount of time resting at home. They may not be truly ambulant and thus may be at increased risk of DVT.

There is no conclusive evidence to form recommendations for ambulatory patients. Nevertheless, it is important to be cautious with early discharge patients as they may still be at risk and may need continued prophylaxis during their convalescence. Patient groups where the value of extended prophylaxis has been demonstrated and where prophylaxis should be continued for 4-6 weeks include patients following hip fracture or hip replacement surgery and major curative surgery for cancer.

3.2 Neuraxial Block (Epidural/Spinal)

The use of epidural/spinal anaesthesia has been increasing in recent times. While the incidence of DVT may be reduced by neuraxial anaesthesia, the requirement is still high for appropriate prophylaxis. The risk of DVT and the importance of prophylaxis is not diminished with the use of neuraxial anaesthesia. However, anaesthetists have become increasingly concerned about the development of the complication of epidural haematoma in patients who are receiving pharmacoprophylaxis.

It is important for the individual patient that the risk of VTE is weighed against the risk of an epidural haematoma and discussions between the anaesthetist and the surgeon should take place early enough for appropriate planning of prophylaxis. While not being able to provide definitive recommendations from the literature, options for the management of such patients would include delaying systemic pharmacological anticoagulants until after the insertion of the epidural catheter or ensuring that pharmacological anticoagulant agents are not administered within 12 hours prior to the insertion or 6 hours following

withdrawal of an epidural catheter (see American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines www.asra.com/).

4 MECHANICAL DEVICES

Two main types of mechanical devices are widely used in the prevention of VTE – Graduated Compression Stockings (GCS) and Intermittent Pneumatic Compression (IPC).

4.1 Graduated Compression Stockings

GCS reduce the incidence of DVT. Studies have generally involved full-length stockings. Although it is anticipated that below knee stockings should also provide a degree of protection against DVT, there are few comparative studies.

There are two distinct and non-interchangeable types of GCS, one for DVT prophylaxis and the other for treatment of CVI. In order to achieve optimal benefit from the use of GCS, some general recommendations are provided in Table 2.

Table 2. General recommendations for the use of graduated compression stockings for DVT prophylaxis

- Should be worn continuously during the period of immobility to the return of full ambulation
- Patient compliance is essential eg. ensuring stockings not rolled down
- Are contraindicated in critical limb ischaemia
- Should be measured and fitted for the individual patient

There are a wide variety of GCS available in Australian and New Zealand. However, there are no Australian standards regulating their manufacture and clinical performance. Ideal characteristics for GCS are set out in Table 3.

Table 3. Ideal characteristics for the selection of GCS stockings for DVT prophylaxis

- Evidence of clinical efficacy
- Pressure of 16mmHg to 20mmHg at the ankle in the supine position with graduated compression to the knee or above
- Appropriate and individual sizing for each patient
- Sizing range should be suitable for a large percentage of the population and the window of coverage should be clearly defined
- Washing and reuse guidelines should be provided
- Appropriate manufacturing standards to ensure quality control
- Independent testing and compression profile of each stocking brand using internationally accepted methods

4.2 Intermittent Pneumatic Compression

IPC reduces the incidence of DVT and is more effective than GCS in high risk patients in combination with anticoagulants or when anticoagulants are contraindicated.

The use of IPC devices for DVT prophylaxis is similar to the GCS recommendations in that they should be used during the period of immobility to the return of full ambulation and not used in limbs with critical ischaemia.

4.3 Pharmacological & Mechanical Combinations

Combinations of agents (for example, subcutaneous heparin with GCS and/or IPC) may be more effective than single interventions alone. Although studies have generally been too small to draw strong

conclusions for prophylaxis in high-risk patients, a combination of pharmacological & mechanical therapy is recommended (see Tables 5, 6 & 7).

5 **ADDITIONAL CONSIDERATIONS**

There are a number of other conditions worthy of consideration when determining the risk of VTE.

5.1 **Pregnancy & Postpartum**

Several factors increase the risk of VTE during pregnancy including Caesarean section, obesity, advanced maternal age and thrombophilia. Although there is insufficient data on optimal timing and dosage, LDUH or LMWH are commonly considered for use in pregnant women with a history of idiopathic proximal VTE, thrombophilia or other high-risk factors. In these patients thromboprophylaxis should be continued for four weeks post-partum. Women undergoing Caesarean section should receive thromboprophylaxis irrespective of their past history or risk for venous thrombosis as long as there are no contraindications for anticoagulant therapy.

5.2 **Oestrogen Preparations**

It is considered prudent to stop hormone replacement therapy (HRT) and the oral contraceptive pill pre-operatively if the patient is in the high risk or moderate risk categories. In the absence of other risk factors, there is insufficient evidence to support routine pre-operative cessation of oral contraceptives or HRT. Appropriate prophylaxis should be used when these agents have not been stopped. Ideally, the oral contraceptive pill should be ceased the cycle before planned surgery and other methods of contraception considered. HRT should cease six weeks before planned surgery.

5.3 **Thrombophilia**

There are many types of thrombophilia (Table 4) but the presence of thrombophilic factors alone do not greatly increase the risk of VTE. However, patients with thrombophilia and a strong family history of

VTE, recurrent DVT, or documented unexplained thrombosis before the age of 40 years are at increased risk of VTE and should receive prophylaxis during any surgical or medical condition. Screening for thrombophilia before surgery is not required and specialist advice should be sought before screening is considered.

Table 4. Causes of thrombophilias

Higher Level of Risk:

- Antithrombin III deficiency
- Protein S deficiency
- Protein C deficiency

Lower Level Risk:

- Activated protein C resistance (Factor V Leiden)
- Prothrombin gene mutation
- Hyperhomocysteinaemia
- Lupus anticoagulant
- Antiphospholipid antibodies
- Hyperhomocysteinaemia
- Myeloproliferative disease

6

RISK STRATIFICATION AND APPROPRIATE PROPHYLAXIS

This section provides recommendations for VTE prophylaxis in a wide variety of clinical situations.

6.1 Non-Orthopaedic Surgery

In non-orthopaedic surgical patients, a prior history of VTE is a most important predictor for the development of VTE post-operatively. Other risk factors include malignancy, obesity, increasing age, varicose veins, the use of oestrogen containing preparations or the presence of thrombophilic factors. The duration and type of operation is most important (eg. intra-abdominal and intra-thoracic versus non-body cavity surgery). Additional risk factors include immobility, dehydration and the presence of sepsis. The risk classification based on the IUA consensus statement is shown in Table 5.

Table 5. Recommended prophylaxis in surgical patients (General and Vascular Surgery, Gynaecology, Urology)

Risk category	Clinical features	Recommended prophylaxis
High	<ul style="list-style-type: none">• Major surgery #, age > 60 years• Major surgery, age 40-60 years with cancer or history of VTE or other risk factors• Major surgery, history of VTE	LMWH** and GCS &/or IPC
Moderate	<ul style="list-style-type: none">• Major surgery, age 40-60 years without other risk factors• Minor surgery, age > 60 years• Minor surgery, age 40-60 years with history of VTE or on oestrogen therapy or other risk factors	LDUH or LMWH
Low	<ul style="list-style-type: none">• Major surgery, age 16-40 years with no other risk factors• Minor surgery, age 16-60 years with no other risk factors	Consider GCS

Major surgery is any intraabdominal operation and all other operations lasting more than 45 minutes.

**10 days minimum prophylaxis

6.2 Orthopaedic Surgery and Trauma

Major elective orthopaedic surgery and major trauma are high risk for DVT. Recommendations on the management of these patients is summarised in Table 6.

Diagnosis	Recommended prophylaxis
Elective hip replacement Hip fracture Total knee replacement	LMWH* or Fondaparinux* AND GCS &/or IPC
Multiple trauma	LMWH* AND GCS &/or IPC

* 10 days minimum prophylaxis

6.3 Medical Patients

Up to 75% of fatal PE in general hospitals occur in non-surgical patients immobilised by medical illness, yet there are fewer trials on VTE prophylaxis for hospitalised medical patients compared to surgical patients. Available data suggest that prophylaxis can prevent approximately two thirds of VTE in medical patients, a reduction rate similar to prophylaxis in surgical patients.

Patients suffering an acute stroke with paralysis of a lower limb, decompensated cardiac failure, acute on chronic lung disease, acute inflammatory disorders or active cancer are at highest risk of VTE (Table 7). Medical patients with additional risk factors should be considered for prophylaxis.

Table 7. Recommended prophylaxis in acute medical illness

Risk category	Risk Factors	Recommended prophylaxis
High	<ul style="list-style-type: none">• Age > 60 years*• Ischaemic Stroke• History of VTE• Decompensated cardiac failure• Active cancer• Acute on chronic lung disease• Acute on chronic inflammatory disease	LDUH or LMWH or GCS &/or IPC if heparin contraindicated

*While patients aged over 60 years are currently classified as high risk, those that are otherwise well and ambulant may not be at high risk for VTE in the absence of other risk factors.

6.4 Travel Related VTE

The risk of travel related DVT is not confined to air travel. There is little information available in the literature with recent studies indicating that the incidence of travel related PE appears to be small and is estimated to be about 1:1 million arrivals although possibly increasing to 1:70,000 arrivals for flights longer than 12 hours. Further studies are required to fully define the risk of travel related VTE. However, based on current information and knowledge, the majority of the travelling public are at low risk of developing a DVT and some common sense suggestions should be followed:

- Ensure adequate hydration by drinking sufficient fluids
- Regularly mobilise ankles, massage the calves and exercise leg muscles when seated for prolonged periods
- Avoid combining sedatives with excess alcohol
- Wear non-restrictive clothing
- Exercise eg. walking, before and after travel and during stop-overs.

Considered at high risk are those travellers with a history of previous VTE, those with known pro-thrombotic states, recent surgery, significant medical illness or with multiple risk factors. In these patients the administration of prophylactic LMWH and use of properly measured and fitted GCS (20-25mmHg) is suggested. Lower compression (e.g 16-20 mmHg) does not offer adequate protection

when the legs are in a dependent position. Non-graduated stockings are not recommended.

Aspirin is not likely to be appropriate as at best it may have a weak protective effect and in some people excess bleeding may negate any benefit.

7 COST EFFECTIVENESS OF VTE PROPHYLAXIS

Currently recommended prophylactic methods have been demonstrated to be cost effective in patients at moderate and high risk of VTE due to the high cost of diagnosis and treatment of VTE in these patients. There are no data on the cost effectiveness of prophylaxis in low risk groups. Effective VTE prophylaxis and treatment should also reduce the costs of managing the post-thrombotic syndrome and its consequences, especially chronic venous leg ulcers.

8 DIAGNOSIS AND TREATMENT OF VTE

Best Practice Guidelines for the diagnosis and treatment of VTE have been published in booklet form by the Australian and New Zealand Working Party.

In summary, the clinical diagnosis of DVT and PE is inaccurate and if suspected, should be confirmed by objective investigations although treatment may be commenced in the meantime. The current recommendation is to perform venous duplex ultrasound scanning for suspected DVT. For the diagnosis of suspected PE, ventilation perfusion scanning, CT angiography or pulmonary angiography is recommended according to local practice. Reliance on D-Dimer without pre-test probability assessment is not recommended.

Swift and effective diagnosis and treatment of active VTE helps to prevent thrombus extension, leg swelling, potentially fatal PE and the development of the post-thrombotic syndrome. Therapeutic heparin is required (usually low molecular weight heparin). Oral anticoagulants should overlap heparin therapy for at least 2 days. Thrombolysis, thrombectomy or insertion of an IVC filter may be required in selected patients.

Following a DVT, consideration should be given for the use of long term GCS (>20mmHg). Several studies have shown that GCS can reduce the incidence of post-thrombotic syndrome by up to 50%, yet many patients do not receive GCS.

9

IMPLEMENTATION OF BEST PRACTICE VTE PROPHYLAXIS GUIDELINES

There are a number of studies in the literature that suggest inpatient VTE prophylaxis is sub-optimal. A major challenge, therefore, is to implement appropriate systems and policies in hospitals that ensure compliance with best practice guidelines. Further recommendations include:

- Prophylaxis should be used routinely
- Hospital policies should include VTE prophylaxis guidelines
- VTE prophylaxis guidelines should be included in clinical pathways, ward and specialist unit guidelines and staff manuals.
- Hospitals should undertake regular audit of the extent and quality of VTE prophylaxis
- Clinicians should ensure that individual patients have a VTE risk assessment documented in the case notes
- The application and use of mechanical methods of prophylaxis should be recorded
- Familiarisation of VTE prophylaxis guidelines should be included in senior and junior medical staff orientation, hospital grand rounds and hospital newsletters
- Liaison should occur with community care physicians particularly for patients receiving extended prophylaxis out of hospital

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APPLICABILITY

There are many clinical situations where the literature provides little information to direct VTE prophylaxis recommendations. In these circumstances, the Australia and New Zealand Working Party has applied recommendations based on expert judgement and experience.

FURTHER READING

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