IVC Filters: Indications and Evidence

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Abstract

The role of anticoagulants in the treatment of venous thrombo-embolic disease is well established. The use of inferior vena cava filters as a second line treatment is increasing, most recently with the popularity of retrievable filters. However, the indications and evidence for their safety and efficacy are not clear-cut. There are few absolute indications. The majority of evidence originates from single-center series studying a preferred few genres of filters. Generalizability and meta-analysis are difficult. Important questions remain to be answered, particularly regarding extended indications for insertion, the long-term safety of retrievable devices, and the relative efficacy and safety of different genres of devices. Thus, filter insertion should be a careful and considered process in a multidisciplinary environment.

Introduction

Venous thromboembolism (VTE) and its sequelae are an important problem. VTE occurs at a rate of 1/1000 in the general population, rising to 1/100 in the high-risk subpopulations. Without treatment, patients with VTE are at high risk of developing pulmonary embolism (PE), which can be fatal in as many as 25% of patients. There are now multiple agents available for treating VTE, from unfractionated heparin to low-molecular-weight heparins and fondaparinux. However, oral vitamin K antagonists remain the mainstay of long-term treatment.

There are a number of situations where such forms of anticoagulation are not sufficient or possible. Anticoagulation can fail with breakthrough PE while on “therapeutic” anticoagulation therapy quoted at 4%. Anticoagulation may also result in serious complications, and may need to be discontinued. It is associated with death in up to 5% of patients. Heparin-induced thrombocytopenia (HIT) can occur in up to 3% of patients, 25% of whom will develop new venous and some arterial thrombosis, including PE. When anticoagulation is contraindicated or otherwise ineffective, interruption of the inferior vena cava (IVC) with a filter device may need to be considered.

In the past, mechanical interruption of caval flow had been surgical. Around 80% of all VTE results from lower-limb thrombosis and ligation of the femoral veins to prevent clots from reaching the pulmonary arteries. This was first suggested by Hunter as far back as 1874. Later, ligation of the IVC was performed, which had a high operative mortality rate of up to 15%, with recurrence of PE in 6% of patients and chronic venous insufficiency in 33%.

In the 1960s, newer methods of partially interrupting the IVC were developed to reduce the effects of venous stasis using suture application and caval clips. Operative mortality and recurrent PE were still similar to those of caval ligation, and the rate for limb edema was reduced, but IVC occlusion rates remained high.

Such problems inspired the development of the Mobin-Uddin umbrella, an endovascular device developed in 1967 to partially interrupt the flow in the IVC and to prevent PE. This was followed by the Greenfield filter in 1971, both of which still required a surgical venotomy. The first widely available, truly percutaneous device was launched in 1981 by Greenfield and quickly replaced all open surgical procedures.

Since then, there has been rapid evolution in technology with smaller devices and flexible delivery systems, allowing delivery from multiple venous access sites under fluoroscopic guidance. There is now also the option of cases being performed under ultrasound guidance in an intensive care setting. These devices, however, are not without their long-term risks; this has driven the development of retrievable IVC filters, providing an option for short-term caval interruption. Today in our institutions, the majority of filters used are temporary.

Such developments in technology have encouraged a shift in “indications” for filter placement with increasing trends to utilize prophylactic filter placement and retrievable IVC filters. This has resulted in an explosion of the number of IVC filters placed. In the United States, this has increased almost 25-fold, from an estimated 2,000 placed in 1979, to an estimated 49,000 placed in 1999.
Indications

There are limited robust data on the precise and correct indications for filter placement. Thus far, there has only been one randomized, controlled trial, the Prevention du Risque d’Embolie Pulmonaire par Interruption Cave (PRECIP) study. The majority of the available data are from case series or retrospective case reports. Following a systematic review of comparable data, the Cochrane group concluded that no firm recommendations could be made for filter placement and data from the PRECIP study could not be extrapolated to general use. The Cochrane group supported the use of IVC filters only in patients in whom anticoagulation was not feasible or where there was breakthrough PE. No recommendations could be made for many of the other indications that are widely practiced.

Similar guidelines have been produced independently by the American College of Chest Physicians (ACCP) who recommend IVC filter placement only in those patients with proven VTE and with (i) a contraindication for anticoagulation; (ii) a complication of anticoagulation treatment; or (iii) recurrent VTE, despite adequate anticoagulation (Table 1).

The British Committee for Standards in Haematology (BCSH) subsequently produced weighted evidence-based guidelines very similar to those of the ACCP. They concluded that there was Grade B/Level III evidence for filter placement in those patients with contraindications for anticoagulation, Grade C/Level IV evidence for breakthrough or recurrent emboli, despite “adequate” anticoagulation, and similarly, Grade C evidence for pre-operative patients who require protection from PE during surgery. Unlike the ACCP, however, they also concluded that temporary filter placement should be considered in pregnancy immediately prior to delivery.

Despite these relatively tight recommendations, there has been a general expansion over time to include a much larger group of non-evidence-based indications (Table 1). Some of these expanded indications were also reviewed by the BCSH. In patients with free-floating ilio-femoral or IVC thrombus, the data have been mixed. Ilio-femoral thrombus has been associated with a 60% rate of PE in some studies and, therefore, is often considered an indication for IVC filter placement. However, other studies have failed to show this increased risk. In a prospective study of 95 patients, the incidence of PE was not greater in patients with free-floating thrombus (n = 62) compared to those without (n = 28), 3.3% versus 3.7% (Level III). Therefore, the BCSH concluded that there were insufficient data to support routine filter insertion in patients with free-floating thrombus.

There are case reports of patients with DVT treated with systemic thrombolysis who subsequently developed fatal PE. However, IVC filters have not been shown to reduce the incidence of fatal PE during thrombolysis, and the BCSH also concluded that filter placement as an adjunct to thrombolysis was not indicated (Grade C, Level IV).

Indications for temporary and permanent filters are identical, although there is a perception of a loosening of the criteria for placement of temporary filters. Temporary filters and their indications are discussed in more detail below.

Filter placement is occasionally being used inappropriately as the first line in the management of thromboembolic disease and as the primary treatment for PE prophylaxis in patients who are otherwise suitable for standard anticoagulation.

Efficacy

The PRECIP study is the only randomized controlled trial to examine the efficacy and indications for IVC filter insertion. The vast majority of studies are single-center studies examining the efficacy of a single genre of filters consisting mainly of uncontrolled, retrospective cohort studies or case series. Data collection from
such studies has been too heterogenous to allow for meta-analysis and systematic review.\textsuperscript{21}

Follow-up post-placement is, in our experience, generally haphazard; when it does occur, it has tended to consist of clinical examination, a review of notes, and telephone consultations with no regular radiological follow up.\textsuperscript{9} This is similarly true for temporary filters that are, as a consequence, being left \textit{in situ} with little evidence for their long-term safety. Event rates, particularly for DVTs in patients with a filter, may be underestimated due to a lack of data. Currently, there is a drive in the U.K. to encourage radiologists to enter data onto the U.K. British Society of Interventional Radiologists (BSIR) Caval Registry so that a representative picture of current practice can be obtained.\textsuperscript{11}

**PRECIP**

Patients were randomly assigned to receive one of four genres of permanent IVC filter (n = 200) or no filter (n = 200), and all received an anticoagulant, either unfractionated heparin (n = 205) or low-molecular-weight heparin (n = 195). At 12 days, there was a significant reduction in PE in patients who had had a filter inserted; however, there was no significant improvement in mortality.

At 2 years, recurrent PE was still reduced with filter placement; the incidence in the filter group decreased by 50\% compared to that in the non-filter group. However, recurrent DVT was significantly increased (20.8\% vs. 11.6\%, \(p = 0.02\)). At 8 years, the overall numbers of VTE were similar between groups, however, the number of symptomatic PEs were lower in the filter group, with the risk decreased by 63\%. Again, recurrent DVT was seen to be higher in the filter group. However, of particular note, the occurrence of post-thrombotic syndrome was similar in both groups.

Thus, the conclusion of this study was that IVC filters reduce the number of PEs at the expense of more DVT; with no mortality or morbidity difference. This study confirmed that there were no additional benefits of filter insertion in the general patient on anticoagulation. However, there may be a subgroup of patients who benefit from combined treatment (\textit{i.e., as 42\% of breakthrough PE in the “no filter” group occurred within the first year, compared with 22\% in the “filter” group.}). It may be the case that optimal treatment for this small group is actually combining anticoagulation with a temporary filter to cover this window.\textsuperscript{22}

There are constraints to this study that make it difficult to generalize further. Firstly, patients received different anticoagulants, including unfractionated heparin. There is controversy as to whether patients with filters should receive anticoagulation at all.\textsuperscript{22} A large proportion of the patients in the “filter” arm of the study received concomitant anticoagulation for the duration of the study out to 8 years, which may explain the small difference in long-term morbidity and mortality rates between groups.

**Other Evidence**

Where anticoagulation is not feasible, IVC filters appear to be effective in reducing the risk of fatal and non-fatal pulmonary emboli, but this risk is not completely obliterated. In a review of permanent filters (mean duration of follow up ranging from 6–18 months) the incidence of recurrent PE ranged from 2–5\%, and fatal PE from 0.3–1.9\%, depending on the type of filter.\textsuperscript{9,23}

Retrievable filters are thought to have similar outcomes, although there have been no comparative studies to date.\textsuperscript{23} In one single-center, retrospective study, it was shown that retrievable filters have similar protection and complication rates to permanent filters.\textsuperscript{24} Of the 702 patient in the study, 427 had retrievable and 275 had permanent IVC filters. There was a 4\% vs. 4.7\% PE rate for retrievable and permanent filters with a DVT, and an IVC thrombosis rate of 11.3\% and 12.6\%, and 1.1\% vs. 0.5\%, respectively. This study, like many others, suffers from the lack of a routine surveillance protocol.

Given all of this, retrievable filters should ideally be used only when the indication for filter placement is transient. Anticoagulation may be contraindicated due to imminent surgery or in obstetric emergencies. Alternatively, a filter may be instituted during a temporary, high-risk phase for protection against PE. The advantage of retrievable filters is that they allow retrieval following such a transient change. The BCSH recommends that filters in such circumstances be removed within 10–14 days, although there is increasing evidence that delayed retrieval is possible with certain genres of filters.

Temporary IVC filters are frequently placed in patients who have suffered trauma due to the perception that these patients are at higher risk for pharmacologic prophylaxis. There is no evidence to support this practice.\textsuperscript{19} On the contrary, a large randomized clinical trial has shown that pharmacologic prophylaxis is both safe and effective in these patients.\textsuperscript{6}

Obese patients undergoing bariatric surgery represent another group in which filter insertion is common, however, controversial. There are undoubtedly obese patients who are at high risk of PE, and there are small case series that describe safe insertion and retrieval of filters in such patients.\textsuperscript{30} However, the exact role of filter use in relation to other methods of prophylaxis, and whether it confers any added benefit, have not been convincingly defined.

Retrievable filters may circumvent the long-term risks
of permanent filters, particularly in younger, fitter patients. However, retrievable filters have variable rates of removal from different centers reported in the literature, ranging from 10.7 to 88%. Failure to remove filters may be for a variety of reasons, ranging from clinical necessity to technical inability to remove. There is, as yet, little evidence for the long-term efficacy of temporary filters. Therefore, the aim for current evidence should be to remove all retrievable filters.

What about anticoagulation following filter placement? As examined above, the PRECIP studied a population that received combined therapy. The general opinion is that anticoagulation should be re-started as soon as is feasible, as filters do nothing to treat the underlying thrombosis. In a recent meta-analysis, it was concluded that filters could be placed safely in patients in whom concomitant anticoagulation cannot be given, raising the question of whether these patients need anticoagulation at all.

Complications

There is also heterogeneity of the data describing complications. The rates of complication immediately associated with insertion are low, and an authoritative review of IVC filter use quotes a major complication rate of 0.3% which is consistent with other published data. Ongoing post-insertion complications are less well defined due to variable surveillance rates and incomplete follow up.

The most common complications are thrombotic, including insertion-site thrombosis (2–28%) and IVC thrombosis (4–28%). An increased frequency of recurrent DVT (6–46%) and post-phlebitic syndrome (13–59%) have also been reported, most notably by PRECIP, possibly because IVC filters impair venous drainage.

The US Society of Cardiovascular and Interventional Radiology recently published guideline thresholds for recurrent PE and IVC occlusion of 5 and 10%, respectively. From the literature, it is clear that some centers may be exceeding this range.

The use of retrievable filters can, theoretically, avoid some of the thrombotic complications associated with permanent filters. The evidence for the safety of retrievable devices stems from small studies, with preliminary data suggesting they are as safe as established filters. However, as yet, there is a paucity of data to support their long-term safety. There are specific anatomic and technical considerations that may preclude retrieval. Epithelialization of the struts occurs after implantation and may be seen within 12 days; thus, IVC wall damage might occur during the retrieval process. Migration and tilting of the filter may technically prevent its capture. Captured thrombus may be too extensive to allow retrieval. Documented retrieval complications are of the order of 1%. A high mortality rate has been described in patients with filters. Filter insertion has been described by some as a pre-terminal event. Patients may be coagulopathic with disseminated malignancy and physiological frailty, precluding the use of routine anticoagulants. Thirty-day mortality figures of at least 6% and overall mortality of 26% probably underestimates the numbers. Acute procedural mortality is very low.

Summary

The role of IVC filters in the treatment of VTE is still unclear. What we can say with some certainty is that in most patients IVC filters do not confer additional benefit compared to being treated solely with anticoagulation for DVT with or without PE. However, there are certain absolute indications that have good evidence basis. These are embraced by most major guidelines. Extended indications remain to be tested in a systematic way. Furthermore, there may still be a role for a combination of anticoagulants and filters in a super-selected group.

The literature is clouded with studies that examine certain filters and make meta-analysis difficult. The question of which IVC filter to use still remains largely unanswered. It is still unclear as to whether anticoagulation should be concomitantly instituted with filter insertion.

The advent of temporary filters adds yet a further level of complexity. There is currently no RCT evidence examining the efficacy of temporary filters. Such devices are in vogue, however, the evidence for their
References


