



## Patients with inferior vena caval filters should receive chronic thromboprophylaxis

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*A 32-YEAR-OLD MAN with testicular carcinoma is diagnosed with an acute left leg deep venous thrombosis (DVT) during his fourth cycle of combination chemotherapy. Because of anticipated moderate to severe thrombocytopenia, anticoagulation is initially avoided and an inferior vena cava (IVC) filter is placed to prevent pulmonary embolism (PE). After completion of all chemotherapy he is deemed to be in remission and anticoagulation is begun. The optimal duration of anticoagulation in this patient is pondered.*

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### A PROTAGONIST'S PERSPECTIVE

Inferior vena cava filters are placed in patients with thromboembolic disease who have a contraindication to anticoagulation (eg, patients with recent bleeding before starting anticoagulation or those at high risk of bleeding with anticoagulation). Examples of such poor-risk patients are one who develops a DVT several days after an upper gastrointestinal bleed or a patient with melanoma metastatic to the brain or who is in the immediate postoperative period after neurosurgery. IVC filters are also placed in patients at high risk of thromboembolism who have a high risk of bleeding (eg, multiple trauma patients). The third indication for IVC filters is in

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patients who have failed anticoagulation (ie, those who have had a thromboembolic event while on therapeutic levels of anticoagulation). Although it is clear that over the short term PE is largely prevented by IVC filter placement, the incidence of later thrombotic complications and the need for chronic thromboprophylaxis to prevent these have not been defined. This question has not been addressed directly in the literature. Most of the published studies describe the outcomes in terms of short-term or long-term risk of thrombotic complications in patients with filters, but not all of the reports indicate whether patients were maintained on anticoagulation. There are no randomized studies of anticoagulation versus no anticoagulation in patients with filters in place. This article reviews the literature on thromboembolic events in patients with IVC filters and literature on postphlebotic syndrome in patients with filters, with reference to anticoagulation where it was used.

In 1998 Rogers et al [1] presented their experience and a review of the literature on prophylactic filters in multiple trauma patients. There was a 2% incidence of PE in the acute phase in patients with filters in their own series and a 3.1% insertion-related DVT. They had abdominal ultrasound data on 47 patients up to 3 years after filter placement. Life-table analysis predicted 97% patency of the filter up to 3 years. In the series they reviewed from the literature, there was a 10% IVC thrombosis rate and a 5% PE rate in spinal cord injury patients with filters in the series by Jarrell et al [2] and in multiple trauma patients with filters reported by Rodriguez et al [3] and a 17% leg edema rate at 18 months in the series of patients with acetabular fractures reported by Webb et al [4]. Other series reviewed by Rogers et al [1] reported no PEs in patients with filters and did not comment on filter complications. Filter failure was believed by Rogers et al [1] to be caused by strut malposition.

Streiff [5] presented a comprehensive review of vena caval filters in 2000. He reviewed one randomized trial (see later) and also compiled several case series of patients with different types of filters in terms of incidence of PE, DVT, and IVC thrombosis and of postphlebotic syndrome. The range of PE incidence was up to 9% of patients (fatal up to 1.9%). The range of DVT incidence was up to 36%, and the range of IVC thrombosis was up to 31%. The mean duration of follow-up in these reports ranged from 6 to 18 months, with a maximum of 81 months. Postphlebotic syndrome was reported in up to 59% of patients in the various series. The randomized trial was published by Decousus et al [6] in 1998. Patients with lower-extremity DVT were randomized to filter or no filter and to intravenous heparin versus low-molecular-weight heparin (LMWH), both followed for 3 months by warfarin or acenocoumarol. The primary outcome was occurrence of PE in the first 12 days. Secondary outcomes included PE, recurrent DVT, death, major filter complications, and major bleeding during a 2-year follow-up period. Although anticoagulation after the initial 3 months was not part of the protocol, 38% continued to receive anticoagulation through the follow-up period. Filters prevented PE in the initial phase of the study (1.1% versus

4.8%;  $P = .03$ ). Recurrent DVT was more prevalent in the filter group (20.8% versus 11.6%,  $P = .02$ ), and the incidence of recurrent thrombosis increased over the 2 years of follow-up. The paper by Decousus et al [6] did not provide information about the anticoagulation status of patients with recurrent thrombosis.

Greenfield and Proctor [40] in 2001, published the Michigan Filter Registry data on experience with IVC filters. Information on anticoagulation was available for 465 patients with at least one follow-up visit, 241 of whom received anticoagulation. They found no difference in rates of new PE, DVT, vena cava occlusion, or venous ulceration, but the survival rate was significantly different, as was the rate of needing support stockings to control symptoms of venous insufficiency, in the group without anticoagulation.

Ballew et al [8] reviewed vena cava filters in 1995 and suggested several potential benefits to combining chronic anticoagulation with filters, although they recognized that the data are only suggestive. Potential benefits to combining anticoagulation with IVC filters include the following:

- Prevention of insertion-site DVT
- Prevention of vena cava obstruction
- Prevention of venous insufficiency
- Prevention of embolization of a clot from an occluded filter
- Prevention of propagation of DVT
- Prevention of recurrence of DVT

The following arguments can be made for continuing anticoagulation in patients with IVC filters who do not have a contraindication to anticoagulation, despite the fact that there are no randomized, controlled trials that address this issue.

1. There is a demonstrated high incidence of recurrent DVT and postphlebotic syndrome in patients with filters. In patients with recurrent DVT without filters, usual practice is to prescribe long-term anticoagulation to prevent PE and decrease the likelihood of further recurrence of both DVT and PE and postphlebotic syndrome.
2. Many IVC filters are placed in patients who have already had a DVT, and many of these patients are at risk for recurrence by virtue of having an underlying state that precipitated the initial DVT or because of damage to the vein wall by the existing DVT.
3. One can make the analogy between a filter and a congenital or acquired hypercoagulable state, where there is clear precedent for long-term anticoagulation, after an initial DVT. For individuals with no DVT history who have a filter inserted because of multiple trauma, the argument for prolonged anticoagulation is less strong. This situation could be considered to be similar to finding that an asymptomatic patient has a hypercoagulable risk factor.

## AN ANTAGONIST'S PERSPECTIVE

Inferior vena cava filter devices have been available for clinical use as a mechanical method to prevent PE originating from the lower extremity veins for over three decades. Since the introduction of the Mobin-Uddin “umbrella” in 1969, several improvements and refinements in filter design, delivery systems, and insertion techniques have occurred, leading to greater ease of IVC filter insertion and a reduction in the cost and morbidity of percutaneous placement procedures [8–11]. Currently available permanent IVC filter models most commonly used in the United States include the Greenfield filters (stainless steel, titanium, and percutaneous steel models; Medi-Tech/Boston Scientific, Watertown, MA); the Bird’s Nest filter (Cook, Bloomington, IN); the Vena Tech filter (Vena-Tech/B. Braun, Evanston, IL, also known as LGM filter in Europe); the Simon Nitinol filter (Bard Radiology, Covington, GA); and the recently introduced TrapEase filter (Cordis Endovascular, Miami, FL).

The original indication for IVC filter placement was to prevent recurrent PE after pulmonary embolectomy, and the list of indications has expanded considerably since then (Table 1) [11–14]. It is surprising to note, however, that this expansion has not resulted from evidence-based recommendations derived from prospective controlled trials [5,12,15–17]. The two most widely accepted and least disputed indications for IVC filter placement (complication or contraindication to anticoagulation therapy) were defined as “grade 1C+” by the American College of Chest Physicians Consensus

Table 1

Indications for interior vena cava filter placement as recommended by the American College of Chest Physicians Consensus Conference on Antithrombotic Therapy - January 2001

Indications	Grade of recommendation
Contraindication of anticoagulant therapy	
Complication of anticoagulant therapy (in individuals with or at high risk for proximal vein thrombosis or pulmonary embolism)	1C+ <sup>a</sup>
Recurrent thromboembolism that occurs despite adequate anticoagulation	
Chronic recurrent pulmonary embolism with pulmonary hypertension	1C <sup>b</sup>
Concurrent performance of surgical pulmonary embolectomy or pulmonary thromboendarterectomy	

<sup>a</sup> Clear benefit, supported by overwhelming evidence from observation studies despite the lack randomized controlled trials.

<sup>b</sup> Intermediate-strength recommendations derived from observations studies alone.

From Guyatt G, Schunemann H, Cooke D, Jaeschke, R, Pauker, S, Buchar H. Grades of recommendation for antithrombotic agents. *Chest* 2001;119:3S–7S; and Hyers TM, Agnelli G, Hull RD, et al. Antithrombotic therapy for venous thromboembolic disease. *Chest* 2001;119:176S–193S; with permission.

Guidelines because they are considered of clear benefit and supported by “overwhelming evidence from observational studies” [14,18]. In fact, most (nearly two-thirds) clinical data on the efficacy and safety of IVC filters is derived from case reports and retrospective, uncontrolled case series, with only 7% of the available literature consisting of prospective studies [17]. Despite this, IVC filter placement for primary and secondary PE prophylaxis (either in high-risk individuals without venous thromboembolic events [VTE]; or with VTE but without a contraindication, failure, or complication of anticoagulation therapy) has been increasingly reported [11,12,15,19]. Although these indications have been listed as “reporting standards” by a Vena Caval Filter Consensus Conference, the appropriateness and the long-term risks of IVC filter insertion for such prophylactic indications are a matter of ongoing debate [5,8,12,15,20].

In 1998, the first and only prospective randomized controlled trial evaluating the efficacy and safety of IVC filters was published by Decousus et al [6]. The French Prévention du Risque d’Embolie Pulmonaire par Interruption Cave (PREPIC) study randomized 400 patients using a  $2 \times 2$  factorial design, comparing the use of IVC filter versus no filter and the LMWH enoxaparin versus unfractionated heparin (UFH) [6]. It included patients with DVT confirmed by contrast venography, with or without concomitant PE, who were considered by their physicians to be at high risk for PE. Because all patients were to be anticoagulated, those with a contraindication, complication, or failure of anticoagulation therapy were not included in the study. The primary end point was the incidence of all PE (symptomatic and asymptomatic) within 12 days after randomization, with all patients undergoing ventilation-perfusion lung scan or pulmonary angiography. Secondary end points were only symptomatic, and included the rates of PE and recurrent DVT at 2 years of follow-up [6].

Regarding IVC filters, the PREPIC study showed that they provided statistically significant short-term protection against PE in anticoagulated patients compared with those who were anticoagulated but did not receive an IVC filter (Table 2) [6]. At 2 years, no differences in symptomatic PE were observed, but patients with IVC filters had significantly more symptomatic recurrent DVT than those without a filter (20.8% versus 11.6%,  $P = .02$ , odds ratio 1.87, 95% confidence interval 1.10–3.20) [6]. These findings have raised the question of whether patients with IVC filters should or should not receive chronic anticoagulation therapy [6,12].

In this author’s view, two conditions must be met before prescription of long-term anticoagulation therapy can be justified and based solely on the presence of an IVC filter. First, there has to be unequivocal evidence of the role of IVC filters as independent risk factors for DVT recurrence. In addition, even if IVC filters did increase the risk of DVT recurrence, this increased risk has to be of such a magnitude that the benefit of prolonging anticoagulation outweighs the risk of oral anticoagulation-related major hemorrhage.

Table 2

Interaction between filter and anticoagulation regimen in the Prévention du Risque d'Embolie Pulmonaire par Interruption Cave Study

Primary end point event	UFH versus LMWH groups number of patients (%)	Filter vs no filter groups number of patients (%)
All pulmonary embolism (symptomatic and asymptomatic) within 12 days of randomization	8 (4.2) versus 3 (1.6) $P = .14$ (OR = 0.38, 95% CI 0.10–1.38)	2 (1.1) versus 9 (4.8) $P = .03$ (OR = 0.22, 95% CI 0.05–0.90)

*Abbreviations:* LMWH, low-molecular-weight heparin; OR, odds ratio; UFH, unfractionated heparin.

*Data from* Decousus H, Leizorovicz A, Parent F, et al. A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. *N Engl J Med* 1998;338:409–15.

Do IVC filters undoubtedly increase the risk of DVT recurrence? To answer this question, the following key issues need to be discussed: (1) the initial antithrombotic therapy and the model of oral anticoagulation management used in the PREPIC study, (2) the issue of insertion-site DVT postfilter placement, (3) determinants of DVT recurrence, and (4) the different IVC patency rates associated with the different filter models.

The impact of the initial UFH on the rates of VTE recurrence has been well substantiated by several randomized controlled trials and subgroup analyses of such trials [14,21–24]. Failure to exceed an activated partial thromboplastin time threshold of 1.5 times the control within 24 hours of initiation of UFH therapy has been associated with as much as a 15-fold increased relative risk of long-term (3 months) VTE recurrence despite adequate oral anticoagulation therapy [22,23]. The use of a weight-based UFH nomogram results in a greater proportion of patients achieving an activated partial thromboplastin time within the target therapeutic range, both at 6 and 24 hours following the weight-based UFH bolus dose, than if a “standard of care” UFH nomogram is used. Weight-based UFH dosing was also associated with significantly lower rates of recurrent VTE [24]. Furthermore, the risk of late recurrence is also dependent on the total daily dose of UFH [14,21]. Higher recurrence rates are seen in patients who receive less than 30,000 IU of UFH per day [14]. Of those who receive at least 30,000 to 35,000 IU of UFH per day, recurrence rates seem to be lower even if activated partial thromboplastin time results are subtherapeutic within the first 24 hours [14,21]. Although it is unknown whether failure to perform appropriate adjustments in UFH infusion increases late VTE recurrence rates, most experts agree that UFH therapy needs to be given so that a minimum activated partial thromboplastin time threshold is achieved in a timely fashion [14,21,22].

Evidence also indicates that the use of LMWH is at least as safe and effective as UFH for initial VTE treatment, and may indeed result in slightly lower rates of VTE recurrence [25,26]. Compared with UFH, LMWH

compounds have greater bioavailability and longer plasma half-lives, more predictable anticoagulant dose-response relationship following subcutaneous administration based on body weight, no need for laboratory monitoring or dose adjustments in most patients, and the potential to facilitate outpatient DVT treatment in selected patients [25,26]. In a recent study comparing the LMWH enoxaparin with UFH for VTE treatment, the mean dose of UFH administered on the second day of treatment was 29,000 IU and almost 25% of the patients in the UFH group failed to achieve an activated partial thromboplastin time within the therapeutic range by that second day of treatment [27]. This underscores the fact that proper administration of UFH can be a challenge, even in the setting of a randomized controlled trial.

In the PREPIC study, patients randomized to the UFH group did not receive a weight-based bolus dose, but the total daily infusion dose was weight-based (500 IU/kg daily) [6]. Although it could be assumed that most patients (at least those weighting 60 kg or more) did receive at least 30,000 IU of UFH per day, data on the adherence to and efficacy of such an UFH regimen are unknown because the study did not ensure proper UFH monitoring. Even though the rates of DVT recurrence at 2 years were not different between the LMWH and UFH groups [6], the  $2 \times 2$  factorial design used in the study does make it possible that some of the differences noted between the “filter” and “no filter” groups were at least in part influenced by the type of initial anticoagulant regimen used. Although the study reported that the interaction between the filter and the anticoagulation regimens was not significant for any of the outcome events, the available data do give rise to two examples of a possible therapeutic interference. First, there was a nonstatistically significant trend toward less PE events in patients who received LMWH as opposed to UFH (see Table 2) [6]. The analysis of the same outcome for the filter versus no filter groups did reveal a significant difference in favor of IVC filters (see Table 2). Interestingly, however, among the nine patients in the no filter group who had a PE, seven (78%) had received UFH and two (22%) LMWH [6]. Moreover, among the four deaths caused by PE in the no filter group, three occurred in patients treated with UFH, whereas only one patient receiving LMWH died from PE [6]. No data are known as to the number of patients receiving UFH or LMWH among the 37 patients in the filter group and the 22 in the no filter group who had DVT recurrence at 2 years. Nevertheless, it is clear that some of the differences between the filter and the no filter groups may not be solely attributed to an effect of IVC filters, and may in part have resulted from differences between the types of initial anticoagulant therapy used. Lack of statistically significant differences regarding the interaction between filter and anticoagulant regimens may have resulted from small sample sizes.

Management of oral anticoagulant therapy is a key issue that can impact the rates of both VTE recurrence and hemorrhage. The two most important factors dictating therapeutic effectiveness and reducing bleeding risk in

orally anticoagulated patients are the intensity of therapy and the maximal time in therapeutic range (TTR) [28]. The 2001 American College of Chest Physicians Consensus Guidelines recommended a target international normalized ratio of 2 to 3 for the treatment of acute VTE [14,28]. Achieving maximal TTR minimizes the risk of both VTE recurrence and hemorrhage, with deviations from the target international normalized ratio range increasing the risks in an exponential manner [28]. Ranges of TTR vary widely (33%–93%) among studies using different models of anticoagulation management (including usual physician monitoring, anticoagulation clinics, patient self-monitoring, and so forth), but it seems that outcomes are worse when the patient's personal physician manages oral anticoagulation therapy [28]. Typically, patients enrolled in recent randomized controlled trials spent 60% to 64% of the time with an international normalized ratio between 2 and 3 [29,30]. In a retrospective analysis of two prospective trials comparing LMWH and UFH for DVT treatment, the TTR was even lower (50%–54%) [31]. In addition, cancer patients have been shown to spend less than 45% of the time with an international normalized ratio within the target range of 2 to 3 [32].

In the PREPIC study, management of oral anticoagulation was performed by the patients' personal physicians [6]. The TTR is unknown, and 14% of patients had cancer at the time of enrollment [6]. Although the study reported no significant differences between groups in terms of number of patients on or off anticoagulation at 2 years, the manner in which this therapy was managed clearly could have impacted outcomes. Because the intensity of anticoagulation is the major determinant of the risk of oral anticoagulation-related hemorrhage, it is possible that patients in the filter group, particularly those considered by their physicians to be at high-risk for bleeding, received an overall lower intensity of oral anticoagulation exactly because they already had an IVC filter in place.

Insertion-site DVT is defined as DVT occurring at the vascular access site used for percutaneous filter insertion [5,33]. Incidences ranging from 19% to 41% have been reported by earlier studies of percutaneous filter placement using large-bore insertion catheters [33]. Because most patients (50% to 70%) with insertion-site DVT are asymptomatic, however, the incidence associated with currently available filter models varies according to the study methodology [5,33]. The frequency is lower (9% to 16%) when only symptomatic patients undergo objective imaging assessment, and is higher (23% to 36%) when routine ultrasound surveillance of all enrolled patients is used [5]. It is likely that lack of active surveillance for insertion-site DVT leads to an underestimation of this complication.

Although it is true that the clinical significance of asymptomatic insertion-site DVT is unknown (because there are no prospective studies with long-term follow-up in this special patient population), it is reasonable to believe that this iatrogenic DVT can still be associated with the same short- and long-term complications seen with any DVT, including the

postthrombotic syndrome (PTS). Postthrombotic syndrome results from residual venous obstruction and thrombus-induced venous valve damage, which then lead to venous reflux and venous hypertension [34,35]. The clinical manifestations of postthrombotic syndrome (chronic limb edema and pain, skin hyperpigmentation, and venous stasis ulceration) are the result of those venous functional abnormalities [34,35]. Postthrombotic syndrome develops in up to 70% of patients following an acute DVT event, most cases develop within 2 years of the initial DVT, and the incidence is increased sixfold following an ipsilateral recurrent DVT [34–36].

In the PREPIC study, 35% of enrolled patients had a history of prior VTE [6]. The locations of any previous DVT, of the DVT that led to patients' enrollment, and of the recurrent DVT during follow-up are all unknown. In addition, the study did not use objective imaging assessment following filter placement. It is likely that a number of cases of insertion-site DVT went undetected. Without knowing the incidence of this complication, a number of patients who developed it may actually have become symptomatic during follow-up because of the postthrombotic syndrome rather than a new DVT. Moreover, a number of the initially undetected insertion-site DVT may have only been visualized when patients became symptomatic during follow-up, hence being incorrectly interpreted as a new, recurrent DVT. Lack of surveillance for insertion-site DVT may have led to misdiagnoses of "symptomatic DVT recurrence." If the same frequencies of insertion-site DVT reported in the literature were to be applied to the PREPIC study data, it is possible that the differences between the filter and no filter groups in terms of rates of DVT recurrence would no longer exist [33].

The risk of recurrent DVT for an individual patient can be influenced by a multitude of variables, such as the nature of the index VTE event, the efficacy of the initial heparin therapy, the intensity and duration of oral anticoagulation therapy, the presence of active malignancy, and the presence of inherited or acquired predispositions to hypercoagulability. Patients with idiopathic (ie, spontaneous) VTE have higher recurrence rates (12%–15% per year) than those with situational (ie, triggered by a known risk factor) VTE (2%–4% per year) [37,38]. VTE recurrence rates have also been shown to be higher in patients with active cancer; antiphospholipid antibodies; deficiencies of natural anticoagulants (protein C, protein S, and antithrombin); and hyperhomocysteinemia [29,31,36,37,39]. Treatment with oral anticoagulation for 3 months suffices for patients with situational VTE without known hypercoagulable states or cancer, whereas therapy for a minimum of 6 months is recommended for those with idiopathic VTE, cancer, or selected hypercoagulable states [14].

More than a third of the available filter literature focuses on the short- and long-term complications associated with these devices [12]. The long-term rates of DVT following filter placement vary widely depending on the filter model, and have been reported as follows: Greenfield filter (all models),

6% to 15%; Bird's Nest filter, 6%; and Vena Tech/LGM filter, 32% [5,40]. These rates, however, are likely inaccurate because most reports present data from retrospective and uncontrolled series in which a number of patients are lost to follow-up or dead at the time of the analyses [5]. Also, data on the timing of DVT development in relation to the filter placement procedure, how the DVT diagnoses were made, and whether concomitant anticoagulation was used are, for the most part, unknown. In a large retrospective analysis of prospectively collected data on 2109 patients from the Michigan Filter Registry, no association between IVC filters and DVT recurrence was observed [7]. Objective analysis was available, however, in only 40% of the cohort, and data on the timing and type of initial anticoagulation and management of oral anticoagulation (in those patients who were eventually started on such therapy) are unknown [7].

Inadequate oral anticoagulation after the initial heparin therapy has been associated with a risk of recurrent DVT approaching 50% [41]. Most patients who undergo IVC filter placement have either a contraindication or a complication of anticoagulant therapy, and many cannot be started on anticoagulation soon after the procedure. If such patients develop VTE recurrence, it becomes impossible to discern whether the new, recurrent event was caused by the device itself or was simply a reflection of the natural history of venous thromboembolic disease.

In the PREPIC study, all groups had a similar frequency of a previous history of VTE and of known cancer at the time of enrollment [6]. Data are lacking, however, on the nature of the DVT events and on the presence of other hypercoagulable states. Differences in the underlying thrombotic risk between the filter and the no filter groups could indeed explain their different rates of DVT recurrence. Although it could be assumed that the randomization process equally distributed the patients' underlying thrombotic risks, it is impossible to determine whether the groups were truly similar without objective data, especially considering that known cancer and prior history of VTE are only two of a multitude of factors that can determine a patient's risk of VTE recurrence. Despite randomization, if any differences indeed existed, adjustments to the outcome analyses would have been necessary to confirm or refute a causal relationship between IVC filters and DVT recurrence.

Considering the significant methodologic limitations of the available studies on IVC filter-related DVT, and despite the yet unparalleled level of evidence provided by the PREPIC study, there is no convincing evidence to date that supports the conclusion that an IVC filter is, by itself, an independent risk factor for DVT recurrence. The answer to the question "Do IVC filters undoubtedly increase the risk of DVT recurrence" should be, in this author's opinion, a prudent "no."

An additionally interesting aspect of the PREPIC study and of the filter literature in general pertains to the different rates of IVC thrombosis associated with different filter models. IVC thrombosis at the filter site is

another potential thrombotic complication associated with IVC filters [5,8,12,15]. Similar to insertion-site DVT, some cases may be asymptomatic, and studies using active imaging surveillance report higher incidence rates than studies that use imaging assessment of symptomatic-only patients [5,8,15]. An added challenge to the diagnosis of IVC thrombosis and determination of its incidence stems from the fact that contrast cavography, the gold-standard diagnostic test, is not used in most studies because it is invasive. Duplex ultrasound, CT, and MRI have been used most frequently, but their reliability to diagnose IVC thrombosis accurately is another matter of debate, particularly in cases of partial IVC occlusion [42]. Nonetheless, compilation of IVC filter study data indicates that the rates of IVC thrombosis at the filter site are lowest with the stainless steel Greenfield filter (3.6%); higher with the Bird's Nest (3.9%–4.7%) and titanium Greenfield filters (6.5%); and highest with the Vena-Tech/LGM filter (11.2%) [5,43,44]. Data on the stainless-steel Greenfield filter may reflect underestimation of the true rates of IVC occlusion because, in the largest published series, even though some patients had been followed-up for 20 years, approximately 20% of patients were lost to follow-up [43]. Best evidence to date, however, does suggest that the Vena Tech filter has the worst long-term IVC patency profile, with IVC thrombosis rates of 33% reported after a 9-year follow-up in the prospective study by Crochet et al [42] using objective imaging assessment every 2 years.

In the PREPIC study, 56% of the patients received a Vena Tech/LGM filter, 26.5% a titanium Greenfield filter, and 15.5% received a Bird's Nest or Cardial filter [6]. The study reported that 16 (43%) of the 37 patients in the filter group who had DVT recurrence were also found to have IVC thrombosis at the filter site, but the rate of thrombosis according to filter model is unknown [6]. Although it is possible that the excess of DVT recurrence seen in the filter group could be attributed to the observed rate of IVC thrombosis, this cannot be proved without knowing the rate of asymptomatic IVC thrombosis in the group of patients who received a filter but did not have symptomatic DVT recurrence. Even if IVC thrombosis did explain the increased rate of DVT recurrence, it still does not support the conclusion that all IVC filters increase the rates of DVT recurrence long-term because it is possible that a specific filter model accounted for most of the IVC thromboses (and DVT recurrences) observed in the study.

Assuming that IVC filters do increase the risk of DVT recurrence (disregarding all of the previously discussed arguments), this does not necessarily mean that long-term oral anticoagulation is justified. In recent large-scale randomized controlled trials of VTE therapy, recurrence rates were indeed lower in patients on long-term (>6 months) oral anticoagulation, but this benefit was partially offset by an annual incidence of major and fatal bleeding of 2%–4% and 0.6%, respectively (15% case-fatality ratio) [14,29,38,45,46]. Conversely, approximately 5% of all recurrent VTE events were fatal [29,30,38,46]. Furthermore, even if patients

are not continued on prolonged oral anticoagulation, the annual rates of DVT recurrence, which are higher in the first 1 to 2 years following the index event, tend to decline thereafter [36,37]. The balance between the clinical benefit and the risk of long-term anticoagulation is likely to change over time. Some authors have suggested that the annual risk of VTE recurrence should exceed 12% before the benefits of prolonged anticoagulation therapy outweigh its risks [38].

In summary, patients who receive IVC filters should not necessarily be treated with long-term oral anticoagulation. This opinion is based both on the lack of conclusive evidence showing that IVC filters are independent risk factors for DVT recurrence, and on the fact that even if these devices did increase the risk of DVT recurrence, the appropriateness of prolonged anticoagulation depends on the balance between the benefits and risks of such therapy for each individual patient. The ideal duration of oral anticoagulation should be guided most of all by the nature and location of the index VTE event, and also by the presence of concurrent cancer and selected hypercoagulable states, but not by the simple presence of an IVC filter. Even if filters are deemed hypercoagulable devices, analogies with hypercoagulable states should be avoided because not all hypercoagulable states increase the risk of VTE recurrence and require long-term oral anticoagulation [14,38].

It is extremely important to emphasize that the question in debate is whether patients with IVC filters should receive chronic anticoagulation and not whether anticoagulation is appropriate following filter placement. These are two very distinct questions. In the large retrospective study by Greenfield and Proctor [7], a survival advantage was noted in patients who received a filter and were subsequently anticoagulated, compared with those who were not anticoagulated. Despite the lack of prospective data to support the benefit of initiation or resumption of anticoagulation as soon as contraindications have passed after IVC filter placement, this practice is logical and recommended by most experts [14,15,47]. After all, the benefits of anticoagulation for the treatment of VTE have been demonstrated by a number of randomized controlled trials since 1960 [12,14,17]. Anticoagulation prevents mortality from PE, DVT extension, and DVT recurrence, and facilitates restoration of venous patency (mediated by the endogenous fibrinolytic system) [12,14,35,47]. Moreover, contraindications or complications of anticoagulation, which represent the most widely accepted indications for IVC filter placement, are in many (if not most) cases transient. IVC filters do not halt the thrombotic process, hence should not be viewed as an alternative treatment for VTE but as a mechanical means to prevent fatal PE, instead.

Prospective controlled studies are clearly needed to determine the exact incidences and clinical significance of the three potential thrombotic complications associated with IVC filter placement: insertion-site DVT, IVC thrombosis at the filter site, and DVT recurrence. Until such data are

available, this author believes that the PREPIC study findings should not serve as evidence supporting long-term anticoagulation in patients with a filter, but rather as strong evidence in favor of a more conservative approach to IVC filter use. Concerns that IVC filters may be associated with long-term thrombotic complications are valid and justifiable. Any recommendations for placement of an IVC filter in high-risk patients without VTE (and in those with VTE but without an absolute contraindication or a complication of anticoagulation therapy) should ideally be based on the results of prospective controlled trials designed to assess objectively the short- and long-term risks and benefits of IVC filter use in those settings, and not on the findings of observational, uncontrolled studies.

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