Inferior Vena Cava Filters in the Cancer Patient: Current Use and Indications

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Abstract
Deep venous thrombosis and thromboembolism are significant health risks, with high rates of morbidity and mortality. Chronically ill and hospitalized patients, particularly those with cancer, have a high risk for developing these conditions. Mechanical inferior vena cava (IVC) filtration has been standard care for patients with these conditions in whom anticoagulation therapy is contraindicated or has failed. This article reviews caval filters and the current indications for using mechanical IVC filters, including retrievable versus permanent filters, focusing on their use in treating venous thromboembolism in cancer patients. (JNCCN 2006;4:881–888)

Current Treatment of Venous Thromboembolic Disease
Venous thromboembolic disease (VTE), which includes deep venous thrombosis (DVT) and pulmonary embolism (PE), is a common problem in hospitalized patients. Reported incidence of VTE is 100 per 100,000 people per year, or approximately 355,000 diagnoses per year. Two thirds of these occurrences are DVT and the remainder are PE. Overall, VTE causes as many as 240,000 deaths per year.1,2 Some patient populations, notably those with cancer, are at high risk for VTE and are disproportionately affected. Treatment of VTE has evolved into 2 distinct entities: pharmacologic anticoagulation and inferior vena cava (IVC) interruption.

Historically, pharmacologic anticoagulation is the preferred treatment for DVT and venous thromboembolism. Oral warfarin has been the mainstay of treatment since the 1950s and is used together with intravenous heparin, which has been used in humans since the 1930s. Recently, the development of low molecular weight heparins with longer half-lives and subcutaneous administration has simplified treatment of DVT and PE. With fractionated heparins, patients no longer must remain in the hospital on intravenous heparin while warfarin is being titrated. Low molecular weight heparins may also have other advantages. Experts recently proposed that fractionated heparins may improve survival in cancer patients by decreasing tumor angiogenesis and interfering with tumor thrombus formation that potentiates tumor metastasis.3 Other newer agents, such as the direct thrombin inhibitor, ximelagatran/melagatran, and the specific factor Xa inhibitor, pentasaccharide, are promising for future use.

Current Indications for IVC Filters
Although pharmacologic treatment of VTE is evolving, a subset of patients remains in whom pharmacologic anticoagulation therapy fails, who develop complications related to anticoagulants, or who have an unacceptably high risk for complications from anticoagulants. Mechanical IVC filtration is indicated for these patients (Table 1).

Anticoagulation therapy failure is defined as the inability to titrate to the target international normalized ratio or partial thromboplastin time; recurrent or new PE despite adequate and therapeutic anticoagulation; or the propagation or new development of DVT despite therapeutic anticoagulation. Complications of anticoagulation are typically related to bleeding, including persistent or large gastrointestinal hemorrhages, intracranial hemorrhages, and hemoptysis. Development of significant bleeding complications typically precludes further anticoagulant use unless the underlying cause can be adequately treated.

Key Words
Deep venous thrombosis, pulmonary embolus, inferior vena cava filter
Generally, patients believed to have unacceptably high risks for bleeding complications and, are therefore poor candidates for anticoagulant therapy include those with 1) recent cerebrovascular accidents, 2) significant risk for falling (with consequent risk for intracranial hemorrhage from minor head trauma), 3) pre-existing gastrointestinal bleeding or lesions that are known to be at high risk for bleeding, 4) brain tumors or other high-risk intracranial lesions, and 5) thrombocytopenia. Patients with acute DVT who will undergo or have undergone major surgery often cannot be treated with anticoagulation. Thus, they are believed to be at risk for PE and considered reasonable candidates for IVC filters. Multisystem trauma patients with DVT and head injury, splenic lacerations, or liver lacerations are in this category.

Free-floating iliocaval thrombi prompt an occasional request for filter placement. Several authors evaluated this issue, with conflicting results. One report evaluated 5238 consecutive venous duplex studies to identify 73 patients with 82 free-floating thrombi. Of these thrombi, 13% were associated with clinically significant pulmonary emboli. The authors concluded that most do not embolize, but instead adhere to the vein wall. Additionally, a prospective study evaluating relative risks of embolism (PE) among 57 patients with free-floating thrombi and 28 with occlusive thrombi found no higher risk for PE in patients with a free-floating thrombus compared with those with a nonocclusive thrombus. Conversely, Radomski et al. reported pulmonary emboli in 27% of patients with free-floating iliocaval thrombi, despite adequate anticoagulation. Although free-floating thrombi are currently an accepted indication for filter placement, this is still debated and a subject for further investigation.

A relatively new trend in filter use is the placement of prophylactic filters. These are typically placed in patients who are at high risk for VTE but have no existing diagnosis or symptoms of DVT or PE, and in those who are at risk for VTE who cannot safely undergo anticoagulation for DVT prophylaxis with low-dose heparin. Trauma is a common indication for prophylactic IVC filter placement, especially in high-risk patients with pelvic or long bone fractures who will undergo surgical fixation. This indication is a primary force driving the development of retrievable IVC filters. Rutherford recently examined this trend, concluding that medical evidence is insufficient to support the broad use of prophylactic filters and that filter use for this purpose needs further objective study (Table 1).

### Currently Available IVC Filters

The first widely successful percutaneously introduced IVC filter, the Kimray-Greenfield filter, became available in 1973. This filter used a 30 French introducer large enough to require surgical exposure of the femoral vein. Subsequent refinements have resulted in the 14-French stainless steel and titanium Greenfield filters (Boston Scientific, Natick, MA). The over-the-wire stainless steel Greenfield filter is currently the benchmark to which all filters are compared and has more than 20 years of patient follow-up data supporting its use.

Numerous other permanent IVC filters have been developed. Most parallel the conical design of the Greenfield filter, whereas others more radically depart from this prototype. These include the Gianturco-Roehm Bird’s Nest filter (Cook, Bloomington, IN), which is 1 of 2 filters indicated for caval diameters greater than 28 mm; the Bard filters (i.e., Simon Nitinol filter, discontinued Recovery Nitinol filter, and the G2 filter; Bard, Tempe, AZ) with dual filtration levels; the B. Braun Vena Tech LGM and LP filters (B. Braun, Bethlehem, PA), which have a conical design similar to the Greenfield filter with added stabilizing struts (the Vena Tech LP is the second filter indicated for caval diameters greater than 28 mm); and the
Several filters with retrieval indications were recently introduced, known as either retrievable filters or optional retrievable filters, which allow temporary placement and retrieval or may remain permanently.

Retrievable Filters

The Günther Tulip vena cava MREye filter set (Cook) has an apical cone design similar to the Greenfield filter, with a small hook at the top to allow snaring for retrieval. The filter comes in femoral and jugular insertion kits with an 8 French introducer sheath. The filter can be retrieved through the jugular route only using a 12 French retrieval system. The OptEase filter (Cordis Corporation) is a dual cone (symmetrical) design nearly identical to the TRAPEASE and can be inserted from jugular or femoral routes with the same 6 French introducer sheath (by reorienting the filter). This filter is retrieved only through the femoral vein by snaring a small hook at the caudal end of the filter. The Günther Tulip and the OptEase filters are the only filters currently approved by the U.S. Food and Drug Administration (FDA) as retrievable devices. A third retrievable filter, the Recovery Nitinol (Bard), is no longer marketed. The Recovery was placed through femoral or jugular routes, and was retrievable through a jugular approach using a unique cone capturing device. Although the Bard G2 filter is currently available as a permanent filter, it is being evaluated by the FDA for retrieval use.

Retrievable filters have a limited recovery time before they become substantially incorporated into the caval wall and cannot be safely retrieved. All retrievable filters currently available are also approved by the FDA for permanent placement indications and may be left in place if the need for caval interruption becomes life-long or other factors arise that prevent either retrieval or resumption of anticoagulation. Unfortunately, studies of retrieval rates have found that, at best, only approximately 50% of retrievable filters are actually removed when contraindications to anticoagulation resolve.10

Permanent Versus Retrievable Filters

Retrievable filters seem to be attractive options for patients with a definable risk period for VTE and a
limited contraindication to anticoagulation. The use of retrievable filters depends on several assumptions (Table 2).

Retrievable filters have other perceived advantages, including some of the smallest delivery systems available, which theoretically may reduce insertion-site thrombosis. The PREPIC (Prévention du Risque d’Embolie Pulmonaire par Interruption Cave) study\(^ {11,12}\) concluded that retrieving filters when the risk for DVT or inability to anticoagulate resolves would provide protection from PE during the vulnerable time while theoretically eliminating the late risk for DVT. Several factors regarding the use of retrievable filters are unknown. For example, whether the risk for DVT as defined by the PREPIC study justifies the cost of retrieving these filters and the risk to patients is unclear. Unfortunately, all of the available retrievable filters lack long-term efficacy and safety data comparable to those of the Greenfield filter or even newer permanent filters. Retrieval windows are continually being revised upwards, and newer technology, such as paclitaxel coating, may further lengthen them. Retrieval times were initially within days to a few weeks, whereas now they are reported several months and, in some cases, more than 1 year after placement.\(^ {13}\)

IVC Filter Placement Procedure

IVC filters may be placed through several routes. All commonly used filters come in jugular or femoral kits, or in a single kit that can be used for either route. Some filters allow greater flexibility in placement, such as the Simon Nitinol, which can be placed from the antecubital vein approach if necessary, with a small-diameter, long delivery system (7 French, 103 cm). The authors have placed a Simon Nitinol filter through an upper-extremity peripherally inserted central catheter (PICC) line site in a patient with extensive body surface burns (replacing a new PICC line after the filter was deployed) and a Günther Tulip filter through the great saphenous vein, using intravascular ultrasound (IVUS) guidance in a morbidly obese patient in the intensive care unit (ICU). Probably only a few patients truly do not have access suitable for filter placement.

After obtaining venous access, a marker flush catheter is placed in the IVC and a contrast or CO\(_2\) (in the event of renal failure) venacavogram is performed. Positioning the catheter in the left common iliac vein increases the likelihood of identifying a duplicated IVC. The venacavogram is evaluated for the presence of intraluminal thrombus; vascular variants such as IVC duplication or a circumaortic left renal vein; and the location of both renal veins (Figure 2). Identifying vascular variants is of vital importance, because a duplicated IVC or circumaortic left renal vein can provide an alternative route for thromboemboli to bypass the filter and cause PE. If the IVC is free of thrombus, the vena cava diameter is determined and the filter is positioned in the infrarenal

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<th>Table 2 Assumptions Guiding Use of Retrievable Filters</th>
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<td>• Equivalent function of retrievable filters and permanent counterparts</td>
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<td>• Short, defined period of susceptibility to thromboembolism</td>
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<td>• Low likelihood of recurrent pulmonary embolism after retrieval</td>
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<td>• Safety of retrieval procedure</td>
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Figure 2 The left panel depicts a normal venogram of the inferior vena cava (IVC). Note the presence of both the left and right iliac veins, ruling out a duplicated vena cava. Opacification of the right renal vein reveals its location, whereas the level of the left renal vein can be identified by the "wash out" of contrast within the IVC by unopacified blood from the left renal vein. The right panel illustrates proper placement of a Greenfield IVC filter within the IVC.
Source: Images courtesy of Kyung J. Cho, MD.
reviewed numerous case series. If any circumstance prevents the use of fluoroscopy, alternative imaging methods for guiding placement include IVUS and transabdominal ultrasound in carefully selected patients. The use of IVUS or transabdominal ultrasound for IVC filter placement allows filters to be deployed at the bedside, which is an advantage in the ICU setting for patients who may not be stable enough to travel to the fluoroscopy suite.

When a vascular variant or IVC thrombus is identified, changes in filter position are mandated. For a duplicated IVC, options include placing a filter in each IVC or simply placing a suprarenal filter (the left IVC typically draining to the left renal vein). For a circumaortic left renal vein, the IVC filter is positioned below the lowest renal vein inflow or, if the infrarenal cava is not long enough, the filter is placed suprarenally. Finally, if caval thrombus is identified, the filter is placed above the thrombus, suprarenally if necessary. Care must be taken to ensure that the filter legs do not land in the renal vein ostia because this can cause filter instability. At the completion of filter placement, venous access is removed. Typically, little bleeding occurs with hemostasis by manual pressure for a few minutes, even with 15 French delivery systems.

Caval Filtration Efficacy, Morbidity, and Mortality

In 1992, Becker et al. reviewed numerous case series on the 7 filters available or in testing at that time (Original Greenfield, Titanium Greenfield, Simon Nitinol, Bird’s Nest, VenaTech LGM, Amplatz, and Günther), evaluating safety, indications, and effectiveness. The combined individual series evaluated 2557 patients, of whom 64% received Greenfield filters. In this group, 8 deaths were reported from recurrent PE after filter placement, and 4 deaths were related to filter complications. The authors concluded that, when possible, anticoagulation should be continued or reinstituted after filter placement.

The PREPIC study by Decousus et al., which was the only prospective randomized trial of filter efficacy, evaluated the effectiveness of filters for preventing recurrent PE. The study used concomitant anticoagulation with either unfractionated heparin or enoxaparin; no group received filters without undergoing anticoagulation, and no control was untreated. This study randomized 200 patients per group into those who were treated with a filter and those who were not, and then randomized them again into groups receiving unfractionated heparin or enoxaparin. Four filters were used, including the VenaTech LGM, Titanium Greenfield, Cardial (Bard, Saint-Etienne, France), and Bird’s Nest, with the VenaTech LGM most commonly used (56%).

Patients have now been followed-up for 8 years, with findings first published at 2 years. Initially, patients treated with a filter experienced fewer recurrent pulmonary emboli, with relatively no instances of major filter-related complications. No difference in mortality was noted between the filter and no filter groups, either immediately or at 2 years. The study also found that at 2 years, filter-related morbidity (recurrent DVT, filter site thrombosis) increased significantly (20.8% in the filter group vs. 11.6% in the no filter group). Findings at 8 years again showed early protection against pulmonary emboli, but no change in mortality. Recurrent DVT remained higher in patients treated with a filter, probably because of insertion-site thrombosis; however, this did not result in a significantly greater incidence of post-thrombotic syndrome.

Previous evaluations of filter-related morbidity and mortality have reported widely varied incidence. Several authors analyzed the potential complications related to IVC filter placement, identifying events immediately related to placement and later complications. Short-term complications include standard percutaneous risks for infection and bleeding, and procedural mishaps, such as pneumothorax (for jugular placement), arterial injury, and artery–vein fistula formation. Also included in this category is filter misplacement or maldeployment (tilting greater than 14°, found to reduce efficacy of filtration) and failure to identify collateral pathways of thromboembolus migration (circumaortic renal vein, duplicated IVC, upper-extremity source). Later complications include filter migration, caval penetration, recurrent pulmonary emboli, caval occlusion, and guidewire entanglement during subsequent venous access placement. Cava perforation from retention hooks is a common event with all filters, although it is rarely clinically significant and is the subject of isolated case reports.

Recurrent pulmonary emboli and caval occlusion are the most significant post-placement complications
of IVC filters. However, in studies reporting recurrent PE after filter placement, some of those events may have been caused by alternative embolic pathways and not necessarily a failure of the filter. One study of 318 patients treated with IVC filters reported a recurrent PE rate of only 3.1%.\textsuperscript{17} Athanasoulias et al.\textsuperscript{18} reported on a 26-year experience with filters placed in 1731 patients, observing a 5.6% rate of recurrent PE. This study also reported a caval thrombosis rate of 2.7%.

Greenfield and Proctor\textsuperscript{19} examined prospective data on 2109 patients, identifying 465 with long-term follow-up (mean, 9 years) from the Michigan filter registry. In this group, the rate of recurrent DVT was found to be 12% of 241 patients treated with anticoagulation in addition to filter, and 15% in 224 patients treated only with filter (Table 3).

**IVC Filters in Patients with Malignancy**

Malignancy is known to carry a significantly increased risk for venous thromboembolism. Trousseau\textsuperscript{20} first noted this association in the mid-19th century. Although poorly understood for decades, several contributing factors have been identified recently, including procoagulant factors produced by tumor cells, stimulation of normal coagulant and thrombotic factors in the blood by tumor cells, inflammatory mediators, and even chemotherapy.\textsuperscript{21} The reported incidence of PE in the literature is somewhere between 7% and 50% in patients with malignancy.\textsuperscript{22} Two studies estimated that the risks for PE in cancer patients were approximately 3.6-fold higher than in those without malignancy.\textsuperscript{23,24} The patients at increased risk for VTE also appear to be at increased risk for bleeding while undergoing anticoagulation therapy.\textsuperscript{25,26}

One of the large studies mentioned earlier\textsuperscript{27} evaluated the use of anticoagulation therapy in patients with and without cancer. Not surprisingly, the recurrence of thromboembolism in patients with cancer was significantly greater than in those without cancer. At 12 months, 20.7% of patients with cancer had experienced recurrent thromboembolism compared with 6.8% of those without. The same study also found a much higher rate of major bleeding complications related to anticoagulation in patients with cancer. At 12 months, the incidence of major bleeding in patients with cancer was 12.4% compared with 4.9% in patients without cancer. Based on these findings, it is reasonable to state that cancer patients have a high risk for thromboembolic disease and a high risk for significant complications if the standard paradigm of anticoagulation is used.

Debate about the use of IVC filters in malignant disease has persisted since the 1990s. Despite frequent use in this setting and continued attempts to clarify their role, their proper use in malignancy remains controversial. A retrospective study in 2002 questioned the clinical benefit of vena cava filter placement in patients with malignant disease.\textsuperscript{28} In this study, 116 patients with typical indications for filter placement and a wide array of primary tumors (25 gastrointestinal, 24 lung, 14 breast, 14 gynecologic, 12 prostate, 8 hematologic, 4 genitourinary, and 15 other) underwent Greenfield filter placement over 8 years (1993–2000). Most patients had stage IV disease. Procedural complications were negligible, and late complications included 2 patients with clinically apparent recurrent PE and 2 patients with progressive DVT after IVC filter placement. Survival rates were 68.8% at 30 days, 49.4% at 3 months, and 26.8% at 1 year. Of 91 patients with stage IV disease, 42 had died at 6 weeks and only 13 were alive at 1 year. Jarrett et al.\textsuperscript{27} suggested that IVC filter placement may not clinically benefit patients with cancer and may not be cost-effective given overall survival rates.

Another recent retrospective study that examined the benefit of IVC filters for cancer patients\textsuperscript{22} clearly showed the association between newly diagnosed PE and the presence of metastasis. This study included 99 patients, 55% with PE as the presenting symptom of new metastatic disease. In 12% of patients,
the diagnosis of PE predated malignancy. Acute PE was present in 52% of patients at cancer diagnosis, and 34% of PE events were associated with new metastasis. These patients had a 40% rate of recurrent PE, with the presence of new metastasis, history of PE, and multiple neutropenic episodes identified as risk factors for recurrent PE. Mean survival was 30 months and was significantly worse in patients with PE at cancer diagnosis and those who could not tolerate anticoagulant therapy in conjunction with IVC filter placement. The study suggests that patients with newly diagnosed metastatic disease, a history of PE, or multiple episodes of neutropenia may benefit from filter placement, assuming their quality of life and life expectancy are reasonable.

Regarding expense and cost-effectiveness of IVC filters in cancer patients, Marcy et al. reviewed data from 1994 to 2000 for 30 patients from one hospital. Six of the 30 patients died before discharge, and 2 died from renal vein thrombosis after suprarenal IVC filter placement. Even allowing for these deaths, 76%, 56%, and 40% were alive at 1, 3, and 6 months, respectively, with an improved quality of life in at least 53% of the patients. The authors concluded that the low complication rate and low cost (relative to the mean cost of hospitalization for PE, 2%) favor IVC filter placement if medically indicated.

This complex issue has no simple answer. Undoubtedly, a subset of cancer patients, even some with metastatic disease, will benefit from IVC filter placement. However, large groups who have advanced disease and short life expectancy are unlikely to derive any clinical benefit from filter placement. The authors contend that patients with cancer who have standard indications for an IVC filter should not be denied the procedure on a purely fiscal basis.

**Recommended Use of IVC Filters in Patients with Malignancy**

The best strategy for treating thromboembolic disease in cancer patients depends on the severity of underlying disease and life expectancy. If possible, patients should undergo anticoagulation. In patients with advanced disease, poor life expectancy, and significant contraindications to anticoagulation, nontreatment is a reasonable course and has been proposed by other authors. Patients with VTE and right heart failure, those with pulmonary hypertension, or others unlikely to tolerate PE may undergo prophylactic filter placement in addition to anticoagulation.

Nonterminal patients with contraindications to anticoagulation would benefit most from filter placement. VTE may be clinically detectable in as many as 15% of cancer patients; recurrent thromboembolism is also twice (or more) as likely to occur in cancer patients. A subset of patients with a limited period of susceptibility to DVT or PE (e.g., during the perioperative period) or with a limited period in which they cannot undergo anticoagulation (i.e., during the perioperative period or while undergoing chemotherapy) may benefit from optional filter placement with subsequent retrieval, assuming that treatment of their malignancy has a reasonable likelihood of success. This latter category may become more prevalent in the future, as treatment for malignancies improves. For patients with suspected or known incurable disease, the best plan currently seems to be a permanent filter when caval interruption is indicated.

**Conclusions**

The frequency of and indications for caval filter placement are increasing, with concurrent increases in the number and types of IVC filters. Sound evidence indicates that IVC filters reduce the risk for recurrent PE. Published reports regarding morbidity related to IVC filters (e.g., recurrent DVT, extension of DVT, iliocaval thrombosis) conflict, although the overall complication rates associated with IVC filters are considered acceptable, especially considering the morbidity and mortality of historical surgical methods for preventing PE included up to 50% incidence of lower extremity edema, almost 8% incidence of recurrent PE, and 15% hospital mortality. IVC filters are useful for treating VTE in patients with contraindications to or complications associated with anticoagulation. Recent studies suggest that IVC filters may also benefit patients with cancer and markedly higher risk for VTE (assuming sufficient life expectancy). Retrieval filters are an excellent option for patients, with a short, definable period during which anticoagulation is contraindicated. Retrieving the filter when the patient can safely undergo anticoagulation would theoretically reduce the major shortcoming of permanent filters.
References