

# Is Market Growth of Vena Cava Filters Justified?

A review of indications, use, and market analysis.

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Caval interruption to prevent pulmonary embolism (PE) is a concept that is more than 100 years old, and at that time, an invasive vein ligation surgery was warranted because it was believed to confer tremendous benefit to the critically ill. So, when the significantly less invasive inferior vena cava (IVC) filter was invented, it was accepted and adopted rather quickly. In the 20-year period between 1979 and 1999, there was a 20-fold increase in the use of IVC filters according to the National Hospital Discharge Survey.<sup>1</sup> This trend was driven in part by the advances and miniaturization in filter delivery systems and IVC filters themselves. The growth trend only continued in the late 1990s and into the 21st century and was mirrored throughout the world, as confirmed by Hammond et al.<sup>2</sup>

Although the indications for IVC interruption have not changed significantly in the past 30 years, and the filter delivery profile has remained relatively constant in

the last 10 years, there continues to be a commercial drive toward filter development, despite a host of available and acceptable IVC filters. In 2007, the United States market for IVC filters was valued at under \$200 million, with expected growth to top \$300 million in 2012. The more recent growth trend coincides with, and is linked to, the advent of retrievable IVC filters.

## INDICATIONS

PE is a potentially preventable cause of death in hospitalized and high-risk patients. The probability of PE increases with the development and progression of deep vein thrombosis (DVT), which can be caused by immobility, hypercoagulability, and trauma to veins. Definitive treatment for both PE and DVT is anticoagulation. However, in instances in which anticoagulation is contraindicated, inadequate, or has failed, IVC filters are relied on to prevent PE. Table 1 lists the categories

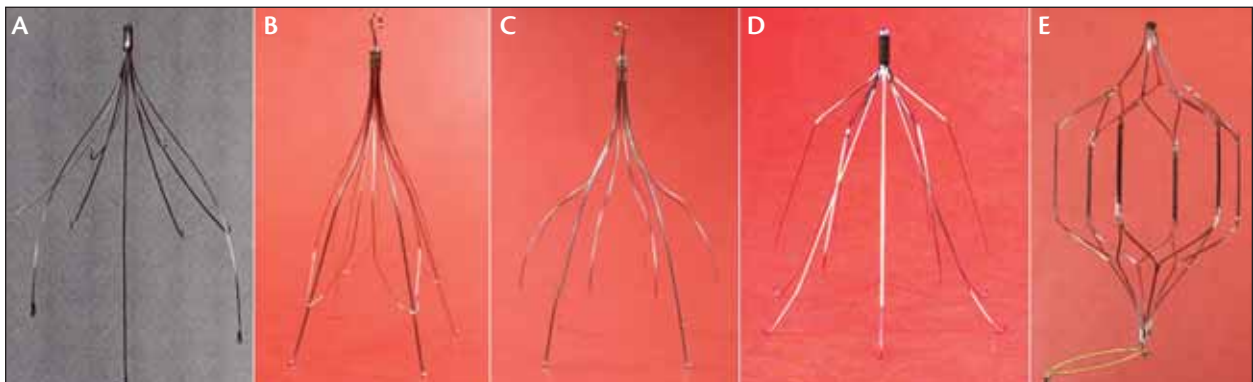


Figure 1. Several optional IVC filters that are commercially available in the United States: ALN (A), Günther Tulip (B), Celect (C), G2 (D), and OptEase (E).

for disease states and scenarios in which filter use is indicated.<sup>3</sup>

### TYPES OF OPTIONAL FILTERS AND THEIR COMPLICATIONS

The first well-studied filter that was adopted was the permanent stainless steel Greenfield IVC filter (Boston Scientific Corporation, Natick, MA), for which there is long-term follow-up data of up to 20 years and longer.<sup>4</sup> This was followed by a host of temporary IVC filters tethered to the skin to allow direct removal without snaring. These filters were used for hospitalized patients and by definition, were used for a short time period and had to be removed. Today, optionally retrievable filters, made of stainless steel, nitinol, titanium, or conichrome (Elgiloy), are available. Eight retrievable filters have been approved by the United States Food and Drug Administration (FDA): the ALN (ALN Implants Chirurgicaux, Ghisonaccia, France), Celect (Cook Medical, Bloomington, IN), Eclipse (Bard Peripheral Vascular, Tempe, AZ), Günther Tulip (Cook Medical), G2 (Bard Peripheral Vascular), G2X (G2 modified with hook, Bard Peripheral Vascular), Option (Angiotech [designed by Rex Medical], Vancouver, BC, Canada), and OptEase (Cordis Corporation, Bridgewater, NJ) (Figure 1).

Unlike the temporary filters that preceded them, the optional filters do not need to be tethered to the skin and thus have a lower rate of infection.<sup>5</sup> Tethered filters also must be removed within a few days, whereas optional retrievable filters present the attractive option of being left in place indefinitely or removed when they are no longer needed. Currently, there are no guidelines on the time frame in which to retrieve these filters, but the data seem to indicate that delayed removal is possible for most of the brands.<sup>6,7</sup> Smouse et al reported successful retrievals out to 17 months with the Günther Tulip filter, with a reliable retrieval success rate of 94% at 12 weeks after implantation without interim filter manipulation (Figure 2).<sup>8</sup>

Retrievable filters are used more frequently today than permanent filters, but data are lacking to indicate their efficacy and safety. One case was reported in which a fractured wire from a retrievable filter migrated to the heart and caused pericardial tamponade.<sup>5</sup> This should serve as an indication that optional filters, like all other new devices left in place for a long period of time, may cause complications. The most common complication with all filters left in the body over an extended period is progression of DVT, as reported in the PREPIC trial.<sup>9</sup> The reasons for this include the thrombogenicity of the device itself, entrapment of emboli within the filter, and natural progression of the DVT. Other reported compli-

**TABLE 1. CATEGORIES FOR DISEASE STATES AND SCENARIOS IN WHICH FILTER USE IS INDICATED**

#### DVT or PE With Contraindication to Anticoagulation Therapy (38%–77%)

- Hemorrhagic stroke
- Recent neurosurgical procedures or other major surgery
- Major or multiple traumas
- Active internal bleeding
- Intracranial neoplasm
- Bleeding diathesis
- Pregnancy
- Unsteady gait or tendency to fall
- Poor patient compliance with medications

#### DVT or PE With Anticoagulation Complication (6%–18%)

##### Failure of Anticoagulation (3%–33%)

- Progression of DVT despite adequate anticoagulation.

##### Free-Floating Iliofemoral or Caval Thrombus

- This has been associated with a 27% to 60% rate of PE, however, somewhat controversial. Pacouret et al did not find a higher PE rate in their study in patients with free-floating proximal DVT.<sup>3</sup>

##### Prophylaxis (Controversial)

- The prophylactic use has accounted for the largest growth in optional type IVC filters because the guidelines for filter placement in these instances are less clear.
- Patients with DVT about to undergo surgery.
- Chronic pulmonary hypertension and low cardiopulmonary reserve.
- Patients with cancer, although this was disputed in 1998 by the American College of Chest Physicians Consensus on Pulmonary Embolism.
- Trauma patients:
  1. Severe head injury with prolonged ventilator dependence.
  2. Major abdominal or pelvic penetrating venous injury.
  3. Spinal cord injury with or without paralysis.
  4. Severe head injury with multiple lower extremity fractures.
  5. Pelvic fracture with or without lower extremity fractures.

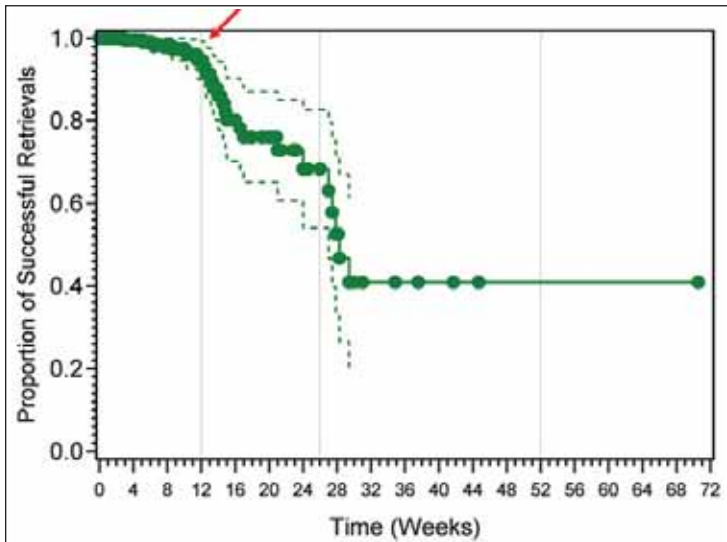


Figure 2. Kaplan-Meier survival curve showing 94% retrieval success of the Günther Tulip vena cava filter at 12 weeks (arrow).

cations include recurrent PE, filter migration, tilt, break or embolism, or IVC perforation or occlusion.<sup>5,6,10</sup> Despite the relatively low risk of these complications, IVC filters offer a great benefit to those at risk of a PE and are thus used quite regularly.

**FDA AND OPTIONAL FILTER CONCERNS**

Literature reviews performed by Food and Drug Administration (FDA) agents have found that the majority of optional filters are not retrieved. The working consensus is that no more than 25% of filters will actually be removed. Because of this relatively low percentage of removal, new filter applications are scrutinized to the same degree as applications for permanently implanted medical devices. The FDA realizes that all filter types, permanent or optional, have reported complications and failures, some leading to death. However, with optional filters, design elements are built into the filter construction to allow eventual retrieval. These include flexible hooks, fewer and smaller hooks, filter collapsibility and flexibility, and unrestrained anchor legs, as well as other elements. These design iterations have placed some optional filters at risk for fatigue failure with fracture, migration, and filter travel into the heart with embolus trapping, as well as IVC wall penetration or perforation.

Items of priority for the FDA include fatigue resistance and migration risk (with and without trapped emboli). It is up to the

manufacturer to satisfy safety concerns using a combination of bench testing and animal trials. Safety factors are built into the filter design to prevent failure, fracture, and embolization in the face of catastrophic embolus burdens and mechanical fatigue from breathing and Valsalva maneuvers. In human clinical trial designs, the primary endpoint is a composite of several endpoints, including the lack of PE, IVC thrombosis, filter fracture, and filter migration (usually described as > 2 cm, caudal or cranial, from the implant site), and the success of accurate filter implantation without significant tilting. The FDA determines the acceptability of a submitted clinical vena cava trial design on a case-by-case basis. Of particular interest are the expected enrollment numbers, the number of retrieval attempts, and the composite endpoint success rate. In the authors' experience, the FDA has accepted enrollment numbers

from between 109 to 200 patients, with a minimum of 50 filter retrieval attempts and a composite endpoint success rate of 80%.

Because the greatest drive for filter use is prophylactic use, the FDA is looking hard at a prophylactic filter indication. At present, prophylactic filter use is considered an off-label indication. Several start-up and established companies that are developing optional IVC filters have been approached by the FDA to apply for prophylactic indication. The number of patient enrollments will be larger than what is currently used for existing filter indications, but the exact number is unclear. It is also unclear at present what the primary and secondary endpoints will be or what will be considered a successful outcome.

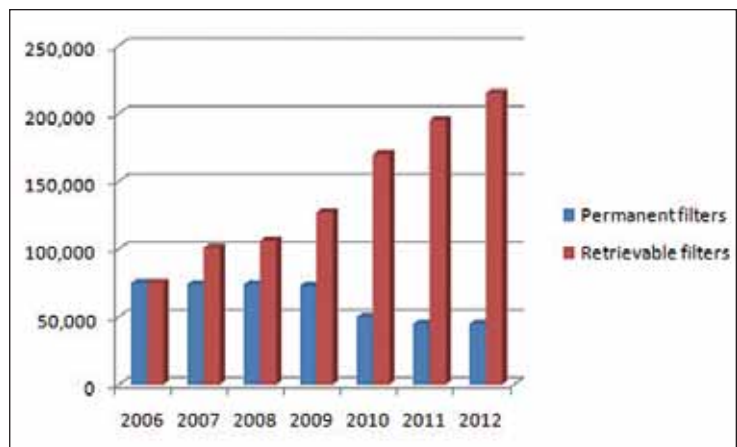


Figure 3. IVC filter market projected change from 2006 to 2012.

## CURRENT MARKET LEADERS AND THE MARKET POTENTIAL

Because IVC filters are seen as a second-line agent for the prevention of PE in patients with DVT (or who are at risk of DVT), the minimally invasive design of the new introducer sheaths (and the ease of filter deployment) have lowered the threshold for IVC filter utilization, and the market share has proliferated. This fact, coupled with the option to remove them at a later time when they are no longer required, has led to an expansion in the indication for the use of retrievable filters. In 1979, only 2,000 IVC filters were used, and in 1999, the number had risen to 49,000.<sup>1</sup> Jumping ahead to 2007, close to 167,000 filters were placed, and by 2012, it is estimated that the number of filters deployed will be around 259,000. Today, the IVC filter market is worth \$190 million and is growing at a compound annual growth rate of 11% per year (Millennium Research Group [Toronto, Ontario, Canada], personal communication, October 2009). The market value of vena cava filters in the United States continues to increase despite a reduction in the use of permanent filters. This is due to two factors: first, the acceptance and use of the optional vena cava filters, which has outpaced permanent filter use, and second, the higher cost of retrievable filters compared to permanent filters (Figure 3).

Retrievable vena cava filters are finding an expanding prophylactic application in new patient populations who may be at temporary risk for venous thromboembolism. Those at risk may include bariatric, orthopedic, trauma, neurosurgical, and cancer patients. They are also being increasingly used by physicians who are afraid of lawsuits. Retrievable filters now represent 50% of the IVC filter market and, at the current growth rate, will represent 75% of the IVC market in 2012. It is estimated that the IVC filter market will be worth close to \$320 million in several years. Determining market leaders is challenging and varies depending upon which research group is polled. Industry leaders for optional IVC filters are Cordis Corporation, Cook Medical, and C.R. Bard, according to Medtech Insight (Irvine, CA, personal communication, October 2009) and Millennium Research Group. Medtech Insight has Cordis as the market leader, with \$64.7 million in sales and a 45.2% estimated market share for 2008, whereas Millennium Research Group has C.R. Bard as the market leader, with an estimated 36.9% market share for 2007.

## CONCLUSION

It seems that transient contraindications to anticoagulation have become an off-label indication to deploy retrievable IVC filters. These transient contraindications

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include trauma, peripartum state, bleeding peptic ulcers, surgical bleeding complications, and recent biopsies or pending surgeries. The bottom line is simple: as retrievable IVC filter designs improve so that they become easier to deploy and remove, and their perceived increased risk of fracture, embolization, and IVC wall penetration declines, their benefits will continue to outweigh their risks, and we will see a continued growth in their use. ■

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