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A NOVEL APPROACH TO VENA CAVA INTERRUPTION: THE ALN FILTER

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Pulmonary thromboembolism is the primary cause of death in in-hospital patients and the third cause overall.
In spite of the keen attention that disease is receiving and the important results pharmacology has achieved, mortality is constantly on the increase. Some patients (but medical data are in disagreement and range from a hard to believe one out of fifty to an alarming one out of five), when treated with low molecular-weight heparin according to internationally accepted protocols, experience recurrent episodes of pulmonary thromboembolism. Among others, patients with threatening deep-vein thrombosis – the precursor of pulmonary thromboembolism – and simultaneous haemorrhage – such as some trauma patients – may not be treated safely with anticoagulants. In any case, there is no drug capable of preventing a thrombotic embolus from reaching the pulmonary circulation once the thrombus breaks and leaves the venous wall. Many new molecules are being investigated and look very promising in preventing thrombus formation; still none of them will be able to stop an embolus. As a consequence, a non-pharmacological solution must be applied to these cases.

The first surgical approach to thromboembolic prophylaxis dates back to 1784, when John Hunter, a Scottish surgeon, performed a ligation of the femoral vein. Although 11% of the patients suffer subsequent pulmonary embolism, a few surgeons have not yet abandoned the procedure. Inferior vena cava ligation, performed successfully for the first time by the Italian surgeon Enrico Bottini in 1893, results in clinical failure in up to 50% and causes venous stasis problems in almost all patients. Collateral veins enlarge considerably with time, thus providing an alternative pathway for large embolizing thrombi. Surgical techniques for caval fenestration by sutures or by specially designed peri-vascular clips have managed to reduce pulmonary embolism relapses down to 4% and to preserve caval patency in about three quarters of the patient, but long-term problems with venous stasis cannot be overcome. A further danger with these techniques is the major surgery they require with its attendant morbidity in patients who are often seriously ill. In spite of that, a few surgeons still subject their patients to such treatments.

Intravenous caval filters represent a brilliant solution to the problems listed above.
Their history, all ups and downs, is made mostly of incomprehension, either for what is expected from these devices and for their demonization that still continues in some milieus. In order to avoid any misunderstandings, it must be clear that the only function a filter can carry out is to keep an embolus - and only when that embolus is a thrombus - from reaching the pulmonary arteries. That embolus must be above a certain size, below which the filter cannot capture it. The function occurs according to simple, universal mechanics laws that do not depend on individual reactions and therefore occur in any case. It must also be understood that, contrary to what many users

believe, caval filters vary greatly from one another, in terms of function, efficiency and safety, and the pretension of grouping them in a single category, as is often the case, and expressing opinions on "vena cava filters" as a Platonic idea is at best naïve from a scientific standpoint. Unfortunately, the operator implanting the filter does not always have the technical training to wholly evaluate the efficiency and safety of the device and the ease of use is often the only consideration regarding the choice of a filter. This has the effect of diverting the manufacturers from what should be the real goals of their research. Evidence of this is the existence of filters flawed by obvious design errors, such as, for example, the presence of a caudal, inverted cone (thrombogenicity, poor capture, corrosion), or stasis volumes (thrombogenicity), or cones manifestly too short that fail to trap clinically significant embolizing thrombi. Further evidence of this is filters that enjoyed a great popularity due to their ease of use but that were then hurriedly withdrawn because of the problems they "unexpectedly" brought on. Those devices, so easy to spot and to condemn by a good technician, yet generally accepted by clinicians, are responsible for much of the bad press lumping together what is good, not so good and not good at all with regard to vena cava filters. And yet what is not good at all may still enjoy commercial success.

The first filter to receive widespread application was the so-called Mobin-Uddin "umbrella" (1967-1986). It prevented all clinically significant thromboembolic migrations by partially interrupting the vena cava across its whole section, allowing eighteen 3-mm diameter passages for the blood.
The Kimray-Greenfield filter (1972) represented a major improvement over the Mobin-Uddin, its main advantage, among many others, being that of a lesser occlusivity, i.e. the percentage of caval section it occupies. Instead of interrupting the entire vascular section, the Greenfield filter captures the passing thrombi inside a 6-leg conical skeleton with its vertex lying on the vena cava axis which coincides with the vector of maximum velocity, i.e. the pathway followed by the emboli. This family of filters is called "hydrodynamic" as opposed to "sieves" (e.g. Mobin-Uddin).

The result of an 11-year study at ALN Laboratory (ALN Implants Chirurgicaux – Ghisonaccia, France) is a hydrodynamic vena cava filter, highly efficient in capturing emboli down to a diameter of 2-3 mm, and in terms of occlusivity and of quantity of metal used, occlusivity and quantity of metal being basic factors - though not the only ones - to assess the thrombogenicity of the device. In addition to that, the architecture causes no flow turbulence and has no points where the blood flow is slowed down, hence its virtual absence of thrombogenicity. In a number of cases, particularly in nephrectomy patients and pregnant women, this design feature has made it possible to perform supra-renal implantations without compromising renal flow. The ALN filter is manufactured from AISI 316 L stainless steel, an alloy widely used for many years in the prosthetic field that has long proved its usefulness in this particular application. Other metals were tested, but offered no advantage in any respect and in particular no advantage at all as to thrombogenicity, which seems to depend exclusively on design. Diamond-like carbon coating was experimented a few years ago in a French filter which is no longer available, but the results in terms of thrombogenicity were identical to the ones obtained from the non-coated Phynox version. Elasticity plays a major role, as too stiff a filter damages the vascular wall and a too supple one may easily migrate. The exclusion of any welding points gives the device an excellent corrosion resistance, the most common, though not the sole, cause of vena cava filter failure upon time. In the eleven-year history there have been no documented fractures in ALN filters. Other design solutions are applied to guarantee an acceptably coaxial positioning -an "aesthetic" feature doctors seem to appreciate very much - and to preserve the filter's shape memory unchanged during shelf life.

For a long time, many industries have tried to produce temporary filters, i.e. catheters with a distal filtering element to be kept inside the patient's vena cava purely for the length of time necessary to heal a deep vein thrombosis. The idea was also tried briefly by myself, without enthusiasm, and proved an utter failure. The main reasons were the very difficult management such systems require and, above all, the biologically limited time the catheter can stay in place before having to be removed. In a vast majority of cases, that time was far from enough to treat a deep vein thrombosis and the temporary filter was habitually replaced by a permanent one.

A model which enjoyed a good commercial success proved to be particularly dangerous as in a small number of cases the distal filtering section capsized and/or migrated close to or into the right atrium. Improper use was a further, fairly common problem inherent in these devices, as some physicians employed them without administering any drug to prevent blood clotting around the device.

Another method the manufacturers attempted was to make a permanent filter that could be explanted, a solution whose results were not particularly brilliant, as the explant must be carried out within too short a time before the filter becomes irreversibly permanent. So the filters proposed by Pietri, Amplatz, Dibie-Musset and the D.I.L. never passed pre-clinical tests or were clinically unsuccessful, while the Günther model enjoys a modest diffusion.

In a non-negligible number of cases, a few months after a pharmacological treatment has been started or the patient has suffered a trauma, including surgery, the presence of a caval filter may become unnecessary. Hence it is desirable to remove the device, which, though scarcely ever dangerous, is still a foreign body and, though correctly designed and manufactured, sooner or later may fracture due to fatigue and corrosion. Additionally a few patients show a psychologically adverse reaction to something implanted inside their body, even if they are perfectly asymptomatic and can lead a completely normal life. The main technical problem is time: in most cases there is no indication to remove a filter before a few months have elapsed from implant and in all filters mentioned above cellular growth is rapid and exuberant enough to forbid any non-surgical removal.

In every respect, ALN is a permanent filter and it must be managed as such. It has, nevertheless, the unique characteristic of being removable when and if it is no longer needed and that, unlike all other devices, apparently without any time limit. Its particular structure allows cells to grow up to as long as 15-20 days and to an extension of 0.5-2 mm from the point were the legs emerging from the caval wall. Being the cellular growth so limited and reaching a stable state after no longer than three weeks, ALN filters can be removed as easily after a few days or after many months, and probably for ever.

While implanting the ALN filter is carried out via jugular, basilic or femoral approach by means of a 7F system, it can be removed, regardless of implantation route, only from the jugular approach with a 9F sheath containing a coaxial, longitudinally movable crampons system mounted distally on a pre-formable steel wire. Once the crampons cone is positioned at the apex of the filter, the sheath is advanced over the filter retracting its hooks from the vascular wall and the filter can be withdrawn without any difficulty.

The time during which the filter was in vivo had no influence on the extraction procedure and the look of the filter seemed not to depend on it. For the time being, the procedure has been used only in France, Germany and Italy. ALN filters have been implanted in other countries as well, but have not yet been removed. Since November 1999, when the first filter was explanted in Florence, Italy, more than 150 ALN devices should have been removed in Italy. Collecting the relevant data though is not easy, as the procedure is uneventful and passes unnoticed. In a documented series from 30 Italian centres between late November 1999 and November 5, 2001, 44 extractions or repositioning manoeuvres were carried out on patients whose age ranged from 17-81 years, with an in-vivo time ranging from 0-332 days. During the implant time no patient, pharmacologically treated or not, showed any signs of pulmonary thromboembolism. Cavography and tomography investigations, when performed, showed a consistently whole cava in all patients and no patient ever showed any clinical sign of caval lesions. When the manufacturer's directions for use were followed, the average extraction time was around 8 minutes, but a short apprenticeship reduces the time to one or two minutes, or event down to a few seconds when the operator is good, experienced and lucky. All changes to the approved procedure, such as, for instance, the use of a Goose Neck snare, prolonged the operation time and made the procedure more difficult to perform. Twice the removal was not possible due to mal-position of the filter. In both cases, the correct implant procedures were not followed and the legs were pushed into two separate vessels, therefore making the sheath advancement impossible once the crampons system had surrounded the filter apex.

Once the removal proved very difficult as the filter was so tilted that its head touched the caval wall. Some tissue had grown around the head, making the capture very hard.

From the histological point of view, the filters removed show that very often the legs, where they emerge from the cava wall, are covered with a short (~ 0.5-2 mm) and thin layer of fibrinohematic tissue with granulocytes and inflammatory cells. In some instances, we found inflammatory cells associated with giant cells. Occasionally, leukocytes or fibroblasts were present. An inconstant finding, apparently not associated with the time during which the device stayed in situ, is a monocellular layer of fibrinohematic tissue with fibroblasts on the outer surface of the ogive or fibro-connective tissue. Those tissues may be interesting as they supply information about how human tissues behave when confronted with foreign bodies, but do not influence the removal procedures at all. A series of explanted filters is under investigation at the Laboratory of Biomaterials of the University of Modena, Italy.

The system briefly described above offers the interesting possibility to reposition an ALN filter in case its placement had not been satisfactory, thus enhancing the overall safety of the device.
In summary, the ALN vena cava filter is not a temporary but a permanent device, and an excellent one, at that, in whose history no documents exist of thromboses, fractures (a problem that may yet occur in the future), or accidents that led to patient injury. No thromboembolic recurrence has ever been observed even in patients who have had the filter in situ for many years. As to a pharmacological treatment, the ALN filter is neither an indication nor a contraindication for any drug therapy as it is biologically inert. In case the filter is deemed to be no longer necessary, its removal is a straightforward interventional procedure.

Such a filter, which is in no way meant to be an alternative to pharmacological treatments, seems particularly indicated in young patients, in those difficult or impossible to treat with drugs such as trauma patients, surgical patients in general and orthopaedic patients in particular, puerperae and subjects with behavioural or family problems that hamper the correct intake of drugs. Trauma is a particularly important, yet neglected, issue. In the year 2000 our country (Italy, 56 million people) suffered more than 100,000 serious traumas and more than 6,000 casualties from road accidents alone, a large number of which was due to pulmonary thromboembolism.

It should not be forgotten how, for simple chemical reasons, protracted pharmacological therapies with the same drug, beside the wanted action carry out unwanted side effects. These occur in all cases and are often accumulation phenomena; they are harmful, very little known and even less studied. The responsibility for that does not rest with the anima alone, but, and in no negligible way, with the particulate inorganic excipients as well, whose presence is all but indispensable in tablets, pills and so on. So, when dealing with a deep vein thrombosis or a pulmonary embolism patient, the opportunity to help him with a filter like the one described above should always be taken into consideration.