

# Vena Caval Filter Use in Patients With Sepsis

## Results in 175 Patients

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**Background:** Septic patients are at risk of thromboembolism. However, the Food and Drug Administration guidance for intravascular filters states that “filters should not be implanted in patients with risk of septic embolism.” The purpose of this study is to evaluate this restriction.

**Hypothesis:** There is no difference in outcomes following filter placement in patients with and without septicemia.

**Data Sources:** A registry of vena caval filter experiences containing information regarding filter placement and annual examinations of more than 2600 patients obtained during a 15-year period was reviewed. We conducted a MEDLINE search of publications reporting clinical sequelae of filter placement in septic patients.

**Data Extraction:** The registry was searched for patients with a diagnosis of sepsis at filter placement; survival rates, adverse events, and recurrent sepsis or thromboembolism were noted. The MEDLINE search joined results from 7 MeSH headings (vena cava filter,

sepsis, septic thromboembolism, vena caval filter contraindication, and filter adverse events) related to filters and sepsis.

**Data Synthesis:** One-hundred seventy-five patients (6.7%) met the criteria and received Greenfield filters. None of the adverse events were related to sepsis, and no filter was removed. Follow-up data were available for 56 patients, with a combined recurrent pulmonary embolism and caval occlusion rate of 1.7%. The 30-day mortality rate was 33%. We noted a significant difference in survival related to the use of anticoagulation therapy ( $P = .001$ ) and to age ( $P = .004$ ). The MEDLINE search did not identify any clinical reports of septic filters or the need to remove a filter because of sepsis.

**Conclusions:** Based on our review, the Greenfield filter is a safe method of prophylaxis for septic patients. Rescinding the restriction for use of vena caval filters in septic patients should be considered by regulatory bodies.

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**S**EPSIS IS a recognized risk factor for thromboembolism and frequently coexists in patients with venous thrombosis and a contraindication to anticoagulation therapy. This is especially true for patients with multiple injuries, surgical patients, and patients with malignancy. When these patients develop thromboembolism, a vena caval filter is the only available prophylaxis against potentially fatal pulmonary embolism (PE). However, the Food and Drug Administration guidance for intravascular filters states that manufacturers must list sepsis among the contraindications for use and include the following statement<sup>1(p12)</sup>: “Vena Cava filters should not be implanted in patients with risk of septic embolism.”

In the past, septic thromboembolism was routinely treated by inferior vena cava ligation, but the combined insult of

ligation and septicemia often resulted in death. In the early 1970s, following introduction of the first intravascular vena caval umbrella, Fullen et al<sup>2</sup> raised the question of potential complications associated with plastic and/or metallic implants in patients with septicemia. Later,

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Scott et al<sup>3</sup> described a patient who developed septicemia 2 years following placement and thrombosis of the Mobin-Uddin filter. However, in nearly 30 years of experience with the Greenfield filter (GF), we have not observed this complication. The purpose of this study was to document this experience and to determine whether the GF could be a source of ongoing sepsis or whether it has ever required removal from septic patients.

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### Characteristics of 175 Patients With Septicemia Receiving Intravascular Filters

Characteristic	Patients, %
Male sex	54
Age, mean (range), y	53 (14-89)
Diagnosis	
Recent surgery	31
Recent trauma	12
Venous disease	12
Malignancy	12
Sepsis	6
Other	27
Indication for filter placement	
Anticoagulant contraindication	45
Prophylaxis	29
Anticoagulant complication	21
Other	5
Diagnosed DVT	66
PE prior to filter placement	15
Percutaneous placement	87
Filter type	
Original stainless steel	20
Percutaneous stainless steel	34
Titanium	46
Filter position	
Infrarenal	84
Suprarenal	15
Superior vena cava	1
Retrieval	0
30-Day mortality	33
Follow-up visits	72*
Recurrent PE	1
New DVT	5
Caval occlusion	1
Stockings	29
Ulceration	5
Lower extremity edema	43
Insertion site patent	96

Abbreviations: DVT, deep vein thrombosis; PE, pulmonary embolism.

\*Percentage of those alive at 1 year.

### METHODS

To understand the basis for the contraindication labeling requirement, we reviewed both MEDLINE (1960-2002) and Current Contents periodical listings (1998-2001) for references relating to adverse events occurring after filter placement in septic patients or patients with septic thromboembolism. We used the following terms in our literature search: vena cava filter, sepsis, septic thromboembolism, VCF contraindication, and VCF adverse events.

We also reviewed the Michigan Filter Registry, which contains information for more than 2600 patients, and selected cases for whom sepsis was listed as the primary or secondary diagnosis at the time of filter placement. We reviewed adverse events encountered during filter placement or during the follow-up period, the status at discharge, the time and cause of death, and any report that attempts at filter removal were made. Sepsis was defined by the clinical service treating the patient, generally on the basis of positive findings from blood culture samples. Statistical analyses were conducted using SAS statistical software version 8.2 (SAS Institute Inc, Cary, NC). Product-limit estimate curves were used to analyze survival. Hypothesis tests were evaluated using the log-rank test. Logistic regression models were developed from variables that were significant in univariate tests.

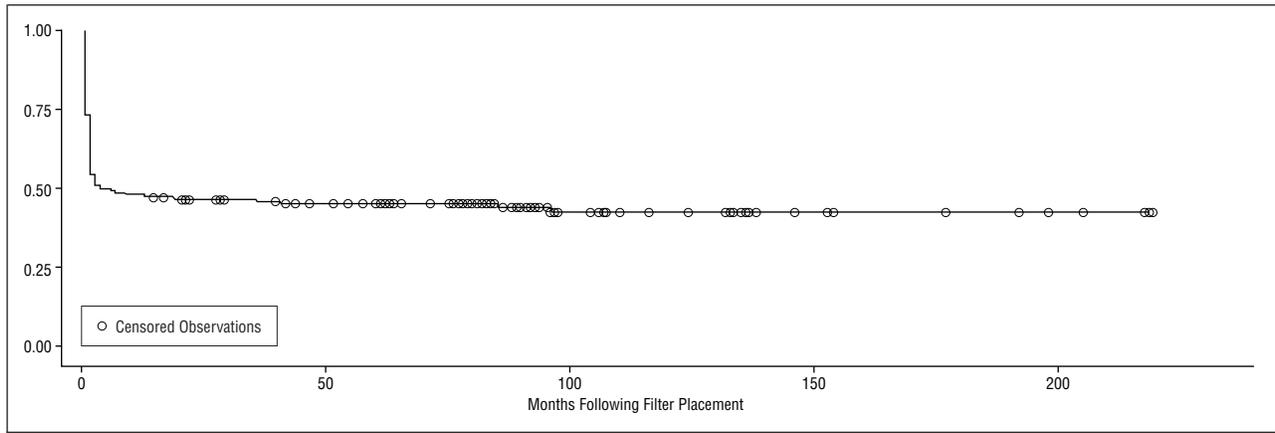
Review of the Michigan filter registry identified 175 patients with sepsis as a primary (10 patients) or secondary (165 patients) diagnosis at the time of filter placement. **Table 1** lists the demographic characteristics of these patients. The diagnosis of deep vein thrombosis had been made in 66%, and 15% had sustained PE. Both stainless steel (54%) and titanium (46%) GFs were used, and noncustomary placement included suprarenal (15%) and superior vena cava (1%) locations.

There was one attempt at device retrieval that took place immediately following placement, but this was due to inappropriate positioning of the filter and was not because of septic complications. The attempt was aborted due to procedural difficulty, and the filter was left in place. Procedural complications included 1 instance each of air embolism, tilt, and filter misplacement; 2 incomplete filter openings; and 7 reports of asymmetrical distribution of the filter limbs. Three adverse events were reported: 1 wound hematoma, 1 wound infection, and 1 bleeding episode, all of which resolved without operative intervention.

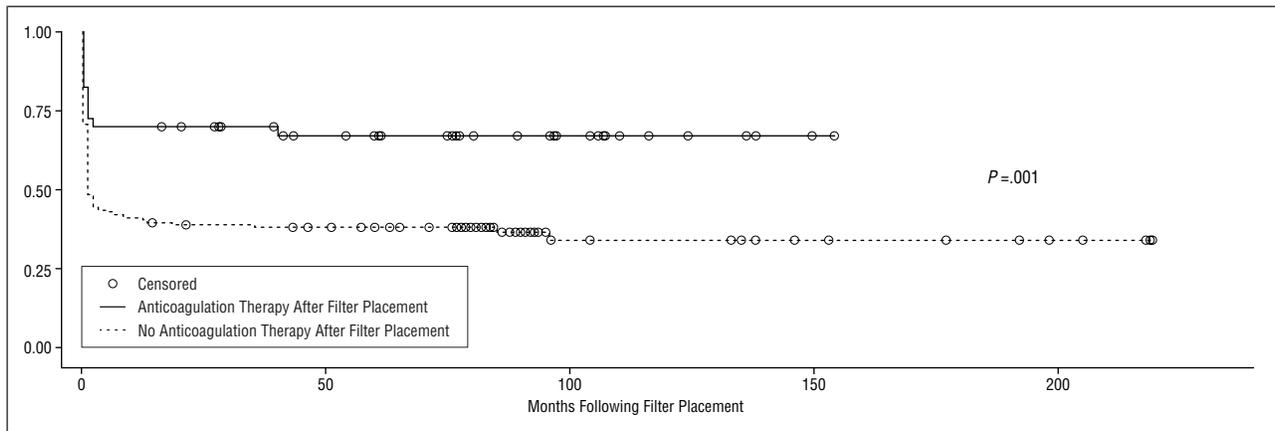
Mortality was high, with a 30-day survival of only 117 (67%). Among the 30-day survivors, 56 returned for routine late follow-up examinations. The mean length of follow-up was 12.9 months (range, 1-133 months). There was one incidence of recurrent nonfatal PE (1%) and one vena caval occlusion (1%). There were no reports of subsequent septic episodes, and none of the filters was removed for any reason. In addition, there were no reports of filter retrieval among the 175 patients. **Figure 1** depicts the mean survival for these patients, which is 44 months (SE, 3.5 months).

To determine the association between anticoagulation therapy and patient outcome, we compared mortality and length of survival when the data were stratified for this treatment. Anticoagulation medication was used in 13 (14%) of the 93 patients who died within 30 days of GF placement and 19 (45%) of the 42 who survived ( $P < .001$ ). Using life table methods, we found a significant difference in mean survival associated with the use of anticoagulation therapy in the postfilter period (**Figure 2**). Five-year survival among those treated was 67% compared with 38% for those who did not receive anticoagulation therapy ( $P = .002$ ).

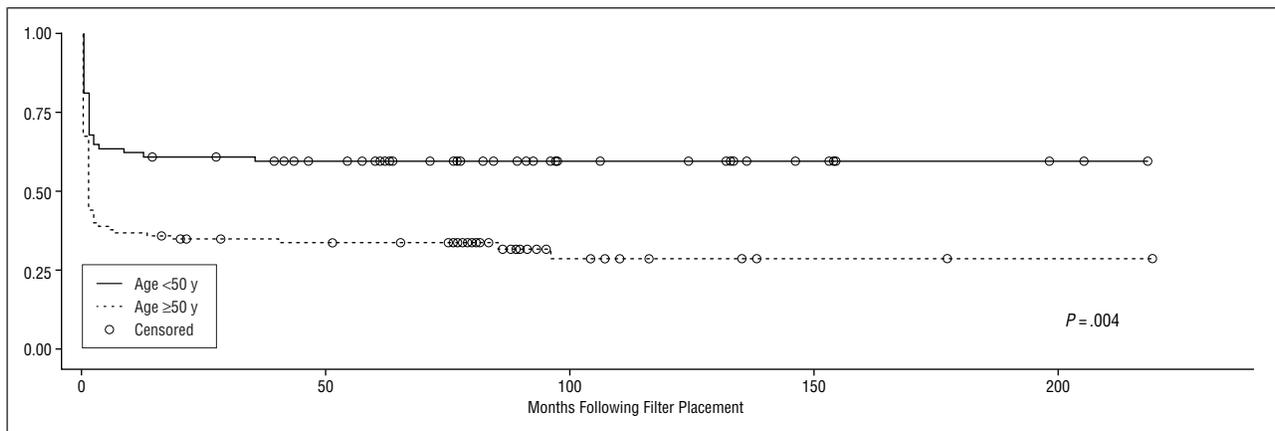
As expected, there was an association between age and the likelihood of survival (**Figure 3**). The mean age of those who survived was 43 years compared with 58 years for those who died within 30 days of onset of sepsis. When we dichotomized age as younger or older than 50 years, the survival duration for those younger than 50 years was 54 months compared with 31 months for those who were older than 50 years ( $P = .004$ ). Using logistic regression to model factors associated with survival, both age (odds ratio, 3.4; 95% confidence interval, 1.6-6.7) and use of anticoagulation therapy following filter placement (odds ratio, 0.29; 95% confidence interval, 0.08-0.55) were independently significant.



**Figure 1.** Product-limit estimate curve for survival with sepsis. Overall mortality in septic patients with vena caval filters is high. However, the cause of death is unrelated to thromboembolism following filter placement.



**Figure 2.** Effect of anticoagulation. Septic patients who receive anticoagulation therapy following filter placement have lower mortality than those who do not receive anticoagulation therapy.



**Figure 3.** Age older than 50 years is associated with a higher 30-day mortality rate among septic patients who have received Greenfield filters.

### COMMENT

We were aware of 2 articles dealing with the evaluation of filters and septic thromboembolism.<sup>4,5</sup> A search of the bibliographies from these articles led to the 2 additional reports cited earlier.<sup>2,3</sup>

The first report, published in 1983, is an in vivo study of sepsis in a dog model.<sup>3</sup> The purpose was to compare

the effectiveness of inferior vena cava ligation with GFs in the prevention of septic thromboembolism, to evaluate the risk of sepsis with GF placement, and to determine the effects of antibiotic therapy on the outcome of infection. For the animals with infected thrombus in filters, antibiotics successfully sterilized the filter, the embolus, and the vena caval wall. This occurred whether the filter trapped a septic embolus or whether sepsis was

induced after capture of a sterile embolus. In contrast, following vena caval ligation, pockets of infection and abscess were found despite antibiotic therapy.<sup>4</sup> This is most likely due to stasis below the ligation. In addition, recurrent embolism is noted to occur in up to 50% of clinical cases by means of collateral vessels that open in response to pressure from the caval occlusion.

The second article reported a successful outcome for a patient who received a filter and who demonstrated sterilization of a septic thrombosis following filter placement, thrombectomy, and a course of amphotericin for a *Candida* infection.<sup>5</sup>

We found no clinical reports of patients requiring filter removal secondary to sepsis or any other adverse events in patients with septicemia following filter placement or those who became septic after filter placement.

For septic patients with a contraindication to anticoagulation medication, the prohibition of inferior vena cava filter placement leaves the physician on the horns of a dilemma. Either the patient is left without prophylaxis for PE or the physician is open to criticism for disregarding the directions for use of the filter. It is disconcerting that there are no clinical data to support this restriction among a group of patients who are at high risk for PE. We were unable to find a single clinical study or a case in our registry to suggest that the filter failed to respond to a course of antibiotic therapy or that any patient required removal of the filter to resolve sepsis. In fact, the opposite occurred. Within this highly thrombotic group, the efficacy of the filter was equivalent to or better than efficacy in lower-risk groups. The explanation is likely a result of the materials used to manufacture the GF—stainless steel and titanium—which are inert. It is only a trapped embolus that could become infected, and the animal study<sup>3</sup> cited herein demonstrates that with adequate antibiotic coverage, the thrombus can be sterilized. This experience is not unusual; wire suture is often used to close an infected wound because its inert properties do not promote bacterial growth but allow healing to occur.

An inflammatory response is associated with both thromboembolism and sepsis,<sup>6-9</sup> and it has been suggested that heparin may modify this response.<sup>10</sup> Our data suggest that further investigation is warranted regarding the association among sepsis, thromboembolism, and anticoagulation therapy. It may well be that the result is confounded by other factors unaccounted for in this analysis such as the acuity of the patients or some other variable that is related to both survival and anticoagulation therapy. However, the highly significant association between survival and the use of anticoagulants following filter placement is intriguing and raises the possibility of causation, which needs to be addressed in further studies.

Although the mortality rate in this population is high, if the patient survives the initial episode, the life table (Figure 1) shows that survival is constant over the remainder of the follow-up period. This confirms that the filter is not contributing to additional sepsis episodes, and,

once the sepsis has resolved, the filter remains capable of long-term protection without added risk.

In conclusion, patients with septicemia are at high risk of deep vein thrombosis and PE possibly related to the inflammatory process that underlies both conditions. For those patients who have an absolute contraindication to anticoagulation therapy, the GF is a safe and effective method of prophylaxis for PE. Filter placement is also warranted when the patient with septicemia is hemodynamically unstable and cannot tolerate further respiratory compromise associated with PE. Once the contraindication for anticoagulation therapy has resolved, it seems to be important to initiate its use. The benefit of anticoagulation therapy following filter placement in septic patients seems to be greater than in other groups, with statistical evidence in this series demonstrating a significant survival benefit. Rescinding the restriction for use of wire-based vena caval filters should be seriously considered by regulatory bodies.

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## REFERENCES

1. Food and Drug Administration Web site. *Guidance for Cardiovascular Intravascular Filter 510(K) Submissions*. Rockville, Md: Center for Devices and Radiological Help, Interventional Cardiology Devices Branch; 1999. Available at: <http://www.fda.gov/cdrh/ode/24.pdf>. Accessed September 5, 2003.
2. Fullen WD, McDonough JJ, Altmeier WA. Clinical experience with vena caval filters. *Arch Surg*. 1973;106:582-587.
3. Scott JH, Anderson CL, Shankar PS. Septicemia from infected caval "umbrella". *JAMA*. 1980;243:1133-1134.
4. Peyton JWR, Hylemon MB, Greenfield LJ, Crute S, Sugerman H. Comparison of Greenfield filter and vena caval ligation for experimental septic thromboembolism. *Surgery*. 1983;93:533-537.
5. Timsit JF, Farkas JC, Boyer JM, et al. Central vein catheter-related thrombosis in intensive care patients: incidence, risk factors, and relationship with catheter-related sepsis. *Chest*. 1998;114:207-213.
6. Esmon CT. Regulation of blood coagulation. *Biochim Biophys Acta*. 2000;1477:349-360.
7. Gando S, Nanzaki S, Sasaki S, Aoi K, Kemmotsu O. Activation of the extrinsic coagulation pathway in patients with severe sepsis and septic shock. *Crit Care Med*. 1998;26:2005-2009.
8. Gando S, Nanzaki S, Morimoto Y, Kobayashi S, Kemmotsu O. Systemic activation of tissue-factor dependent coagulation pathway in evolving acute respiratory distress syndrome in patients with trauma and sepsis. *J Trauma*. 1999;47:719-723.
9. McGilvray ID, Rotstein OD. Role of the coagulation system in the local and systemic inflammatory response. *World J Surg*. 1998;22:179-186.
10. Downing LJ, Strieter RM, Kadell AM, Greenfield LJ, Wakefield TW. Low-dose low-molecular-weight heparin is anti-inflammatory during venous thrombosis. *J Vasc Surg*. 1998;28:848-854.