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# The Inferior Vena Cava Filter

*How Could a Medical Device Be So Well Accepted Without Any Evidence of Efficacy?*

**B**ASED ON THE PATHOPHYSIOLOGIC characteristics of venous thromboembolism (VTE), the inferior vena cava filter (IVC) should work. Placed between the proximal vessels of the lower extremities—the main source of venous emboli<sup>1-3</sup>—and the right side of the heart, the IVC filter should capture a blood clot before it reaches the pulmonary circulation and should improve outcomes. This theory, however, has never been validated by empirical studies. This may seem surprising for a device so well established in medical practice. The history of the IVC filter provides valuable insight into the shortcomings of medical device approval in the United States.

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### THE ORIGINS OF THE IVC FILTER AND MODERN USE

The first percutaneous device used to intercept a blood clot was the Mobin-Uddin umbrella filter. Introduced in the late 1960s,<sup>4</sup> The device was plagued by high rates of IVC occlusion (in over half of patients), pulmonary embolism (PE), and migration. It was replaced by the stainless steel Kimray-Greenfield filter in 1973,<sup>5</sup> a device with lower complication rates. In 1981, Greenfield et al<sup>6</sup> reported results for 156 patients treated with this filter, of which the most common indication was VTE with contraindication to anticoagulation. Greenfield and Michna expanded this series to 469 patients by 1988.<sup>7</sup> At that time, long-term follow-up (mean duration, 43 months) was achieved for 146 patients; 190

were lost, and 133 patients (28%) had died. Greenfield et al<sup>6</sup> noted a 4% rate of PE (17 deaths from PE and 9 cases of nonfatal PE) and a long-term patency rate of 96%, although nearly half (44%) of patients were left with chronic venous stasis. These results—nearly uninterpretable because of the lack of control group and the loss of nearly half of study participants—serve as the evidence base for the IVC filter.

Over the past 3 decades, use of the IVC filter has climbed steadily. Although only 2000 filters were placed in 1979,<sup>8</sup> by 1990, over 120 000 Kimray-Greenfield filters had been implanted in the United States.<sup>9</sup> By the 1990s, nearly 30 000 to 40 000 filters were placed annually.<sup>10</sup> At the decade's end, nearly 50 000 filters were being placed each year.<sup>8</sup>

### GUIDELINES FOR IVC FILTERS

Four major professional groups—the American College of Chest Physicians, the American Heart Association, the British Committee for Standards in Hematology, and the Thrombosis Interest Group of Canada—have published guidelines for the use of IVC filters. All 4 agree that an IVC filter should be placed in patients with VTE and a contraindication to anticoagulation.<sup>11</sup> There is not consensus among the guidelines for other possible indications: VTE despite anticoagulation, patients with recent VTE who must have anticoagulation held for surgery, patients with proximal deep vein thrombosis (DVT) and poor cardiac reserve, patients with free-floating DVT, or primary prevention for high-risk patients.<sup>11</sup>

### EVIDENCE FOR THE USE OF THE DEVICE

To our knowledge, there is only 1 randomized controlled trial (RCT) of the IVC filter—the PREPIC (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) study—published in 1998<sup>12</sup> with an 8-year follow-up reported in 2005.<sup>13</sup> The PREPIC study enrolled 400 consecutive patients older than 18 years, with acute proximal DVT (with or without PE), who were considered high risk for (further) PE by their physicians. Patients were excluded if they were pregnant, undergoing thrombolysis, had liver or kidney failure, or a short life expectancy. Most notably, the trial excluded patients with a contraindication to anticoagulation therapy, the only indication for which the several professional societies agree. Patients were allocated to 1 of 2 types of anticoagulation therapy with or without the addition of IVC filter (in 2 × 2 factorial design). Long-term anticoagulation with warfarin occurred in equal numbers across the groups.

At 2 years, PREPIC found no difference in mortality between the 2 groups but a 10% (95% CI, 11.6%-20.8%) higher rate of DVT among those who received the filter.<sup>12</sup> A nonstatistically significant reduction in symptomatic PE was noted ( $P = .16$ ).<sup>12</sup> At 8 years, the reduction in symptomatic PE met significance. 15.2% of patients without IVC filters experienced symptomatic PE, while only 6.2% of patients with filters did.<sup>13</sup> Deep vein thrombosis had occurred in 35.7% of patients in the filter group but in only 27.5% in the group without the device ( $P = .04$ ). Most importantly, mortality was indistinguishable between the groups.<sup>13</sup>

Even the finding of a decrease in symptomatic PE may be exaggerated. Per trial protocol, a physician phoned patients annually, elicited symptom history suggestive of PE or DVT symptoms, and recommended hospital visits or imaging based on these conversations. Thus, it was not only symptoms that drove patients to the physician. Elsewhere, we have argued that PE exists on a continuum.<sup>14</sup> Improving a symptomatic condition may well be a valid patient-centered outcome, but decreasing a condition, evident only on probing, may not be.

The weak findings of PREPIC and otherwise absence of RCTs supporting the filter may be reflected in the findings of 2 studies in this issue of the journal. White et al<sup>15</sup> show tremendous variation in the use of the device in clinical practice, and, make the case, that the underlying reason for this finding is a lack of evidence based indications. According to Sarosiek,<sup>16</sup> the advent of retrievable filters has done little to change the calculus presented here. Most (91.5%) retrievable filters were not removed in a comprehensive examination of a tertiary medical center.

#### FDA APPROVAL

How did a device with such a poor evidence base garner US Food and Drug Administration (FDA) approval in the first place? The FDA's 510(k) process—in which similarity to an existing product (not safety or efficacy data) is used to make regulatory decisions—has been the basis of IVC filter approvals. In 1976, the Mobin-Uddin filter was cleared by this process, and in 1985, the Greenfield filter was similarly approved.<sup>17</sup> Despite extensive review, the predicate device for approval of these early filters remains unclear. In recent decades many new filters have been developed: the Titanium Greenfield, the Bird's Nest, VenaTech, Gunther Tulip, VenaTech LP. We can find no instances in which such filters were approved through any process, besides the 510(k), an approval mechanism that the Institute of Medicine recommends be discontinued.<sup>18</sup>

#### GROWING AWARENESS OF HARM

While the benefits of the IVC filter are hard to assess, the complications are evident. Complications of the IVC filter may occur at the time of placement or years later. Procedural harms include hematoma (0.6%), misplacement (1.3%), pneumothorax (0.02%), and air embolism (0.2%).<sup>9</sup> One model, the Bird's Nest, has a procedural death rate nearly 3-fold greater than competitors (0.34%).<sup>9</sup> A study of the VenaTech IVC filter found IVC occlusions in 22% of patients at 5 years, and 33% at 9 years.<sup>19</sup> Arguably, PREPIC illustrates the greatest harm, a nearly 10% increased absolute risk of DVT, a powerful risk factor for the postthrombotic syndrome.<sup>9</sup>

A study in this journal<sup>20</sup> brought to public attention the prevalence of fracture and fragment embolization of Bard retrievable filters. Just over 16% of patients (13 of 80) had strut fractures in a single center study, with device debris leading to cardiac tamponade, and possibly ventricular tachycardia and death. These concerns were echoed in a 2010 safety alert by the FDA. From 2005 to 2010,<sup>21</sup> the FDA received reports of 921 adverse events regarding IVC filters. A total of 328 were cases of device migration, 146 were embolization of broken device parts, and 70 were cases of IVC perforation.

#### THE NEED FOR RCTs

Given the known harms and the lack of efficacy data for IVC filter, we need RCTs. Unfortunately there is little incentive for manufacturers of filters to embark on trials that can only eliminate their products' market share. Therefore, we need either the FDA to require current filter manufacturers to perform efficacy studies of their devices as a condition for remaining on the market or a large federally funded study to determine if this expensive device leads to greater benefit than harm. Until then, clinicians and patients face difficult choices. Follow current standard of care and place filters where guidelines advise, or do not place filters, after informed consent informs patients that there is evi-

dence of harm without evidence of benefit.

Vinay Prasad, MD  
Jason Rho, MD  
Adam Cifu, MD

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**Author Affiliations:** Medical Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland (Dr Prasad); Department of Medicine, Northwestern University, Chicago, Illinois (Dr Rho); and Department of Medicine, University of Chicago, Chicago (Dr Cifu).

**Correspondence:** Dr Prasad, Medical Oncology Branch, National Cancer Institute, National Institutes of Health, 10 Center Dr, 10/12N226, Bethesda, MD 20892 (vinayak.prasad@nih.gov).

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