Inferior Vena Cava Filters and Prevention of Recurrent Pulmonary Embolism

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Abstract

Although inferior vena cava (IVC) filters have a clear role in preventing recurrent pulmonary embolism (PE) in patients with venous thromboembolism who cannot be anticoagulated, the role of filters in patients who are candidates for anticoagulation is controversial. With limited and conflicting data, practitioners often have to make an educated patient-specific decision when encountering this scenario. This article reviews the available data on the efficacy and risks associated with adjunctive IVC filter use to prevent recurrent PE.

Keywords

- venous thromboembolism
- deep vein thrombosis
- pulmonary embolism
- inferior vena cava filters
- interventional radiology

Objectives: Upon completion of this article, the reader will be able to (1) distinguish the benefits of adjunctive use of IVC filters to prevent recurrent PE; (2) discuss the risks associated with IVC filters when used in conjunction with anticoagulation; (3) implement patient-specific evidence-based decisions regarding adjunctive filter use to prevent recurrent PE.

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History of Inferior Vena Cava Filtration

The concept of an intracaval barrier to capture migrating deep venous thrombi and prevent pulmonary emboli dates back to 1868.[1] This concept came to fruition with the first surgical interruption of the inferior vena cava (IVC) in 1893. Percutaneous caval filtration became a viable option with the advent of the Mobin-Uddin filter in 1967.[2] Shortly thereafter, the first steel Greenfield IVC filter was used in 1973.[3] In the ensuing decades, numerous different types of IVC filters, both permanent and retrievable, have been developed. The ease of insertion of IVC filters along with expansion of indications for filter use has led to an increased utilization of IVC filters.[4]

Guidelines on IVC Filter Use

The American College of Radiology (ACR)/Society of Interventional Radiology (SIR), American College of Chest Physicians (ACCP), and American Heart Association (AHA) agree that IVC filters are indicated for patients with venous thromboembolism (VTE) who have an absolute contraindication to anticoagulation or in patients whom anticoagulation has failed (recurrent VTE).[5,6]

SIR guidelines propose expanded indications including iliocaval deep vein thrombosis (DVT), large free-floating proximal DVT, difficulty establishing therapeutic anticoagulation, massive PE treated with thrombolysis/thrombectomy, chronic pulmonary embolism (PE) treated with thromboendarterectomy, thrombolysis for iliocaval DVT, VTE with limited

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cardiopulmonary reserve, recurrent PE with filter in place, poor compliance with anticoagulant medications, and high risk of complication with anticoagulation (e.g., ataxia, frequent falls). Additional indications for patients without documented VTE include severe trauma without documented PE or deep venous thrombosis, such as closed head injury, spinal cord injury, and multiple long bone or pelvic fractures; high-risk patients, such as immobilized intensive care patients; and prophylactic preoperative placement in patients with multiple risk factors for VTE.[6]

IVC Filters to Prevent Recurrent PE

Anticoagulation alone can prevent recurrent PE in 95% of patients presenting with a proximal DVT, and therefore, adjunctive use of IVC filters in patients at high risk for PE recurrence is controversial.[7,8] With limited and conflicting data, practitioners have to make an educated patient-specific decision when dealing with this scenario. This article reviews the available data on the effectiveness and risks associated with adjunctive IVC filter use to prevent recurrent PE to aid with this difficult decision.

The PREPIC trial (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) was the first prospective, randomized, blinded trial assessing the role of IVC filters in the prevention of recurrent PE. This landmark trial was structured as a 2×2 factorial intention-to-treat design with recruitment of 400 patients of whom 200 were randomized to IVC filter plus anticoagulation and 200 to anticoagulation alone. A total of 195 patients received low-molecular-weight heparin and 205 patients received unfractionated heparin. Inclusion criteria were hospitalized patients older than 18 years with acute proximal DVT with or without symptomatic PE and being deemed high risk for PE. Twelve-day assessment post filter insertion demonstrated 1.1% of patients with adjunctive filters developed a recurrent PE (symptomatic and asymptomatic) compared with 4.8% of patients treated with anticoagulation alone ($p = 0.03$). Similar findings were seen in patients who initially presented with DVT with concurrent PE. There was a trend toward lower symptomatic recurrent PE at 2 years with 6 events in the filter arm (1 death) and 12 events in the control arm (5 deaths; $p = 0.16$). PE on initial presentation was not a significant prognostic indicator of recurrent PE. A major area of caution in the use of IVC filters resulted from this publication based on the increased rate of recurrent DVT in the filter arm compared with the control arm (20.8 vs. 11.6%, $p = 0.02$). There was no difference in overall mortality.[9] Although this study stated a short-term benefit in the development of recurrent PE and a potential risk of recurrent DVT resulting from IVC filter placement, the study was designed to require 800 patients and may have been underpowered due to poor enrollment. This may have contributed to the lack of a statistically significant benefit in preventing recurrent PE at 2 years.

In an effort to better understand the long-term effects of IVC filters and the potential for increased recurrent DVT risk, the authors of the PREPIC trial performed a follow-up study of the same patients by performing an annual phone call for 8 years after the initial trial to assess for VTE recurrence, postthrombotic syndrome (PTS), and overall mortality. There was an increased rate of symptomatic PE in the control arm that received anticoagulation alone (24 patients, 5 fatalities), compared with the IVC filter placement + anticoagulation arm (9 patients, 2 fatalities; $p = 0.008$). This benefit was confirmed with a multivariate analysis including significant predictive factors of PE including PE at inclusion, transient risk factors, and idiopathic VTE or cancer ($p = 0.014$). Additionally, in distinction to the original trial, initial presentation with PE correlated with recurrent PE presentation ($p = 0.032$). Although the filter arm did not have any increased incidence of PTS, 57 patients with filters developed a symptomatic DVT compared with 41 patients in the control group ($p = 0.032$). Of the patients who developed a DVT in the IVC filter arm, 46% (26 of 57 patients) had associated filter thrombosis. Importantly, there was no difference in overall mortality between the two cohorts.[10] This follow-up study further established the increased incidence of DVT following filter insertion, but without associated PTS or mortality. One of the limitations in the assessment of PTS in this cohort is that a large proportion of patients had PTS at the time of IVC filter insertion and the use of graduated compression stockings was high in both groups during the follow-up time period. The benefit in preventing recurrent PE may have been potentiated by the fact that only 50% of the patients in both cohorts remained on anticoagulation at 8 years with a majority of PEs occurring after anticoagulation was stopped.

Due to the increased utilization of IVC filters to prevent recurrent PE following the initial PREPIC data, the PREPIC 2 study was performed to assess the safety and effectiveness of retrievable IVC filters. The authors hypothesized a similar benefit in PE recurrence with the added benefit of mitigating DVT recurrence with retrieval of the IVC filter. PREPIC 2 was a randomized, open-label, blinded, intention-to-treat study comparing PE recurrence in patients who were at high risk of recurrence and initial presentation of PE. The study arm was treated with a retrievable IVC filter plus 6 months of anticoagulation and filter retrieval at 3 months. The control arm was treated with 6 months of anticoagulation. At 3 months, there was no significant difference in the rate of recurrent PE with six patients in the filter arm and three patients in the anticoagulation arm ($p = 0.50$) (8 fatal). At 6 months, one additional patient in each cohort had a recurrent PE, but there continued to be no significant difference. There was also no difference in both cohorts when comparing major bleeding or death.[11] The control group in this study had an overall PE recurrence rate of 1.5%, far below the expected 8% rate. The authors acknowledged this difference, but stated that the historic rate was from the era of more traditional anticoagulation agents. Recent trials of direct oral anticoagulants demonstrated PE recurrence rates similar to this study.[11] Generalizability of this study is limited by a remarkably high filter retrieval rate (153/193 patients), which has not been achievable in most clinical practices in the United States.

Stein et al retrospectively analyzed a database of over 2,000,000 patients with a diagnosis of inpatient PE showing a mortality benefit in certain populations with adjunctive IVC filter use. They were able to calculate rates of in-hospital

Table 1 Incidence of recurrent PE in patients with DVT or PE, with or without IVC filters

Time	DVT + Filter	DVT − Filter	PE + Filter	PE − Filter
12 d			1.1% (2)	4.8% (9)
3 mo[a]	0.5% (1)	0.5% (1)	3.0% (6)	1.5% (3)
6 mo[a]	0.5% (1)	1.0% (2)	3.5% (7)	2.0% (4)
2 y[b]	20.8% (37)	11.6% (21)	3.4% (6)[c]	6.3% (12)[c]
8 y[b]	35.7% (57)	27.5% (41)	6.2% (9)	15.5% (24)

Notes: All additional data in this table are statistically significant. Incidence in cohort (*n*).
[a]PREPIC2.
[b]PREPIC.
[c]Was not statistically significant. $p = 0.016$.

mortality in cohorts with and without IVC filters. In addition, they were able to stratify these cohorts into stable PE and unstable PE as well as patients requiring thrombolysis or not. They showed a significantly lower hospital case fatality rate in stable PE patients undergoing thrombolysis with adjunctive IVC filter use compared with those that did not receive IVC filters (6.4 vs. 15%, $p = 0.0001$). This study also demonstrated significantly lower hospital case fatality rates in unstable PE patients undergoing thrombolysis with adjunctive filter compared with no IVC filter (7.6 vs. 18%, $p = 0.0001$). Unstable patients with PE who did not receive thrombolytic therapy had a lower in hospital mortality if they had an IVC filter compared with no IVC filter (33 vs. 51%, $p = 0.0001$). Of note, the authors assumed patients who received thrombolytic therapy were also on concurrent anticoagulation and, therefore, recommended adjunctive filter use in these cohorts.[12]

►**Table 1** provides overall risks of recurrent PE in patients presenting with DVT or PE, with or without IVC filters.

Conclusion

The role of IVC filters as an adjunct to anticoagulation continues to be controversial. The PREPIC trial demonstrated short-term benefit and long-term efficacy in preventing PE recurrence at the cost of increased DVT recurrence. The PREPIC 2 study, however, failed to show a similar short-term benefit of reduced PE recurrence with the use of retrievable IVC filters. Both PREPIC and PREPIC 2 highlight the importance of anticoagulation in the management of these patients. The PREPIC study demonstrated lower PE recurrence in patients who were initially on low molecular weight heparin compared with heparin. The PREPIC 2 trial demonstrated overall lower PE recurrence with direct oral anticoagulants compared with vitamin K antagonists. The ability of patients to adhere to a regimen and achieve therapeutic anticoagulation both quickly and reliably may be a critical deciding factor in the individualized decision for adjunctive filter use in patients at high risk for recurrent PE.

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