



**TITLE:** SAFETY AND EFFECTIVENESS OF INFERIOR VENA CAVA  
FILTERS USED TO PROTECT AGAINST PULMONARY EMBOLUS

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## **SAFETY AND EFFECTIVENESS OF INFERIOR VENA CAVA FILTERS USED TO PROTECT AGAINST PULMONARY EMBOLUS**

*A Technology Assessment*

### **INTRODUCTION**

The California Technology Assessment Forum (CTAF) is requested to review the scientific evidence for the safety and efficacy of the use of inferior vena cava (IVC) filters for the prevention of pulmonary embolus (PE). This review was prompted by the Food and Drug Administration (FDA) warning published in August, 2010. Since 2005, the FDA has received a fair number of device adverse reports, some of which led to adverse clinical outcomes in patients. Initially all filters were placed permanently, but more recently filters have been developed that can be placed when needed and then removed once a patient's risk for PE has decreased. Due to concern that retrievable IVC filters which are intended for short term placement, are not always removed once a patient's risk for PE subsides. The FDA recommended that implanting physicians and clinicians responsible for the ongoing care of patients with retrievable IVC filters consider removing the filter as soon as protection from PE is no longer needed.

### **BACKGROUND**

Pulmonary embolism (PE) is a severe and often fatal condition, and occurs when a lower extremity thrombus embolizes to the lungs. Untreated PE can lead to a mortality rate of up to 30%<sup>1,2</sup>. The severity can be variable - some patients can be asymptomatic, whereas others with large PEs can have right heart failure, shock and death. When death occurs, it is usually because of recurrent embolism and so treatment options focus on the prevention of recurrent embolism. The standard treatment is anticoagulation, but in situations where anti-coagulation is contraindicated, interruption of the inferior vena cava is considered.

Initial attempts to interrupt the vena cava were surgical and were initially described by Trousseau in 1868<sup>3</sup>. Several surgical approaches were used up until the 1960s. In 1967, the Mobin-Uddin filter was introduced as the first filter used for transvenous interruption of the vena cava<sup>4</sup>. This filter was associated with a significant incidence of IVC occlusion. Subsequently a new device, the Kimray-Greenfield filter, became the preferred device for IVC interruption.

## Treatment of pulmonary embolism: Role of IVC filters

The treatment of choice for proximal venous thrombosis is anticoagulation. In situations where anticoagulation is absolutely contraindicated or when anticoagulation has failed in the face of an acute proximal venous thrombosis, placement of an IVC filter has been recommended<sup>5</sup>. There are several other situations where there is controversy about whether or not an IVC filter should be considered. These include situations where a pulmonary embolism has already occurred and another one would be poorly tolerated or situations where bleeding risk is high. Inferior vena cava filters are often used for prophylaxis in patients deemed to be a high risk for pulmonary embolism (e.g. bariatric surgery in the super-obese), although whether or not this affects clinical outcomes has not been clear.

More recently, retrievable filters have been introduced. “Retrievable” filters are filters that can be placed in patients at high risk for PE and then removed later when the risk has decreased. There are different types of retrievable filters, G2 and G2X, manufactured by Bard, OptEase, manufactured by Cordis and Gunther tulip and Cook Celect, manufactured by Cook. Although the devices are designed to be retrievable, retrieval can be difficult and is not always successful<sup>6-8</sup>. In a recent study of 240 patients who underwent placement of IVC filters, only 73 (30.4%) had documented plans for filter removal and of 62 who underwent attempted filter retrieval, 25.8% of filters could not be successfully removed [Mission, JGIM 2010: (25 (4): 321-5]. The recommended duration of use varies for each manufacturer, but the longer a filter is in place, the more difficult it is to remove. Filters that are not removed stay in place and may be associated with potential complications.

Several non-retrievable filters are also commonly used. The key areas of differences among the filters are in the diameter of the introducer system and also in the maximal size of the IVC that can be accommodated by the filter.

With the increasing ease of insertion of filters and the possibility of removal, IVC filters are increasingly being placed for prophylactic reasons in patients deemed at high risk for developing a venous thrombus. Sometimes IVC filter placement is used for prophylaxis instead of anticoagulation or mechanical methods (e.g. sequential compression devices), in patients with major trauma and in those having bariatric, neurosurgical or spinal surgery. Whether or not IVC filter placement improves clinical outcomes in this setting is an important question.

### *Placement*

The filters are usually placed percutaneously using a femoral or jugular approach. They are usually positioned inferior to the renal veins, although they are sometimes placed suprarenally. The filters are usually placed with fluoroscopic guidance, which requires patients to go to interventional radiology and receive intravenous contrast. Ultrasound guidance at the bedside has also been used without a significant increase in complication rates, although training is necessary in ultrasound guided techniques<sup>9,10</sup>.

In August of 2010, the FDA reported that since 2005, they had received reports of 921 IVC filter adverse events. The complications included device migration (n=328), embolizations/device component detachment (n=146), IVC perforation (n=70) and filter fracture (n=56). Some of these adverse events were associated with adverse clinical outcomes. Some of the adverse events may also be related to retrievable filters not being removed and staying in past the time when the risk of pulmonary embolism has subsided.

The FDA is currently reviewing the literature to evaluate the risk/benefit profile of IVC filters. In the interim, they recommend that filters be removed when the risk for PE has subsided<sup>11</sup>.

### *IVC filters and anti-coagulation*

It is recommended that anticoagulation be resumed as soon as possible after filter insertion because the filter alone is not an effective treatment of venous thromboembolism (VTE)<sup>5</sup>. However, given that many patients in whom filters are inserted have contraindications to anticoagulation, achieving this goal may be a challenge.

### *Retrievable vs. non-retrievable filters*

Initial filters, that were developed, were permanently placed in the IVC. More recently filters have been developed that are potentially retrievable. Although the filters are designed to be removable, removal can be technically challenging<sup>7,8</sup>. Manufacturers have different recommendations about how long a filter should stay in, but in general the longer it is left in place, the more difficult it is to retrieve.

### *Complications*

Filter placement has been associated with many complications. Some of the short term complications are those seen with any percutaneous procedure and include contrast agent reaction, arrhythmia, air embolization, pneumothorax or hemothorax, extravascular penetration of the guide wire insertion site bleeding, infection at the insertion site, contrast agent induced renal dysfunction, arteriovenous (AV) fistula, insertion site thrombosis<sup>12</sup>. Others are directly associated with the filter-, incomplete opening, tilting and angulation, misplacement, entrapment of the guide wire, embolization of the filter, PE and death. In addition to these short term complications, long term complications include an increased risk of subsequent deep venous thrombosis (DVT), filter migration, filter embolization, filter fracture, IVC occlusion, vena cava stenosis, PE and guide wire entrapment<sup>12</sup>.

#### **TA Criterion 1: The technology must have final approval from the appropriate government regulatory bodies**

Several retrievable IVC filters have been approved by the FDA through the 510(k) process. The Cook Günther Tulip® Vena Cava Filter and the Cook® Celec® Vena Cava Filter both have FDA 510(k) clearance.

The Bard Recovery Filter System (Bard Peripheral Vascular, a division on C.R. Bard, Inc; Tempe, AZ) received FDA 510 K clearance.

The Cordis OPTease® Vena Cava Filter and OPTease® Retrieval Catheter (Cordis Corporation, a J&J Company; Bridgewater, NJ) have received FDA 510(k) clearance. These are a few of the available inferior vena cava filters on the market.

#### **TA Criterion 1 is met**

#### **TA Criterion 2: The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes.**

The Medline database, Cochrane clinical trials database, Cochrane reviews database and Database of Abstracts of Reviews of Effects (DARE) were searched using the key words inferior vena cava filter or tempofilter or vena tech or bard G2 or bard recovery or Greenfield or Birds nest or Cook and Celec or

Gunther tulip or OptEase or TrapEase or Movin-Uddin or Rex medical option or Simon and Nitinol and also with the terms safety or efficacy or adverse or outcome. The search was performed for the period from 1966 to December, 2010. The bibliographies of systematic reviews and key articles were manually searched for additional references. The abstracts of citations were reviewed for relevance, and all potentially relevant articles were reviewed in full.

Inclusion Criteria were that the study had to report outcomes of IVC filter placement, had to report clinical outcomes, had to include humans and had to be published in English.

Studies were excluded if they did not report clinical outcomes. Articles that focused on procedural methods or instrumentation were excluded.

A total of 82 potentially relevant articles were identified. 36 were excluded for not addressing the research question. A total of 46 abstracts were evaluated, and 17 were excluded. Reasons for exclusion included not reporting clinical outcomes of IVC filter placement, focusing on methods or instrumentation, or review articles. The remaining studies (n=29) were included. Of these, 18 were retrospective studies<sup>13-30</sup>, and 11 were prospective studies<sup>8,31-40</sup>. Among the prospective studies, most (n=8) were observational<sup>8,31-34,36,37,41</sup>; two were trials that compared an IVC filter to something else<sup>38,39</sup> and one compared two different types of IVC filters<sup>40</sup>.

Clinical outcomes reported by the identified studies included rates of recurrent VTE, recurrent DVT, mortality and filter related complications.

#### **TA Criterion 2 is met**

#### **TA Criterion 3: The technology must improve net health outcomes**

Several prospective and retrospective non-comparative studies have reported on the outcomes of IVC filter placement. Indications for filter placement have varied and have included absolute contraindication to anti-coagulation, anti-coagulation failure and prophylactic use.

At least 18 retrospective studies have reported on the outcomes of IVC filter placement (Table 1). Study size has varied from 13 to 751. Some studies have included only one type of filter and others have included

more than one type of filter. Importantly, in the majority of studies, patients have had many different reasons for filter insertion. Many included patients who were having filters inserted because of either absolute contraindication to anticoagulation or an anticoagulation failure, but also included patients who had filters inserted for other reasons such as prophylaxis or post-trauma. Only five of the studies have included relatively uniform patient populations (e.g. two studies of trauma patients<sup>23,25</sup>, one of super obese patients undergoing bariatric surgery<sup>19</sup>, neurosurgical patients<sup>20</sup>, and patient sepsis<sup>27</sup>). None of the studies reported on outcomes for particular categories of patients.

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**Table 1:** Retrospective studies of IVC filters and safety and efficacy outcomes

Study	N	Type of study	Treatment	Reasons for insertion	Outcomes Evaluated
Nicholson, 2010 <sup>28</sup>	80	Retrospective single center cross sectional	Bard Retrievable Vena Cava Filter	22% trauma 22% DVT/PE 6% Warfarin intolerance 26% Surgery prophylaxis 3% Malignant neoplasm prophylaxis 23% Unknown	Strut fracture with embolization
Ray, 2006 <sup>13</sup>	197	Retrospective multi-center	Gunther Tulip Filter (73%) Recover filter (28%)	52% prophylaxis 34% anticoagulation contraindication 6% anticoagulation complication 6% poor cardiopulmonary reserve 2% anticoagulation failure	Safety and efficacy of placement and retrieval Retrieval rates Reasons for failure of retrieval
Millward, 1991 <sup>14</sup>	64	Retrospective multi-center	LG-medical Vena Tech Vena Cava filter	36% PE with contraindication to anticoagulation 56% DVT with contraindication to anticoagulation 8% Recurrent PE on anticoagulation	Safety and efficacy of filter placement
Keller, 2007 <sup>15</sup>	172	Retrospective	Gunther tulip or OptEase filter	65% prophylactic multiple trauma 2% prophylactic neurosurgery 9% proximal DVT or PE and trauma 27% proven DVT or PE and neurosurgery or other singular indications	Safety and efficacy of two filters
Hammond, 2009 <sup>16</sup>	507	Retrospective audit of three centers	74% retrievable filters	57% for “absolute indications” (thromboembolism with a contraindication to anticoagulation or recurrent thromboembolism despite adequate anticoagulation) 65 for perioperative or post-traumatic prophylaxis 37% for relative indications	Trends in IVC filter use Complications Rates of removal



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				(proximal thrombus, massive PE and multiple PE with limited cardiopulmonary reserve)	
Yavuz, 2008 <sup>17</sup>	67	Retrospective Single center	Insertion and retrieval of 72 filters in 67 patients	31% Contraindication to anticoagulation with documented VTE 9% complication of anticoagulant therapy with documented VTE 55% prophylaxis without current VTE 3% prophylaxis with VTE in addition to anticoagulation 1% in association with pharmacomechanical thrombectomy for VTE	VTE after retrieval of IVC filter VTE after filter removal Placement of subsequent filter or death
Kim, 2008 <sup>18</sup>	702	Retrospective cohort	Optease Gunther Tulip Bard Recovery TrapEase Vena Tech Greenfield Birds nest	58% Contraindication to anticoagulation 17% primary prophylaxis 1% anticoagulation complication 12% anticoagulation failure 3% catheter directed thrombolysis	PE Complication rates
Piano, 2007 <sup>19</sup>	59	Retrospective	Retrievable VCF	Super obese patients undergoing bariatric surgery	Retrieval success Procedure related complications Pulmonary embolism
Ghanim, 2007 <sup>20</sup>	175	Retrospective cohort	Filters vs. anticoagulation alone	Neurosurgical patients	Mortality
Kalva, 2006 <sup>21</sup>	751	Retrospective cohort	Trap Ease Vena Cava Filter	70% PE and or DVT 30% no VTE	Safety and efficacy of TrapEASE vena cava filter
Greenfield, 2003 <sup>27</sup>	175	Review of VCF registry	Greenfield filters	Patient with sepsis	Adverse outcomes Survival Reasons for filter removal

Mohan, 1995 <sup>22</sup>	195	Retrospective Comparative efficacy and complications of VC filters	Greenfield Vena-Tech Birds Nest Simon Nitinol	31% contraindication to anticoagulation 23% complication of anticoagulation 13% failure of anticoagulation 16% prophylaxis 3% other	Comparison of efficacy and complication rates of different filters
Phelan, 2009 <sup>23</sup>	188  52% had follow-up)	Retrospective	Any permanent prophylactic vena cava filter	High risk trauma patients	Safety and efficacy of IVC filters
McKenzie, 2010 <sup>29</sup>	121	Retrospective single center	Retrievable IVC filters	Established VTE and contraindication to anticoagulation 39% High risk of VTE and need for surgery with high risk of VTE and bleeding 43% Anticoagulation failure 12% Massive PE 4% Multitrauma 2%	Safety and efficacy of IVC filters and Retrieval success
Neuerburg, 1997 <sup>24</sup>	83	Retrospective multi-center	Retrievable Tulip Vena Cava Filter	Anticoagulation failure 30% Contraindication to anticoagulation 10% Free floating thrombus 39% Prophylaxis 1a% Other 11%	Evaluate safety and efficacy of tulip Filter
Karmy-jones, 2007 <sup>25</sup>	446	Retrospective multi-center	Retrievable vena cava filters	Trauma patients (97.5% for prophylaxis)	Major complications Reasons for failure to retrieve
Schutzer, 2003 <sup>26</sup>	189	Retrospective single center	TrapEase IVC filter	Contraindication to anticoagulation (59%) VTE on anticoagulation 11% Free floating DVT 7%	Safety and efficacy

				Propagation of DVT 3% Prophylactic 3% Miscellaneous) 18%	
Lam, 2004 <sup>30</sup>	13	Retrospective single center	Gunther tulip or OptEase	Contraindication to anticoagulation (62%) Prophylaxis (38%)	Success of filter placement and retrieval Recurrent PE

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One important recent study evaluated the potential adverse effects of filter placement and focused on the prevalence of fracture and embolization of the Bard Recovery and the Bard G2 vena cava filters (VCF) Nicholson, 2010<sup>28</sup>. Eighty patients who had filters inserted between 2004 and 2009 had fluoroscopy to assess the filter's integrity. Patients who had fragment embolization underwent echocardiography and cardiac computed tomography. Of the 80 patients, 13 (16%) had at least one strut fracture. Among the 28 Bard Recovery filters, seven (25%) had a strut fracture with embolization. The strut embolized to the heart in five out of seven cases. Three patients had life threatening ventricular arrhythmias or tamponade. There were 52 Bard G2 filters. Six of them (12%) fractured. Two of the six had embolization to end organs although they were asymptomatic. The results of this study show that there are potentially major complications associated with vena cava filters. Although actual population prevalence cannot be estimated from a retrospective study, the relatively high incidence of complications, some of them life threatening, is concerning.

Eight prospective observational studies have evaluated the safety and efficacy of IVC filters. Study size has ranged from 30-220 patients (Table 2) Length of follow up has ranged from six to 35 months. In general, most studies have included patients with varying indications for filter placement, including contraindication to anticoagulation, recurrent VTE on anticoagulation and other prophylactic reasons. More recent studies have primarily focused on retrievable filters. In the largest of these studies<sup>36</sup>, 220 patients were followed for a mean of 338 days. As in most of the prospective studies, participants had a variety of indications for filter placement. Filter insertion was a success in the vast majority of patients (98.6%) but resulted in an immediate complication in 11.8%. Overall, 17% of patients had at least one thromboembolic event. Filter retrieval was attempted in 25% of patients and removal was successful at the first attempt in 92.7%. This study showed that filter insertion could be easily accomplished and easily removed but the extent to which it prevents PE remains unknown since there was no comparison group.

**Table 2:** Prospective studies of IVC filters and safety/efficacy outcomes

Study	N	Design	Inclusion Criteria	Average Length of follow-up	Outcomes Evaluated	Results	Comments
<b>OBSERVATIONAL STUDIES</b>							
Yazu, 2000 <sup>31</sup>	42	Prospective observational	Contraindication to anticoagulation, recurrent VTE on anticoagulation, other prophylactic purposes	35 months	Complications	5% developed symptomatic PE 5% developed asymptomatic PE PE is 16.7% of those who did not receive anticoagulation and 7.4% of those who received anticoagulation	Low rates of PE and filter captured thrombus in those on concurrent anticoagulation
Johnson, 2010 <sup>32</sup>	100	Prospective single arm clinical trial evaluating safety and effectiveness of retrievable option IVC filter	Pulmonary thromboembolism when anticoagulation is contraindicated, failure of anticoagulant therapy in thromboembolic disease (TED), complication of anticoagulation therapy for TED or indication for temporary filter (bariatric surgery or trauma)	180 days For those who had filter removed 30 days after filter removal	“Clinical success”- technical success without subsequent PE, significant filter migration or embolization, symptomatic cava thrombosis or other complications	8 cases of recurrent PE, two cases of filter migration, no filter embolization or fracture Clinical success in 88% of participants 39 subjects had attempted Retrieval	No comparison group



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						successful for 92% patients at a mean of 67 days 17 deaths and 18 DVT were judged not related to filter	
Imberti, 2005 <sup>8</sup>	30	Prospective observational multi-center of ALN retrievable IVC filter	VTE with a contraindication to anticoagulation, primary prophylaxis after major trauma or before surgery in patients with high thromboembolic risk	18.2 months	Efficacy and likelihood of filter removal	3 cases of trapped emboli in filter 1 case asymptomatic filter migration toward heart 2 DVT recurrences ALN removal attempted in 18 patients and successful in 78% Retrieval less successful more than 3 months after implantation Median implantation 123 days	Retrieval safe and efficacious after medium period of placement Retrieval more than three months after placement less successful
Ziegler, 2008 <sup>33</sup>	150	Post-marketing surveillance; multicenter prospective of OptEase IVC filter as permanent	PE with anticoagulation contraindicated; anticoagulation failure, emergency treatment after massive PE, chronic and or recurrent PE where anticoagulation failed or	Six months	Primary endpoints: filter migration and symptomatic thrombosis one month after implantation	At one month 0.9% filter migration and 0.9% filter thrombosis No new filter migration or	55 out of 150 did not complete full six month evaluation



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		filter	was contraindicated and patients at high risk for PE with relative or absolute contraindication to anticoagulation		Secondary endpoints: major adverse events, filter tilting	symptomatic thrombosis at 6 months	
Bovyn, 2006 <sup>34</sup>	103	Multicenter prospective study of patients receiving Tempofilter II	Complications of or contraindications to anticoagulation therapy, ineffectiveness of anticoagulation therapy or prophylactic (high risk surgery or free floating thrombus)	90 days	Rate of retrieval Filter related complications PE	Filter in place for a mean of 29.5 days All filters except one were removed One episode of filter migration followed by PE	Filter retrieval successful when filter in place for relatively short period
Ricco, 1995 <sup>41</sup>	222	Multicenter prospective	PE on anticoagulation PE with contraindication to anticoagulation PE and ileocaval thrombosis Ileocaval /femoral or popliteal thrombosis Thrombosis without embolism Cor pulmonale with lower extremity thrombosis	15 months	Local complications General complications	1.7% 30 day mortality 2.2% recurrent PE 3.6% filter migration Two recurrent PE Seven caval thromboses	
Mismetti, 2007 <sup>36</sup>	220	Single center prospective cohort of patients with retrievable VCF	Recurrent VTE despite anticoagulation, transient bleeding event, definite contraindication to anticoagulation or need to stop anticoagulation due to major surgery trauma or invasive procedure	18 months	Success of filter insertion Clinical events related to filter insertion Filter retrieval	Filter insertion 98.6% successful Complication of filter placement 11.8% Median duration of filter placement 166 days	Largest multicenter study of single type of retrievable filter

						At least one VTE 17% Removal successful at first attempt in 92.7% of patients	
Greenfield, 1991 <sup>37</sup>	186	Prospective multi-center study of modified hook- titanium Greenfield filter	Contraindication to anticoagulation Free floating thrombus, anticoagulation complication Anticoagulation failure Recurrent embolism with pulmonary hypertension Massive embolism requiring vasopressors	30 day	Safety and efficacy	97% filter placement success 22 deaths from PE 9.75 new lower extremity edema No filter occlusion	Study goal was to evaluate modified filter
<b>TRIALS</b>							
Fullen, 1973 J or Trauma 1973;13: 403-10) <sup>38</sup>	129	Single center trial Participants received permanent cava filter or no filter	Proximal femoral fracture	33 days	Mortality PE Filter insertion complications	No difference in mortality Fewer PE in filter group (RR 0.3; 95% C.I. 0.11,.0.82)	No information on long term complications
Decousus, 1998 <sup>39</sup> ; PREPIC, 2005 <sup>42</sup>	400	Randomized controlled trial (RCT) with 2 x 2 factorial design also comparing low molecular weight heparin	Acute DVT with or without PE and if physicians considered them to be at high risk for PE	2 year and 8 year	Recurrent VTE, death and major bleeding	At day 12, fewer PE in the filter group than in the no filter group (OR 0.22: 95% C.I. 0.05, 0.90) At two years more recurrent DVT in	



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		to unfractionated heparin				filter group (OR 1.87: 95% C.I. 1.10, 3.20) Similar results at one year follow up	
Usoh, 2010 <sup>40</sup>	156 (N=84 Greenfield and n=72 Trapease )	Prospective randomized comparative study comparing IVC Greenfield and TrapEase filters	Contraindication to anticoagulation, or failed anticoagulation, high risk trauma patient or high risk procedure with history of VTE	12 months	Access site thrombosis Filter thrombosis Symptomatic PE	Symptomatic IVC/IV thrombosis in 6.94% in the TrapEase group and none in the Greenfield group (P=0.19) No filter migration, access site thrombosis misplacement or IVC perforation Recurrent PE suspected in one of five patients with IVC/IV thrombosis 30 day and 12 month mortality was comparable between the two groups	349 eligible patients during the time period did not participate in the study. Higher rate of IVC/IV thrombosis in those who received TrapEase- effect was not related to anticoagulation

In summary, many retrospective and prospective observational studies have assessed the safety and efficacy of IVC filters. Pulmonary embolism was a common outcome in many studies, but is to be expected since included patients are those at high risk for PE. Filters could typically be placed successfully. Filter retrieval was more successful the shorter the time that the filter was in place. Filter complications were relatively common, although not all complications were associated with negative clinical outcomes. Since there was typically not a comparison group, it is not possible to estimate whether IVC filters are associated with net benefit.

**TA Criteria 3 is not met.**

**TA Criterion 4: The technology must be as beneficial as any established alternatives.**

Two randomized trials have compared the use of IVC filters to no IVC filters. One study done in 1973 was a study of 129 patients with proximal femoral fractures<sup>38</sup>. It was a single center trial where participants received a permanent vena cava filter or no filter and were followed for 33 days. The main outcomes were mortality, PE and complications of filter insertion. There was no difference in mortality and there were fewer PEs in the filter group [RR 0.3; 95% C.I. 0.11, 0.82]. Long term complications were not reported.

Only one RCT has compared the use of IVC filters to anticoagulation in patients at high risk for PE<sup>39</sup>. In this French study, which used a two by two factorial design, 400 patients were assigned to receive either a filter or no filter, and to receive low molecular weight heparin or unfractionated heparin. Outcomes were evaluated at day 12 and at two years and included recurrent VTE, death and major bleeding events. Included patients were those who had an acute DVT confirmed by ultrasound with or without a PE and whose physicians considered them to be at high risk for PE. Patients who had a contraindication to anticoagulation were excluded. Four different types of permanent IVC filters were used (titanium Greenfield, Vena Tech LGM, Cardial and Bird's Nest). All participants received warfarin for at least three months to a target INR (International Normalized Ratio) goal of 2.0-3.0. Those who could not receive warfarin received subcutaneous heparin for at least three months.

The primary outcome was PE (symptomatic or asymptomatic) in the first 12 days. Secondary outcomes included symptomatic PE, recurrent DVT, death, major filter complications and major bleeding during two year follow-up.

At 12 day follow-up, 1.1% of patients in the filter group and 4.8% of patients in the no-filter group had a PE (odds ratio 0.22; 95% C.I. 0.05, 0.90). At two year follow-up, more patients in the filter group had recurrent DVTs than those with no filter (20.8% vs. 11.6%; OR 1.87; 95% C.I. 1.10-3.20). There was no significant difference in mortality or other outcomes. In summary, in these high risk patients, IVC filters led to an early benefit in reduction of PE, but over the longer term were associated with an increased risk of DVT. Overall there was no reduction in mortality. Results were similar. At eight year follow-up- PE was reduced, but DVT risk was increased and there was still no impact on mortality<sup>42</sup>. Thus, overall, although IVC filters reduce the risk of recurrent PE, the incidence of subsequent DVT is increased and there is no impact on mortality. There is no evidence of any clear benefit of IVC filters in the treatment of PE among patients who are receiving anticoagulants. No studies have compared the efficacy of anticoagulation with IVC filter placement in the absence of anticoagulation.

A third clinical trial compared two different types of IVC filters, but did not include a control group who did not receive filters<sup>40</sup>.

Since IVC filters are more commonly used in patients who have major or absolute contraindications to anticoagulation, evaluation of the role of IVC filters in patients who cannot be on anticoagulation is critical. To date no RCT has evaluated the role of IVC filter in this population. In this population, it is also important to define what the “established alternative” is.

There are several patient groups for whom IVC filters are commonly used but for whom clinical trials have not been conducted. These include trauma patients, neurosurgical patients before surgery and super-obese patients undergoing bariatric surgery. These patients are certainly at high risk for TED and often cannot receive anticoagulation. Although it is possible that the use of IVC filters leads to benefit in these patients, this has not been shown in clinical trials.

There are two ongoing clinical trials evaluating the role of IVC filters in prevention of PE. One is a RCT of anticoagulation and IVC filters in cancer patients with VTE. Cancer patients with a radiographically confirmed cardiovascular thrombosis (CVT) or PE will receive fondaparinux alone or with a filter and will be followed for death and event free survival. Secondary outcomes will include PE, major bleeding, thrombophlebitis, cellulites secondary to IVC filter, thrombosis of the IVC filter and quality of life. In the PREPIC 2 study, which is a randomized open label active control safety and efficacy study, retrievable IVC filter will be compared with no filter in patients with PE or DVT. The primary outcome at three months will be

a combined outcome including recurrent PE and fatal PE and death. Secondary outcomes will include recurrent PE, DVT and filter related complications.

In summary, only two clinical trials have assessed the efficacy of IVC filters compared with an established alternative. One is a small study of patients with hip fractures which only reports short term outcomes and has limited generalizability. In the main study comparing IVC filters with no filters although there was a short term decrease in PE, there was a longer term increase in DVT and no overall reduction in mortality. Among other patient populations such as trauma patients, neurosurgical patients and super-obese patients in whom IVC filters are frequently used for prophylaxis, no trials have assessed their use and it is not known whether this is of overall benefit in these populations.

**TA Criterion 4 is not met.**

**TA Criterion 5: The improvement must be attainable outside the investigational settings.**

Since the improvement has not yet been shown in the investigational setting, by definition it cannot be attainable outside the investigational setting.

**TA Criterion 5 is not met**

## **CONCLUSION**

Inferior vena cava filters have been widely used and it is surprising how few studies have evaluated their safety and efficacy. Inferior vena cava filters have been compared to no filters in only two studies, one of which only included patients with hip fractures and the other high risk patients. These studies showed reduced recurrent PE but an increased risk of DVT with IVC filters, and there was not associated reduction in mortality. Although IVC filters are commonly used for prophylaxis in high risk patients including trauma patients, neurosurgical patients, patients with malignancy and super-obese patients undergoing surgery, whether or not their use leads to a net benefit is not known.



## RECOMMENDATION

It is recommended that the use of IVC filters to protect against pulmonary embolism does not meet CTAF criteria 3, 4 or 5 for safety, effectiveness and improvement in health outcomes.

**February 16, 2011**

This is the first CTAF review of this topic.

*The California Technology Assessment Forum panel voted to accept the recommendation as written.*

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## RECOMMENDATIONS OF OTHERS

### **Blue Cross and Blue Shield Association (BCBSA)**

The BCBSA Technology Evaluation Center (TEC) has not conducted an assessment of this technology.

### **Centers for Medicare and Medicaid Services (CMS)**

A review of the CMS web site did not reveal any decisions specific to the use of IVC filters.

### **Society for Cardiovascular Angiography and Interventions (SCAI)**

The SCAI, Society for Vascular Medicine and the CA ACC provided a joint statement regarding this technology. They did not participate at the meeting.

### **Society for Vascular Surgery (SVS)**

The SVS has been invited to provide an opinion on this technology and to have a representative provide testimony at the meeting.

### **Society for Interventional Radiology (SIR)**

SIR provided an opinion regarding the use of this technology. A representative was present at the meeting to provide testimony and participate in the discussion.

### **California Chapter of the American College of Cardiology (CAACC)**

The CAACC provided a joint statement as noted above. A representative did not attend the meeting.

## ABBREVIATIONS USED IN THIS REVIEW

CTAF	California Technology Assessment Forum		
IVC	Inferior vena cava	PE	Pulmonary embolus
FDA	Food and Drug Administration	VTE	Venous Thromboembolism
AV	Arteriovenous	DVT	Deep vein thrombosis
DARE	Database of Abstracts of Reviews of Effects		
VCF	Vena cava filters		
CVT	Cardiovascular Thrombosis		
RCT	Randomized controlled trial		
TED	Thromboembolic Disease		

## REFERENCES

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