Venous Thromboembolism: An Insidious Hazard Part 1: Incidence, Prevalence and Sequelae

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Summary

Venous ulceration continues to be a significant cause of a poor quality of life for patients and a major burden on the Australian health dollar. It is estimated to cost $300-500 million per annum to manage. Prevention of deep venous thrombosis (DVT) and the consequent chronic venous insufficiency (CVI) would have a major impact on the prevalence of venous ulcers. This review examines the incidence of DVT and pulmonary embolism (PE) in the community and determines the consequences of CVI and ulceration. Clinicians are encouraged to consider prophylaxis for this insidious condition.

CVI is an insidious condition with wide ranging consequences. These consequences include symptoms of leg pain, cramps, pruritus and paraesthesia accompanied by signs of chronic oedema, skin induration and hyperpigmentation as well as cellulitis and chronic leg ulceration (Figure 1).

The resultant quality of life of patients with CVI is significantly decreased, particularly in those patients suffering the more overt manifestations e.g. leg ulceration. Not surprisingly, CVI is a substantial drain on the health dollar, requiring large amounts of primary physician and nursing time, contributing notably to inpatient bed days and consuming immense volumes of wound pharmaceuticals [1].

CVI reflects venous valvular incompetence in the superficial and/or deep venous systems of the lower limb. Despite the progression towards chronic leg ulceration being well recognised, all too often the management of CVI is inadequate. The consequent management of leg ulceration costs the Australian health system $300-500 million per annum.

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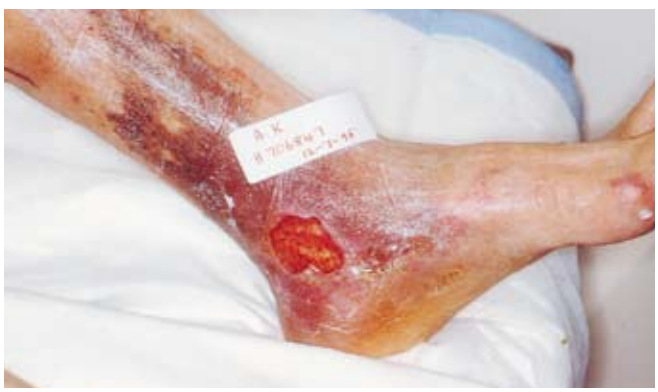
Unquestioningly, the best method of managing CVI is to prevent it in the first instance. One major cause of venous valvular damage is DVT. Regretfully, despite extensive evidence on the prophylaxis and treatment of DVT, clinicians frequently do not follow best practice guidelines. As a result, the sequelae including CVI are much more prevalent than they otherwise should be.

As clinicians dealing with these sequelae, e.g. leg ulceration, it is important to update knowledge of the incidence and prevalence of DVT and CVI. Moreover, many wound clinicians have the opportunity to play a preventative role in CVI by encouraging best practice in DVT prophylaxis and compliance with graduated compression, when appropriate, whether the patient is in hospital or the home. It is expected that the review of venous thromboembolism will stimulate discussion about a problem that receives insufficient attention by clinicians. This

Figure 1. DVT occurred in this patient's leg 20 years earlier. Note hyperpigmentation and venous ulceration.



first article reviews the incidence, prevalence and sequelae of venous thromboembolism and will be followed by articles covering DVT prophylaxis and treatment and a review of graduated compression therapy.

Extent of the thromboembolic problem

The most serious manifestation of thromboembolism is PE. PE continues to be a major cause of death in hospitalised patients. Sandler and Martin found that 9 per cent of patients admitted to a general hospital in the UK died and 10 per cent of these deaths were due to PE, i.e. 0.9 per cent of all admissions [2]. Most concerning was their finding that in these patients dying of PE, preceding non–fatal thromboembolism occurred in 20 per cent but in only 3 per cent was it recognised and treated by clinicians.

In the population at large, the annual frequency of DVT is approximately 160 per 100,000, 20 per 100,000 for non–fatal PE and 50 per 100,000 for fatal autopsy proven PE [2, 3]. There is considerable variation between countries in the incidence of thromboembolism and indeed considerable variation as a result of the prevailing attitude towards DVT prophylaxis.

It has been increasingly recognised that the risk of developing DVT varies between hospitalised patient groups. The risk is dependent on patient related variables including age, immobility, obesity, previous thromboembolism and presence of sepsis (Table 1) [4].

The risk of thromboembolism increases with age in an exponential manner. After 40 years of age, the risk becomes appreciable when coupled with major illnesses, trauma or surgery. A history of previous thromboembolism is also highly concerning as the risk of post–operative DVT is over 50 per cent [5]. If patients developing DVT are less than 45 years of age, have recurrent DVTs or have a family history of thromboembolism, screening for thrombophilias should be undertaken as well as investigations for other causes of hypercoagulability (Table 2) [6].

Many studies have also estimated the risk of thromboembolism within various surgical and medical subpopulations, as well as others including trauma and obstetric. A commonly quoted stratification risk scale for hospitalised patients was developed by Salzman and Hirsh in 1982 [7] and is presented in a modified form (Table 3) [2]. Low risk patients have a risk of DVT of less than 10 per cent and a proportionally low risk of proximal extension into the popliteal, femoral or iliac veins from which emboli more commonly arise. In contrast, high risk patients have an

Table 1. Risk factors for venous thromboembolism in inpatients.

Patient factors	Disease/surgical procedure
Age/obesity	Trauma or surgery, especially of pelvis, hip, lower limb
Varicose veins/immobility (bed rest over 4 days)	Malignancy, especially pelvic, abdominal, metastatic
Pregnancy	Heart failure
Puerperium	Recent myocardial infarction
High dose oestrogen therapy	Paralysis of lower limb(s)
Previous deep vein thrombosis or pulmonary embolism	Infection/inflammatory bowel disease
Thrombophilia	Nephrotic syndrome
Deficiency of antithrombin III protein C, or protein S	Polycythaemia/ paraproteinaemia
Antiphospholipid antibody or Lupus anticoagulant	Paroxysmal nocturnal haemoglobinuria/Behcet's disease

Table 2. Partial list of causes of hypercoagulability.

Genetic	Acquired	Physiologic
Antithrombin deficiency	Surgery	Age
Protein C deficiency	Trauma	Gender
Protein S deficiency	Pregnancy	
Activated protein C resistance	Immobilization	
Hyperhomocysteinemia	Hyperhomocysteinemia	
Prothrombin-20210	Smoking	
Dysfibrinogenemia	Obesity	
Plasminogen deficiency	Antiphospholipid	

incidence of DVT from 40-80 per cent, a high risk of proximal extension (10-30 per cent) and a subsequent risk of fatal PE of up to 10 per cent. High risk patients include those undergoing major orthopaedic operations of pelvis, hips and lower limbs or major pelvic or abdominal surgery. They require the highest level of prophylaxis to reduce the risk of thromboembolism but, unfortunately, it will still not extinguish the risk.

Diagnosis of venous thromboembolism

The diagnosis of venous thromboembolism is not an exact science. Even when clinically suspected, more than half the cases of DVT are not confirmed by investigation. A major diagnostic complication is the fact that DVT can occur with only minimal symptoms and signs and a number of other conditions can masquerade as DVT (Table 4) [8].

Venography remains the 'gold standard' for the diagnosis of DVT. A dorsal foot vein is injected with contrast and an intraluminal filling defect is sought in the deep veins. Problems with venography include its technical difficulty; 20 per cent of venograms are inadequate for diagnosis. Venographic examinations are invasive, can be painful, cause superficial phlebitis and hypersensitivity reactions. Although venography remains the standard against which other diagnostic modalities are compared, in current clinical practice venography is infrequently used.

Ultrasonography is increasingly used to diagnose DVT, particularly in the proximal deep veins. With colour duplex ultrasound, the deep veins can be visualised and the flow characteristics determined. Diagnosis of DVT is based on non-compressibility of a vein, presence of thrombus in the lumen and absence of venous flow augmentation during calf compression. While ultrasound is non–invasive, safe and readily repeatable, its reliability for detecting calf vein thrombosis is lower than for proximal vein thrombosis. However, calf vein thrombosis represents a low risk for venous thromboembolism. Thus, even though the duplex scan may miss infrapopliteal vein thrombosis, the scan is still most useful for detecting the clinically significant proximal vein thromboses.

Table 3. Incidence of venous thromboembolism in hospital patients according to risk group

	Deep vein thrombosis	Proximal vein thrombosis	Fatal pulmonary embolism
Low risk groups	<10%	<1%	0-01%
Moderate risk groups	10-40%	1-10%	0.1-1%
High risk groups	40-80%	10-30%	1-10%
Low risk group:			
• Minor surgery (<30 min); no risk factors other than age			
• Minor surgery (>30 min); age <40; no other risk factors			
• Minor trauma or medical illness			
Moderate/high risk group:			
• Major general, urological, gynaecological, cardiothoracic, vascular, or neurological surgery; age > 40 or other risk factor			
• Major medical illness: heart or lung disease, cancer, inflammatory bowel disease			
• Major trauma or burn			
• Minor surgery, trauma or illness in patients with previous deep venous thrombosis, pulmonary embolism or thrombophilia			
• Fracture or major orthopaedic surgery of pelvis, hip or lower limb			
• Major pelvic or abdominal surgery for cancer			
• Major surgery, trauma or illness in patients with previous deep vein thrombosis, pulmonary embolism or thrombophilia			
• Lower limb paralysis (for example, hemiplegic stroke, paraplegia)			
• Major lower limb amputation			

Table 4. Differential diagnosis of DVT

Venous disorders
• Chronic venous hypertension
- panniculitis
- lipodermatosclerosis
- venous incompetence
• Superficial thrombophlebitis
• Extrinsic compression of the veins
- tumour
- haematoma
- arterial aneurysm
Orthopaedic disorders
• Ruptured Baker's cyst
• Muscle strain, injury tear or haematoma
• Compartment syndrome
Infection
• Cellulitis
Lymphatic disorder
• Lymphoedema and lymphangitis
Others
• Reperfusion oedema or post-bypass surgery
• Leg oedema in a paralysed limb
• Generalised oedematous state

If DVT is clinically suspected, the proper decision should be to treat empirically and then investigate. Even if the clinical suspicion is not supported by duplex scanning, empirical treatment should considered and the scan repeated in 1-2 days. The main period of risk for PE is before leg swelling or other symptoms occur [9] and therefore heparinisation is advised when clinical suspicion arises. If DVT is detected, consideration for a baseline lung scan should also be entertained, particularly if the DVT is present in the proximal veins [10].

Post–thrombotic sequelae

The clinical consequences of DVT are not necessarily short-term. The development of post–thrombolic sequelae, e.g. leg ulceration, can be a long–term debilitating condition, yet it is not well documented in the literature. Recently, one major study followed a cohort of patients for 8 years following their first episode of symptomatic DVT. Of major concern was the authors finding that post–thrombotic syndrome occurred in almost one third of these patients and they also had a high risk of recurrent venous thromboembolism [11]. This study was found to contrast with some earlier studies where the rate of post–thrombotic syndrome was found to be even higher. However, in the earlier studies the use of graduated compression stockings was conjectured to be lower, thus increasing their rate of DVT.

It is obviously of prime concern to wound clinicians that the incidence of post–thrombotic syndrome is so high. It certainly emphasises the importance of both preventative management and appropriate therapy for DVT. In particular, advising patients following a DVT of the benefit of graduated compression hosiery in the prevention of long term problems.

Conclusion

Venous thromboembolism continues to have an insidious presence in the community especially following immobilisation in the hospital or the home. While the high risk groups are generally recognisable, fatal PE still plagues these patients. Appropriate prophylaxis can reduce the incidence of both DVT and PE as well as the long term sequelae of venous thromboembolism.

Regretfully, the sequelae of CVI and venous ulceration continues to haunt patients, reducing significantly their quality of life as well as remaining a major drain on the Australian health dollar. It behoves clinicians, particularly those dealing with venous ulcers, to work towards ensuring that the risk of venous thromboembolism is kept as low as possible. That entails following the well recognised best practice guidelines for DVT prevention [12] and management [10].

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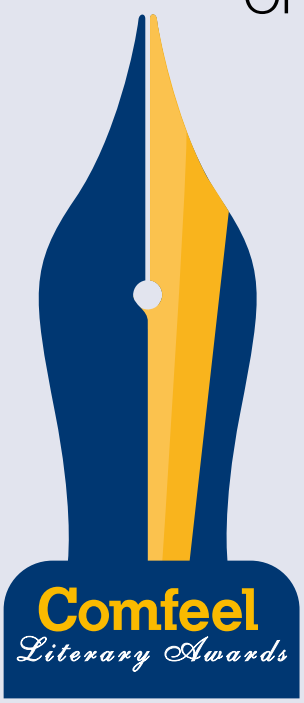

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