

those receiving rt-PA, although this difference was not statistically significant. Two studies compared the efficacy and safety of 0.6 mg/kg body weight of rt-PA given over a period of 15 minutes with 100 mg during two hours (52, 53). Hemodynamic improvement was slightly but significantly faster for the two-hour regimen, although the 0.6 mg/kg dose was associated with a non-significant reduction in major bleeding events.

## The role of inferior vena cava filters in VTE

The role of inferior vena cava (IVC) filters in the management of VTE has recently been reviewed (54). The first IVC filter was the Mobin-Uddin umbrella in the late 1960s and then the Greenfield filter in the early 1970s (55, 56). Compared with IVC ligation and then clips, filters are now easily inserted through a femoral or jugular vein using local anesthesia and fluoroscopic control. However, numerous complications do persist, such as fracture and/or migration of these devices (54). Despite the absence of large evaluations of IVC filters, their rate of implantation has been very high in some countries with, for example, a 50-fold higher rate of implantation in the USA compared with Sweden, during the 1990s (57). A five-fold increase in the number of caval filters implanted in the USA was reported between 1980 and 1996 (58). Furthermore, it is surprising to see in a recent prospective US registry of 5,451 patients with acute DVT that 781 patients (14%) had received filters. Among them, one-third were inserted for prophylaxis rather than accepted indications such as contraindication to anticoagulant treatment (59).

Several IVC filters exist, nine of which have been approved by the FDA (8, 54). There are three kinds of devices: permanent, temporary and retrievable filters. The temporary filters require a permanent catheter to fix the device and tend to be abandoned. Alternatively, the retrievable filters can be left in place like a permanent filter or retrieved as it was the case with a temporary filter. Two of them (the ALN and the RNF filters) can be retrieved up to six months after initial placement; among these new devices the ALN filter is certainly the one that has undergone the most studies (60). However, complication rates and comparison between the different devices are limited due to the small number of studies published to date and their short follow-up.

### Indications for IVC filter placement

Due to their risk of complication, the small number of controlled trials available and the potential cost incurred, filter indications should remain restricted. Table 4 summarizes the indications for IVC filters in VTE. Two indications are widely recognized as being appropriate, despite the fact that most clinical data on IVC filter placement are derived from historic, non-randomized series (1, 8). The first is a permanent or temporary contraindication to anticoagulation in patients with proximal DVT or PE. Absolute contraindications include severe and active visceral hemorrhage, recent history of brain hemorrhage, recent neurosurgical operation or head injury, and the need for major surgery (57). When contraindication to anticoagulants is temporary, the use of a temporary filter and now of a retrievable filter is logical. The second indication is the occurrence of PE or propagation of the thrombus in patients treated for DVT, or recurrence in patients with PE, despite adequate anticoagulation. It is thus

necessary to ascertain the recurrence and that the patient was in the therapeutic range during the period preceding the recurrent event. If not, it is probably more appropriate to equilibrate anticoagulation treatment. Investigation of thrombophilia and/or Trousseau's syndrome is also mandatory in this setting.

Other debated or debatable indications are based on small series, and IVC filter placement in these situations should be addressed by prospective clinical studies. This was realized in a single randomized trial (the PREPIC study) in patients with acute proximal DVT confirmed by bilateral venography, with or without concomitant symptomatic PE, and considered to be at high risk for PE (61). In a two-by-two factorial design, the authors randomized 400 patients with proximal DVT to receive a permanent vena caval filter (200 patients) or no filter (200 patients), and LMWH (enoxaparin, 195 patients) or unfractionated heparin (205 patients), followed by at least three months of vitamin K antagonists. The rates of recurrent VTE, death and major bleeding were analyzed on day 12 and at two years. On day 12, 1.1% of patients assigned to receive filters, compared with 4.8% of patients in the no-filter group, had had symptomatic or asymptomatic PE (OR 0.22; 95% CI 0.05–0.90). By contrast, at two years, 20.8% of patients assigned to the filter group, compared with 11.6% of patients assigned to the no-filter group, had had symptomatic recurrent DVT (OR 1.87; 95% CI 1.10–3.20). There were no significant differences in mortality or in the other outcomes. Recently, the results of an eight-year follow-up of 99% of patients included in the PREPIC study have been reported. Symptomatic PE occurred in nine patients in the filter group (cumulative rate 6.2%) and 24 patients (15.1%) in the no-filter group ( $p = 0.008$ ). DVT occurred in 57 patients (35.7%) in the filter group and 41 (27.5%) in the no-filter group ( $p = 0.042$ ). A similar rate of post-thrombotic syndrome was observed in 70% of both groups, the most common signs reported being edema and varicose veins. At eight years, 201 (50.3%) patients had died (103 and 98 patients

**Table 4: Indications for IVC filters (adapted from ref. 1, 54 and 57).**

<b>Accepted (appropriate) indications</b>
Contraindication (temporary or definitive) to anticoagulant treatment and recent proximal DVT or PE
Failure of adequate anticoagulant treatment: Documented PE Documented propagation of DVT
<b>Debated indications</b>
Pulmonary thromboembolism patients
Post-embolic pulmonary hypertension
Adjuvant preventive treatment before high-risk surgery in high-risk patients or in major trauma patients
<b>Debatable indications</b>
Thrombolysis of ilio-caval thrombus or extensive free-floating iliofemoral thrombus
Proximal DVT or PE and thrombolytic treatment
Cancer patients
Exclusive preventive treatment before high-risk surgery or in major trauma patients