EDITORIAL

Inferior Vena Cava Filter Update

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Despite therapeutic advances and the universalization of prophylactic techniques, pulmonary thromboembolism (PTE) remains a serious, frequent, and difficult-to-manage disease. If not treated properly, it is the third most frequent cause of death. Venous thromboembolism is a serious and complex health problem with an incidence exceeding 1 per 1000 population per year. In the United States of America there are still 300 000 new cases of venous thromboembolic disease each year. According to Heit,[1] 30% of patients with venous thromboembolic disease will die within 30 days of occurrence and 1 in 5 will die of PTE. Of the survivors, 30% will develop recurrent thromboembolism within the following 10 years. A recent study by Stein et al,[2] of Saint Joseph Mercy Oakland Hospital in Pontiac, MI, USA showed that nearly 1% of patients admitted to a general hospital for any reason developed deep vein thrombosis (DVT) of the extremities whether or not they had received prophylactic treatment with low-molecular-weight heparins and that 21% of these patients suffered an episode of pulmonary embolism.

The various types of anticoagulant therapy and fibrinolysis in severe cases constitute the treatment of choice for PTE. At present, the use of inferior vena cava (IVC) filters for the prophylaxis and treatment of PTE is controversial. No definitive evidence has been published to support the efficacy of or need for such devices in treating PTE.[3] There are circumstances in venous thromboembolic disease, however, in which anticoagulant therapy fails or proves insufficient. Traditionally, doctors have turned to IVC interruption (at first through surgical techniques and later through the placement of percutaneous filters) in order to save the patient's life.

Since the appearance of the Mobin-Uddin[4] filter in the mid-1960's, the development and improvement of such filter systems, together with an increasing acceptance of them on the part of the medical profession for treating and even preventing PTE, has led to an enormous increase in their use. Thus, in the United States of America, 2000 filters were placed in 1982, while in the last decade some 90 000 filters per year were implanted.[5] In nearly all cases the filters used are made of steel or nickel and titanium alloys. They are inserted using a femoral or jugular approach and, once deployed in the IVC, are impossible to retrieve. Although the use of such filters has traditionally been regarded as very effective, with few immediate or long-term complications, in recent years various authors have reported complications associated with the use of permanent IVC filters (migration of the filter, thrombosis at the site of insertion, vena cava thrombosis, etc) in a significant number of cases.[6-9] Among the most frequent complications is IVC thrombosis, which occurs in up to 22% to 30% of cases.[5,6] Several studies analyzing outcome in series of patients treated with IVC filters have established a PTE recurrence rate of 2.4% to 2.9%, with fatal embolism in 0.7% to 0.8% of cases.[10,11] A critical moment in the history of IVC filters came in 1998 with the publication of an article by Decousus et al[12] in the *New England Journal of Medicine.* In a randomized trial of 400 patients at high risk for PTE due to proximal DVT, the authors showed that the initial benefit of IVC filters in the prevention of PTE was counterbalanced by an excessively high rate of 2-year recurrence of DVT, with no significant difference in mortality.

The data presented in the study[12] had a decisively negative effect on the use of vena cava filters in Europe, such that in the year 2000, for example, only 10 were placed in all of the Netherlands. In the US, however, they are still much used, with 200 000 implanted in the last year.

Kinney,[13] an authority on intervention techniques at the University of California San Diego Medical Center, while recognizing the importance of the study by Decousus et al,[12] pointed out several grounds for criticism, some of which were also subsequently discussed in the *New England Journal of Medicine*.[14] Originally, the study of Decousus et al[12] was designed for 800 patients but included only 400 due to difficulties in

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enrollment. In Kinney's opinion, the modification of the number of subjects enrolled and the particular indication for filter placement in this study (only high risk for PTE due to proximal DVT) might have affected the rate of 2-year recurrence of PTE and DVT. On the basis of several US series, Kinney challenged the conclusions that might be taken from the fidings of Decousus et al, suggesting that the use of IVC filters, far from being excessive, was insufficient[15]; that increased thrombosis in the IVC was produced by the accumulation of thrombi trapped in the filter rather than by increased thrombogenicity attributable to the metallic device[16]; and finally that the risk of thrombosis was associated not with the IVC filter, but with the thromboembolic episodes themselves and their sequelae.[17]

In view of published findings, it would seem that the tendency in Europe is to view the efficacy and consequently the use of IVC filters as controversial, while in the US they seem to be considered an excellent and underused tool for the treatment and prevention of thromboembolic disease with little risk attributable to the device itself. There is a question of major importance, however, independent of trends or philosophies: Are there more deaths from PTE in countries where IVC filters are used little or not at all, or, on the contrary, are there complications resulting from an excessive and unnecessary use of these filters in other countries? There are no reliable and convincing data to answer either of those 2 questions affirmatively or negatively. What, then, are the real reasons why the use of IVC filters remains so high in the US? Everything seems to indicate that, in addition to the reasons cited by Kinney,[13] medical-legal considerations peculiar to that country also play a role. Finally, can it be affirmed that the study of Decousus et al[12] is alone responsible for the low use of filters in Europe?

No one, not even Decousus et al,[12] denies the initial efficacy and safety of IVC filters. In the light of our present knowledge, any device (used for the correct indications) that is effective during the period of highest risk of embolization and that could later be removed would constitute the ideal filter and few clinicians would question its use. Nearly all the filters on the market meet these criteria, except perhaps for simple and safe retrievability.[18] For this reason, most authors have advocated the development and use of temporary retrievable filters.[5-9]

Vena cava filters may be permanent, temporary, or retrievable. Permanent filters are deployed and remain in place in the vena cava for the rest of the patient's life. Temporary filters, connected to the outside by a catheter or guide wire, remain in the vena cava for a certain period of time, but must always be removed at some point. Retrievable filters, which resemble permanent filters, may either be removed or left in place indefinitely, as clinically indicated.

The vast majority of publications to date have dealt with permanent filters,[19-24] as there has been little experience with temporary filters because of technical difficulties.[25,26]

For some time, efforts have been directed to the design of retrievable filters. Some, like the Amplatz filter[27] have had a minimal presence on the market, due to difficulty of retrieval; others have not gone beyond the experimental prototype stage. The temporary Gunther Tulip filter (William Cook, Europe A/S, Bjaeverskov, Denmark)[28] was the first such device with technical and safety characteristics suitable for clinical use. In the US, other retrievable filters, such as OptEase (Cordis Endovascular, Miami, FL)[29] and the nitinol retrievable filter (Bard Peripheral Vascular, Tempe, AZ)[30] are currently being used on an experimental basis, with acceptable results. The results, however, are not well documented, as little has been written about these filters and they have not been approved for use as retrievables by the US Food and Drug Administration.

Although the indications for retrievable filter placement have not yet been clearly established, they might include prophylaxis after serious injury, documented DVT or pulmonary embolism in patients with temporary contraindications to anticoagulant therapy (postoperative status), pulmonary embolism in patients with critically low cardiopulmonary reserve, and free-floating thrombi.[13] In these circumstances, and possibly others that will emerge with experience, the retrievable filter may play an important role as either a therapeutic or prophylactic measure. The Gunther Tulip filter and 2 prototypes not yet available on the European market[29,30] have designs similar to that of permanent filters and they can, in fact, act as such if necessary; the difference lies in the fact that they have a small retrieval hook which facilitates removal. To prevent migration, all retrievable filters have anchoring hooks that penetrate the wall of the vena cava.[31] As a consequence, the endothelium is disrupted, triggering a fibrous reaction that traps the filter struts in the venous wall and makes the filter difficult or impossible to remove. How long does it take for the fibrous reaction to occur? For the Gunther Tulip filter, the distributor recommends removal within 12 days of placement. Studies in animals have determined that after 14 days a significant fibrous reaction occurs around the struts of the retrievable filter,[31,32] preventing its removal. However, in the case of the Gunther Tulip filter and the 2 prototypes, there have been reports of removal with no difficulty after longer periods ranging from 21 to 134 days.[30,33] Here questions arise that may be of clinical importance: How long should a filter be left in place? Until the thrombi adhere to the wall? Perhaps the most sensible answer would be until adequate anticoagulation therapy can be initiated. But what of patients with permanent contraindications to anticoagulant therapy, or those who, despite adequate anticoagulation, experience further episodes of embolization? For patients in this (probably small) group, a temporary filter might not be the best solution.

In order to extend the dwell time of the Gunther Tulip filter, we have proposed either repositioning the device within the vena cava every 13 to 14 days in order to avoid its being trapped by fibrosis[34] or covering

the filter with a cellular proliferation-inhibiting agent (paclitaxel). Results have been satisfactory with both approaches, both in patients and in animal experiments. With repositioning, indefinite dwell times, ranging from 22 to 62 days in our experience,[34] have been achieved, while covering the device with a cell proliferation–inhibiting agent led to a 30-day dwell time in animal experiments.[35]

With the available Gunther Tulip filter and other such devices that will probably become available in the future, reliable treatment or prophylaxis with little risk to the patient is possible. An additional advantage to this type of filter is that, should a permanent filter be required for any reason (change in the patient's clinical condition, large thrombi trapped in the filter, etc), it can act as such with levels of efficacy and safety similar to those of a conventional permanent filter.

In conclusion, the study of Decousus et al,[12] while raising some still unanswered questions,[13] marked a turning point in the use of IVC filters, and demonstrated both their initial efficacy and their doubtful ability to provide long-term protection against PTE and potential complications. Retrievable filters, in addition to broadening the possible indications for filter placement, may offer initial protection against PTE and, as they can be removed, may prevent the adverse effects of conventional permanent filters. However, clinical trials (randomized ones, if possible) are needed to corroborate this last point.

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