Requiem for Liberalizing Indications for Vena Caval Filters?

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Use of inferior vena cava (IVC) filters has proliferated. In 1979, ≈2000 vena caval filters were inserted. In 1999, the number of IVC filters inserted annually had increased ≈25-fold to 49000. Retrievable IVC filters were first approved in 2003 and gained popularity rapidly. By 2006, retrievable IVC filters accounted for about half of all IVC filters that were inserted. The largest proportional increase in IVC filter use was subsequently in patients at risk for pulmonary embolism (PE) but who had had neither PE nor deep vein thrombosis (DVT).1

Epidemiology

In Medicare fee-for-service beneficiaries ≥65 years of age, ≈17% of PE patients undergo IVC filter placement. The IVC filter use rate in PE patients has remained stable since year 2000. However, the frequency of hospitalization for PE has increased in this population by ≈70%, resulting in a sharp rise in the absolute number of filters inserted. Use appears especially high in blacks, in men, and in octogenarians, but overall use varies markedly across the United States. Filter insertion is highest in the South Atlantic region and lowest in the Mountain States. In this PE population overall, the in-hospital mortality rate has fallen by half, including the subgroup with IVC filters. The in-hospital mortality rate for patients receiving IVC filters fell from 8.2% in 1999 to 4.3% in year 2010. This decrease in mortality is remarkable, especially because those who had filters placed had a greater frequency of comorbidities such as cancer, heart failure, atherosclerosis, and vascular diseases in comparison with PE patients without filters.6

Observational Studies

Patients with massive PEs stand to benefit the most from IVC filter insertion, but such patients are so critically ill that a randomized, controlled trial of management is not feasible. Most PE experts have no enthusiasm to undertake such a trial because of the lack of clinical equipoise. In the International Cooperative PE Registry (ICOPER), 108 (4.5%) of 2392 patients with known systemic arterial blood pressure at presentation had massive PEs. The 90-day mortality rate was 52%. Among patients with massive PEs who received thrombolysis, the 90-day mortality remained high, 46%. The recurrent PE rate at 90 days was 12%. However, none of the 11 patients who received an IVC filter developed recurrent PE within 90 days. Ten of the 11 patients survived at least 90 days. Thus, in this registry, among patients with massive PEs, IVC filters were associated with a reduction in 90-day mortality.7

The Nationwide Inpatient Sample found that patients who had unstable massive PEs (defined as in shock or ventilator dependent) who received thrombolytic therapy had a lower in-hospital case fatality rate than those who did not: 505 of 6630 (7.6%) versus 2600 of 14760 (18%). Similarly, unstable patients with massive PEs who did not receive thrombolytic therapy also had a lower in-hospital case fatality rate with IVC filters: 4260 of 12850 (33%) versus 19560 of 38000 (51%).8 The mortality reduction associated with IVC filters was present in every age group but was greatest among patients ≥1 years of age.8

Patients with venous thromboembolism (VTE) are also at risk if they have a major bleeding risk that may impede the use of anticoagulation. Using the Computerized Registry of Patients with Venous Thromboembolism (RIETE) database of >40000 VTE patients, 344 with a significant bleeding risk were managed with IVC filter insertion. They were matched with 344 VTE patients treated without a filter. Propensity score–matched pairs showed a trend (P=0.12) toward lower risk of all-cause death for filter insertion. The risk-adjusted PE-related mortality was lower for filter insertion (1.7% versus 4.9%; P=0.03). Risk-adjusted recurrent VTE rates were higher for filter insertion than for no insertion (6.1% versus 0.6%). Thus, in patients with VTE and known bleeding risk, IVC filter insertion may reduce the risk of PE-related mortality in comparison with anticoagulation but increase the risk of recurrent VTE.10

In this issue of Circulation, White and colleagues11 from the University of California at Davis School of Medicine report...
the results of a large California hospital registry of acute VTE patients from 2005 to 2010. They excluded patients who had cancer with VTE. Among 80,697 VTE patients with no contraindication to anticoagulation, 9.6% received IVC filters. Among 3017 VTE patients with active bleeding and at least a temporary contraindication to anticoagulation, 36% received IVC filters. Filter use did not reduce the risk of death in nonbleeding VTE patients but did reduce the mortality rate by 32% at 30 days and by 27% at 90 days in VTE patients with active bleeding. The risk of subsequent DVT increased by 50% in nonbleeding VTE patients and more than doubled in VTE patients with active bleeding. In no subgroup did filter use reduce the risk of recurrent PE.

White and colleagues have a lot of experience with this particular California registry and the information it provides on population-based study of the effectiveness of IVC filter use among VTE patients. In year 2000, they published a case-control study of 3632 patients treated with an IVC filter and 64,333 VTE controls in registry data collected from 1991 to 1995. Most of these VTE patients appeared eligible for anticoagulation therapy. Only 20% of the patients in the IVC filter group had a diagnosis of major bleeding during the index hospitalization or preceding 3 months. Among patients who received IVC filters, there was no reduction in rehospitalization for PE. In contrast, the presence of IVC filters more than doubled the likelihood of rehospitalization for venous thrombosis among patients who presented initially with acute PE.

Randomized Trials

Randomized trials of IVC filter placement in VTE patients are extraordinarily difficult to organize and to perform. A French group has managed to achieve this feat twice over a 20-year period. The Prévencion du Risque d’Embolie Pulmonaire par Interruption Cave (PREPIC) study randomly assigned 400 proximal DVT patients either to an IVC filter or no filter. These were permanent filters, because retrievable filters had not yet been invented. All 400 patients were anticoagulated with heparin or low-molecular-weight heparin. The Prevention of Recurrent Pulmonary Embolism by Vena Cava Interruption (PREPIC2) trial randomly assigned 400 PE patients with leg DVT either to a retrievable IVC filter or no filter. All patients received full-dose anticoagulation for at least 6 months.

In the PREPIC trial of acute DVT, by day 12, the IVC filter group sustained a 1.1% rate of acute PE in comparison with 4.8% in the group without filters. However, by 2 years, 21% of the filter group had recurrent DVT in comparison with 12% of the no-filter group. By 8 years, symptomatic PE occurred in 6.2% of the filter group in comparison with 15% of the no-filter group. In contrast, recurrent DVT occurred in 36% of the filter group in comparison with 28% of the no-filter group. There was no difference in rates of postthrombotic syndrome or in survival between the 2 groups. In the PREPIC2 trial of acute PE plus DVT, insertion of a retrievable IVC filter plus anticoagulation in comparison with anticoagulation alone did not reduce the risk of symptomatic recurrent PE at 3 months.

Guidelines

The 2014 European Society of Cardiology guidelines state that venous filters are indicated in patients with acute PE who have absolute contraindications to anticoagulant drugs and in patients with objectively confirmed recurrent PE despite adequate anticoagulation. The European Society of Cardiology guidelines also state that there are no data to support the routine use of venous filters in patients with free-floating thrombi in proximal veins. The guidelines further state that there is no evidence to support the use of IVC filters in patients undergoing systemic thrombolysis, surgical embolectomy, or pulmonary thromboendarterectomy. The 2016 CHEST Guideline and Expert Panel Report simply states, “In patients with acute DVT or PE who are treated with anticoagulants, we recommend against the use of an IVC filter.”

Reconciling Randomized Trials, Observational Data, and Guidelines With the Real World

At the moment, the popularity of IVC filters is declining. There remains consensus to insert IVC filters in patients with absolute contraindications to anticoagulant drugs, in patients who experience major bleeding during anticoagulant treatment of acute VTE, and in patients with objectively confirmed recurrent PE, despite adequate anticoagulation treatment (Table 1). Evidence derived from randomized trials and registries does not support liberalization of IVC filter insertion beyond these strict indications.

However, it is premature to hammer nails into the coffin and to gather as a medical community for a requiem that celebrates no indication for liberalizing indications for placing an IVC filter. Instead, we need to shift the focus of the questions that we investigate and pour resources into further randomized and observational trials of IVC filter insertion in special high-risk populations. There remain important groups of patients who may benefit from IVC filters with reduction in PE and PE-associated mortality (Table 2). In some cases, tantalizing data suggest that these populations warrant filters. In other cases, we lack data to guide us.

Patients with massive PE—accompanied by cardiogenic shock requiring vasopressors to support blood pressure—are desperately ill. They are clinically unstable. An additional PE under these circumstances can be the fatal blow. Data from the National Inpatient Sample and the International Cooperative PE Registry suggest that filters in these patients may be lifesaving.

Patients with severe PE who undergo acute surgical pulmonary embolectomy are vulnerable to recurrent PE, especially during the early postoperative period where full anticoagulation cannot be immediately implemented. I have had personal experience managing this type of patient where the embolectomy is successful but the patient dies of recurrent PE.

Table 1. Generally Accepted Consensus Recommendations for IVC Filter Insertion in Patients With VTE

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Description</th>
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<tr>
<td>Major bleeding on full-dose anticoagulation</td>
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<tr>
<td>Major contraindication to full-dose anticoagulation</td>
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<tr>
<td>New-onset acute PE (especially recurrent PE) despite well-documented full-dose anticoagulation for an existing VTE</td>
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IVC indicates inferior vena caval; PE, pulmonary embolism; and VTE, venous thromboembolism.
Patients who have cancer have been excluded from many of the large registry studies of IVC filters. Patients with cancer are predisposed to VTE and to recurrence despite therapeutic anticoagulation. They are also at higher than average risk of major bleeding because their tumors may be hemorrhagic or their platelet counts may be low because of chemotherapy.

Patients undergoing certain types of surgery, such as neurosurgery or spine surgery, may not be safe candidates for prophylactic low-dose anticoagulation. We should obtain evidence on whether patients in this predicament benefit from perioperative IVC filter placement.

The 2 randomized PREPIC trials enrolled patients in whom most of us would not place filters. The study population consisted of relatively stable patients who were candidates for full-dose anticoagulation.

The results of observational registry studies vary according to the population studied. In the current issue of Circulation, White and colleagues have provided additional evidence that stable noncancer patients who can tolerate full-dose anticoagulation do not benefit from IVC filters. Now, we should turn our attention to less well-studied patients with massive PEs, high-risk submassive PEs, patients who have cancer with VTE or at risk for VTE, and preoperative patients at high risk for VTE in whom standard VTE thromboprophylaxis is ill advised.

The observational studies of White et al facilitate our focusing on unanswered questions regarding special populations who might benefit more often from routine insertion of IVC filters. These patients, who in general will not be good anticoagulation candidates, might experience increasingly frequent DVT after filter insertion, but less frequent PE with its graver morbidity and mortality. Rather than a requiem, we should promote a renaissance in clinical investigations of IVC filter insertion.

Disclosures

None.

References


Key Words: Editorials ■ pulmonary embolism ■ thrombosis ■ vena cava filters
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doi: 10.1161/CIRCULATIONAHA.116.022730

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