REVIEW ARTICLE

Deep vein thrombosis and pulmonary embolism in the Chinese population

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Deep vein thrombosis and pulmonary embolism are well-recognised major health problems in the West. There is a deep-rooted belief among clinicians that deep vein thrombosis is rare in Asians, particularly in the Chinese population. However, it appears that the incidence of venous thrombosis and pulmonary embolism is increasing in Chinese patients. Prophylaxis reduces the incidence of venous thrombosis by 66% and of pulmonary embolism by 50%—prophylaxis should therefore be considered for Chinese patients who have a high risk of developing postoperative deep vein thrombosis. This report reviews the current literature on this subject.

HKMJ 1998;4:305-10

Key words: Anticoagulants; Fibrinolysis; Heparin; Postoperative complications; Pulmonary embolism

Introduction

In 1934, Homans[1] described the relationship between deep vein thrombosis (DVT) and pulmonary embolism (PE). Since then, thromboembolism has been well recognised as a major public health problem in the West. A study performed in the United Kingdom found that 0.9% of all patients admitted to hospital had fatal pulmonary embolism.[2] The prevalence of DVT in surgical patients is 10% to 80%, depending on the type of surgery and individual patient risk factors.[3,4] It is generally accepted that postoperative DVT is rare in Asians, particularly in the Chinese population.

Prevalence of deep vein thrombosis

There have been several recent reports about DVT and PE in the Chinese population in recent years; they cite a prevalence of DVT of 2.6% to 17%.[5-10] A similar figure has been reported for Malaysian and Thai patients.[11,12] In an autopsy study, Chan and Hoaglund[8] reported a prevalence of pulmonary thromboembolism (PTE) of 0.75% in the adult Hong Kong Chinese population. A similar retrospective study by Chau et al[9] reported a prevalence of 2.1%. Recent data from a study performed in Hong Kong between 1990 and 1994 show an increased prevalence of PTE—namely, 4.7%.[13] These figures are within the lower range of the prevalence of PTE in Caucasian patients—reported rates of significant PTE from all autopsies are 3.4% to 9.0% in the United States[14] and 12.8% in the United Kingdom.[15] Interestingly, there seems to be a seasonal variation in the frequency of PTE in Hong Kong (as diagnosed during necropsy), and two troughs can be identified: one in early summer (June and July) and the other in early winter (November and December). The prevalence of pulmonary thromboembolism varies from 1.6% to 5.5%.[16] Seasonal variations have also been found in patients in Birmingham, United Kingdom—namely, the presence of two peaks in spring and autumn. It has been noted that the humidity, which is low in winter in Hong Kong, is similar to that of summer in the United Kingdom[16]; however, its association with PTE is unclear.

The site of DVT also differs in Caucasian and Chinese patients. In the latter, the thrombi are mostly found in the calf veins[5,7,17] whereas in Caucasians, proximal veins are more commonly involved. The probability of PTE complicating DVT has been reported to be 46%, 67%, and 77% for the calf, thigh, and pelvic veins, respectively.[13]

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Prevalence of venous thrombosis in Chinese patients

The explanation for the low prevalence of DVT in the Chinese population is a matter of speculation. Several factors are likely to be responsible; they include race, diet, and climate. Racial factors alone are unlikely to be the explanation. Chinese people who have been living in western countries for several generations may have a much higher incidence of DVT. This is also the case for African Americans, whose prevalence of DVT is similar to white Americans.[18] Fibrinolytic activity in the blood is higher in Africans, Indians, and New Guineans than it is in Caucasians.[19,20] Studies in rats show that fibrinolytic activity can be reduced by a raised plasma lipid level which, in turn, is influenced by the dietary intake of fat.[21] A low dietary fat intake is a possible explanation for the low incidence of DVT in the Chinese population. Lawrence at al[22] have demonstrated a seasonal variation in the incidence of DVT: many more cases of DVT occur in the six cold months of the year than during the warmer months. The tropical climate of south-east Asia may thus be partly responsible for a low prevalence of DVT in Asians.

Risk factors for the development of deep vein thrombosis

Extensive epidemiological studies of patients with thromboembolism have identified several factors that enhance the risk of the development of DVT. These factors include surgery, age, sex, heart failure, history of previous thromboembolism, direct trauma to the leg, use of oral contraceptives, and limb weakness. Patients who are admitted to hospital can be classified into three groups according to their degree of risk, as recommended by the European Consensus Group (Box).[23]

Classification of patients according to the degree of risk

Low-risk patients
<40 years without additional risk factors
Minor surgery (<30 minutes)

Moderate-risk patients
>40 years
Major surgery (>30 minutes)
Oral contraceptives
Immobilised medical patients with active disease

High-risk patients
Previous deep vein thrombosis or pulmonary embolism
Major surgery for malignant disease
Orthopaedic surgery on lower limbs
Stroke, heart failure, or acute myocardial infarction

The prevalence of DVT associated with surgical procedures that last more than 4 hours can be as high as 80%; it is also high in patients undergoing surgery for malignant disease. The prevalence in Caucasians varies for different types of operation, as follows: neurosurgery, 29% to 50%; general surgery, 30%; urological surgery, 50%; and orthopaedic surgery, 54%.[24] The reported figures for Chinese patients are as follows: neurosurgery, 10%; general surgery, 8.5%; colorectal surgery, 4%[9]; and orthopaedic surgery, 53.3%.[17] Surgery causes changes in coagulation and platelet function that may favour thrombus formation. Immobility during surgery causes stasis in the venous sinuses of the calf veins and pressure against the operating table can lead to vessel wall hypoxia. These factors fulfill Virchow's triad of stasis, vessel wall injury, and altered coagulation that initiates thrombus.

An increased incidence of DVT with increasing age, especially in patients aged more than 60 years has been noted in both autopsy and clinical studies. Venous thrombosis is more common in women than in men. This difference is most pronounced during the reproductive age, when there is a two- to three-fold increase. The rate of fatal PE in Chinese women is significantly higher than in Chinese men.[13] The primary site of thrombi in Caucasian patients is the thigh. In Chinese patients, however, the majority of thrombi are limited to the calf veins, and there is a 40% to 53% risk of thrombosis in an injured leg and 25% to 52% in a non-injured leg.[13,17]

Women who use oral contraceptives show a four-fold increase in the incidence of thromboembolism. There is also evidence that contraceptive pills are associated with an increased risk of postoperative thromboembolism when they are taken in the month prior to surgery.[25] Tso et al[6] have reported a 10.5% incidence of DVT in Chinese women who were taking oral contraceptives prior to pelvic surgery.

Limb weakness is a well-known risk factor. In a study of patients who had recently had a stroke, Warlow et al[26] reported an incidence of DVT of 60% in the paralysed leg compared to only 7% in the non paralysed leg in both Caucasian and Chinese patients. An incidence of 17% of DVT in the paralysed limb has been reported in Chinese patients.[7]

Diagnosis of deep venous thrombosis

Some objective diagnostic tests, preferably non-invasive, are needed to screen patients who have a high risk of DVT developing or who have signs and symptoms of

DVT. It is important that clinicians maintain a high level of awareness of the risk so that early diagnosis can be made and treatment initiated to prevent the serious, often fatal complications of PE. Treatment for DVT should not be given without objective confirmation of the diagnosis. Only about 30% of the patients with clinically diagnosed DVT also have the diagnosis confirmed by reliable objective tests.[27]

Venography

The traditional 'gold standard' method used to diagnose DVT has been venography. Ultrasonic imaging has now replaced venography as the new diagnostic standard in many hospitals. All of these tests, however, have limitations as screening tests. Venography is invasive, needs to be done in the X-ray department, and cannot be repeated readily. In addition, asymptomatic thrombi tend to be small, non-occlusive, and limited to the calf; they are thus difficult to detect by using non-invasive tests.

Although morbidity can be associated with venography, there is none associated with ultrasonography, which can be used as an alternative to venography in most patients. Furthermore, even the morbidity from venography is much less than the morbidity associated with anticoagulation therapy.

Non-invasive tests

Non-invasive tests can be performed at the bedside and can be repeated. Real-time B-mode compression ultrasonography is sensitive and specific for diagnosing proximal vein thrombosis and is more accurate than impedance plethysmography. Doppler ultrasonography is a sensitive method for detecting proximal vein thrombosis, but it is less sensitive for the diagnosis of calf vein thrombosis. Impedance plethysmography is both sensitive and specific for diagnosing completely occluded proximal veins, but it is insensitive for diagnosing thrombosed proximal veins that are partially occluded. Leg scanning that uses fibrinogen I 125 has been primarily used as a screening test for medical and surgical patients who have a high risk of DVT developing. It is also used as an adjunct to impedance plethysmography to confirm or exclude the diagnosis of clinically suspected venous thrombosis. Leg scanning that uses fibrinogen I 125 accurately diagnoses DVT, but there is some concern about the possible transmission of blood-borne diseases.

Other techniques used to diagnose venous thrombosis include isotopic methods, blood tests, and other non-invasive tests. However, these tests have not been evaluated fully and their role in clinical practice remains unproven.[27] Radioisotopic techniques include radionuclide venography with technetium Tc 99m–labelled macro-aggregated albumin or human albumin microspheres, technetium Tc 99m–labelled red blood cells, and indium 111–labelled platelets. The limited accuracy of the various isotopic techniques reported in the literature to date, their invasiveness, the radiation exposure, and the high cost of preparing the isotopes argue against their use for the diagnosis of venous thrombosis.

Blood tests can detect the presence of intravascular fibrin by measuring fibrinopeptide A in the plasma or fibrin/fibrinogen degradation products in the serum such as D-dimer and fragment E. These tests have been shown to be sensitive but not specific, and their use is primarily confined to research centres.[27] Other non-invasive tests like phleborrheography, thermography, and strain-gauge plethysmography require further evaluation.

Advances in prophylaxis of venous thrombosis

Prophylaxis of venous thrombosis in Caucasian patients is cost-effective and reduces fatal complications and treatment requirements. Selective prophylaxis in Chinese patients undergoing high-risk surgery should be considered. The physical methods of prophylaxis described below can be safely used for these patients. If one decides to rely on pharmacological methods, however, low molecular weight heparins should be used where possible, as they are effective and safe.

There are several different effective methods available for preventing venous thrombosis and these can be divided into physical and pharmacological methods.

Physical methods

The use of graduated compression stockings is the most popular physical method used to prevent DVT. Intermittent compression devices are more cumbersome to use and less well tolerated by patients. A new method has been introduced recently—that is, the arterial-venous impulse foot pump. The pump is applied to the patient's foot and provides compression to the plantar venous plexus. Its use has significantly reduced the incidence of DVT.[28] One advantage is good patient tolerability compared with conventional intermittent pneumatic compression devices, which enables its use after an operation until the patient is ambulant.

Pharmacological methods

Low-dose heparin is the mainstay of pharmacological prophylaxis. Prophylaxis with low-dose heparin (5000 U, every 8 or 12 hours) reduces the prevalence of DVT by 66% and that of PE by 50%.[3] Other drugs that have varying degrees of success include warfarin, aspirin, and dextran. However, recent interest in heparin prophylaxis has centred on low molecular weight heparins. These are as effective as unfractionated heparin. Because of the longer half-life of low molecular weight heparins, only a once-daily dosage is needed, which is more convenient for patients and nurses. There is also less bruising at injection sites.

Prolonged prophylaxis

Standard prophylaxis for venous thrombosis usually lasts for 1 to 2 weeks after operation. Some patients develop DVT after discharge from hospital and late death from PE is not uncommon after surgery.[29] In recent years, there has been discussion as to whether there is an indication to continue prophylaxis for more than 1 to 2 weeks. There have been several prospective double-blind trials in which low molecular weight heparins were given to patients undergoing hip surgery (ie a 1-month course that started preoperatively and that continued postoperatively). The studies show that prolonged prophylaxis significantly reduced venographically detected DVT approximately 1 month postoperatively.[30]

Orgaran (danaparoid sodium; Durbin, Middlesex, UK) is a new low molecular weight heparinoid that consists of a mixture of heparin sulphate, dermatan sulphate, and chondroitin sulphate; it is chemically distinct from heparin. Although not in widespread use, several studies of patients who had a high risk of developing DVT have shown the drug to be effective and comparable to low-dose heparin.[31]

Treatment of venous thrombosis

The aims of treating patients with venous thrombosis are to prevent death from pulmonary embolism, to reduce morbidity from the acute episode, and to minimise postphlebitic syndrome.

Preventing death from pulmonary embolism

The following four treatment approaches can be used to prevent death from pulmonary embolism:

Anticoagulant therapy

There is good evidence that anticoagulants are effective in reducing mortality from PE. With adequate heparinization, symptomatic PE occurs in only 5% of patients with DVT, and fatal PE in less than 0.5%.[32] If the diagnosis of DVT has been confirmed in a Chinese patient, giving anticoagulants ought to be seriously considered, especially if there are thrombi in the femoropopliteal or ileofemoral veins. These thrombi are prone to becoming dislodged and may cause fatal PE. Anticoagulation is directed at controlling the thrombotic process that has already been initiated. Intravenously injected heparin is the most effective treatment: the preferred method is continuous administration, starting with a loading dose of 5000 to 10 000 U and varying the dose depending on the activated partial thromboplastin time, which should be kept within the therapeutic range (1.5 to 2 times the control). The two advantages of this approach are to achieve a more uniform level of anticoagulation and a lower incidence of bleeding complications.

The duration of heparin therapy depends on the extent of venous thrombosis. For femoropopliteal or ileofemoral venous thrombosis with or without PE, heparin treatment should be continued for 10 to 14 days—even longer if the patient remains at risk. A course of oral anticoagulants should be started while the patient is still receiving heparin treatment, and should be discontinued only when a satisfactory level of anticoagulation has been achieved. The maintenance dose must be monitored carefully to keep the activated partial thromboplastin time approximately between 1.5 to 2 times the control. Chinese patients usually require a lower dose of anticoagulants than do Caucasian patients (unpublished observations).

The duration of the course of oral anticoagulants depends on the severity of thrombosis. For isolated calf vein thrombosis, treatment lasting 4 to 6 weeks is sufficient. However, to treat femoropopliteal or ileofemoral vein thrombosis with or without PE, anticoagulant therapy should be continued for 3 to 6 months.

Vena caval interruption

Vena caval interruption should be considered when anticoagulant treatment is contra-indicated or if it has failed.

Thrombolytic therapy

Thrombolytic therapy is more effective than heparin in preventing death in patients who have massive PE and are in shock, or in those with underlying heart or lung disease in whom even a small or moderate embolus may be life-threatening. Thrombolytic agents usually used are streptokinase, urokinase, or tissue plasminogen activator.

Surgical embolectomy

Urgent pulmonary embolectomy is usually restricted to patients with a saddle embolus that is lodged in the main pulmonary artery, or in patients with massive PE whose blood pressure cannot be maintained despite thrombolytic therapy.

Minimising postphlebitic symptoms

In 60% to 70% of patients with proximal vein thrombosis and 30% to 40% of those with calf vein thrombosis, postphlebitic syndrome can develop even after full treatment with anticoagulants. The frequency and severity of postphlebitic symptoms are lower in patients whose venous thrombosis is treated early with thrombolytic agents. The severity of postphlebitic symptoms can be minimised by about 50% when compression stockings are used soon after venous thrombosis is diagnosed.[33]

Conclusion

Venous thrombosis is a major public health problem in western countries. It would appear that the incidence of venous thrombosis and PE is rising in Chinese patients. Ultrasonic imaging has now replaced venography as the new diagnostic standard in many hospitals. Prophylaxis against venous thrombosis reduces the incidence of thrombosis by 66% and that of PE by 50%, and prophylaxis should be considered for Chinese patients who have a high risk of developing postoperative DVT. Treatment of venous thrombosis should not be undertaken without objective confirmation of the diagnosis.

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