Current management of venous thromboembolic disease

Despite improvements in early diagnosis, medical management, and prophylaxis of venous thrombosis, pulmonary embolism continues to be a vexing and frequently fatal problem. Estimates of the incidence of fatal pulmonary embolism in the USA continue to range from 50,000 to 100,000 or more annually. In spite of this high incidence, the management of patients with established thromboembolic disease remains controversial.

The initial question faced by the clinician managing a patient with a new diagnosis of deep venous thrombosis is whether to treat with conventional anticoagulation or to attempt to remove the thrombus with one of the newer thrombolytic agents or use a surgical approach. While surgical thrombectomy was commonly performed in the past, it has been abandoned for most deep venous thromboses because of the high rate of rethrombosis. Recently there has been a resurgence in interest in surgical thrombectomy for severe iliofemoral venous thrombosis causing phlegmasia cerulea dolens or phlegmasia alba dolens. The incidence of rethrombosis has been reduced in these patients by the creation of a temporary distal arteriovenous fistula. Nevertheless, the use of surgical thrombectomy should be reserved for this very select group.

There have been several studies comparing anticoagulant therapy and thrombolytic drugs for the treatment of acute deep venous thrombosis. Serial venographic studies have shown that heparin is quite effective in preventing extension of the thrombotic process but that only a small amount of thrombolysis occurs during treatment with heparin. In contrast, approximately 50 per cent of patients treated with thrombolytic therapy will have significant lysis of thrombus. It appears that the age of the thrombus is the most important factor in determining the likelihood of lysis. There is a significant cost to this increased lysis, however, and that is the 2-9 times greater incidence of bleeding complications in patients treated with lytic therapy compared with those treated with heparin.

The advocates of lytic therapy for deep venous thrombosis propose that such therapy will result in better preservation of venous valvular function and thus reduce the incidence of late post-phlebitic syndrome and chronic venous insufficiency. As yet, however, there has been no large scale comparative study to support this contention.

Based on current available data, it is recommended that surgical therapy be reserved for patients at immediate risk for venous gangrene due to the phlegmasia syndromes. Fibrinolytic therapy may be considered for patients with extensive venous thrombosis but who do not require immediate surgical decompression and for those in whom lysis of thrombus can occur over 24-48 h. Patients with lesser degrees of venous thrombosis are best treated with conventional heparin anticoagulation and heparin should also be administered to patients following a course of fibrinolytic therapy.

After an episode of venous thrombosis, patients remain at risk of recurrent thrombosis for an undetermined period. Conventionally, patients have been anticoagulated with warfarin following 7-10 days of heparin therapy. The warfarin has been continued for from 3 to 6 months. There is a significant risk of bleeding complications with warfarin and, because of this, recent trends have been to lower the dose to prolong the prothrombin time by a ratio of 1:2:1:5 rather than the previous goal of prolongation by a factor of two. The lower dose appears to be equally effective in preventing recurrence of venous thromboembolism and is clearly associated with a lower incidence of bleeding complications.

The management of established pulmonary embolism is perhaps even more controversial than the management of simple deep venous thrombosis. Heparin has been compared with no treatment for established pulmonary embolism, but this trial had to be discontinued because of the clear superiority of anticoagulation compared with no treatment. The mortality rate for undiagnosed and therefore untreated pulmonary embolism is over 30 per cent, while the mortality rate for acute pulmonary embolism in patients treated with heparin is less than half this figure. Heparin therapy allows the body's actual fibrinolytic system to lyse sufficient volumes of thrombus to restore right ventricular and pulmonary pressures to normal, but this process requires several weeks.

The primary decision facing the clinician caring for a patient with pulmonary embolism is to decide between heparin and one of three thrombolytic agents. Of the five trials comparing fibrinolytic agents with standard heparin therapy, all have shown improved clot lysis in patients treated with fibrinolytic agents compared with patients treated with heparin. However, this has not been translated into improved mortality or...
improved pulmonary function either early or late8. In addition, this fibrinolytic therapy has been used at the cost of an increased incidence of bleeding which may be severe or even fatal. It was hoped that with the introduction of recombinant tissue-type plasminogen activator a more thrombus specific lytic agent would be available and that the incidence of bleeding complications would be reduced. However, recent clinical trials using recombinant tissue-type plasminogen activator have also shown a significant incidence of bleeding complications9. Additionally, it must be realized that all of the fibrinolytic agents require 7–12 h for maximal lysis and improvement in pulmonary haemodynamics.

It is expected that the use of fibrinolytic agents for pulmonary embolism will increase. Because of the increased incidence of bleeding, however, the use of these agents should be reserved for patients with haemodynamic compromise but who do not require immediate surgical pulmonary embolectomy for survival.

Ligation and permanent interruption of the vena cava in an effort to prevent subsequent embolization of lower extremity or lower vena caval thrombi have been previously recommended. However, the high incidence of severe venous stasis and post-phlebitic syndrome subsequent to complete interruption of the vena cava suggests that this should be done only in extreme circumstances. In 1972, Greenfield introduced an intravascular cone-shaped filter for the purpose of trapping larger emboli. This device has become the most popular intravascular device for prevention of pulmonary emboli and thousands have been inserted. However, these devices are not innocuous.

Current design allows percutaneous insertion through the femoral vein. However, the large size of the catheter and thus the degree of injury to the femoral vein is such that exacerbation of the lower extremity venous thrombosis syndrome by femoral vein thrombosis at the site of cannulation may occur in as many as 40 per cent of insertions13. A smaller apparatus for introduction currently being developed may improve this alarming rate, but this new device is not yet available for general use.

The indications for insertion of a filter include pulmonary embolism in the presence of an absolute contraindication to anticoagulation such as recent intracranial hemorrhage or an extensive surgical procedure. It may also be used in patients who experience major bleeding episodes while on anticoagulation for embolism. Recurrent embolism while on adequate anticoagulation therapy is exceedingly rare but is an indication when it occurs. A large number of filters are being inserted for prophylactic reasons14, but in view of the problems mentioned above, this practice can be viewed with circumspection and requires continued reassessment.