FDA INSIGHTS

Regulation of Peripheral Vascular Devices

Current issues in the regulation of IVC filters.

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As discussed in the FDA Insights article published in the August 2005 issue of *Endovascular Today*, the Office of Device Evaluation's Peripheral Vascular Devices Branch (PVDB) is striving to respond to various evolving pertinent clinical and regulatory issues using a set of ongoing initiatives to better evaluate peripheral vascular devices. Current issues regarding superficial femoral artery (SFA) stenting and the PVDB SFA initiative were discussed in the August article. This article discusses another PVDB initiative: to better define the preclinical and clinical standards of evidence needed to evaluate permanent and retrievable inferior vena cava (IVC) filters.

FDA REGULATION OF IVC FILTERS

Examining the history of IVC filters offers an interesting perspective of the regulation and classification of medical devices. The first marketed IVC filter, the Mobin-Uddin umbrella filter, was introduced to the market in 1967 without the clearance currently required by the FDA, 9 years before the Medical Device Amendments were passed. Because the device was already on the market before the FDA began regulating medical devices, IVC filters were classified in 1976 as preamendments devices. Later, IVC filters were reclassified as class II devices based on the FDA's current classification system.

By law, medical devices are classified based on the risks associated with their use. This risk-based classification works to define the level of oversight the FDA exercises in reviewing medical devices. Class I devices are considered to be of low risk to patients and are subject to general controls. Some class I devices may require premarket 510(k) clearance, although many are exempt from premarket submission. Class II devices are more complex, higher-risk devices that are subject to special controls in addition to general controls and usually require premarket 510(k) clearance to demonstrate substantial equivalence to a currently marketed device. Special controls consist of guidance regarding the information needed to allow for an appropriate evaluation of the device and are needed when general controls are insufficient to ensure that the device is safe and effective. Class III devices are the most complex and have the highest risk to patients and therefore require premarket approval to demonstrate safety and effectiveness.

Given that the use of IVC filters can be associated with serious complications such as device migration, caval wall perforation, caval occlusion, and thrombosis, all of which can become sources of morbidity or mortality, you may be wondering why IVC filters are only subject to special controls rather than premarket approval. The answer lies in their long history of clinical use. Although IVC filters are complex implantable devices with serious patient risks, the design, mechanism of action, and testing of IVC filters are relatively well defined. Therefore, IVC filters are class II devices regulated with special controls requiring FDA clearance of a 510(k) premarket notification, which demonstrates that the device under review is as safe and effective as a device already on the market.

This does not mean, however, that the FDA does not review substantive data prior to clearing an IVC filter for the market. The information submitted in 510(k) applications varies widely depending on the type of device being reviewed; some are only a couple of pages requiring minimal amounts of data to obtain clearance, while others, such as 510(k)s for IVC filters, require a considerable amount of preclinical and/or clinical data to obtain clearance.

IVC FILTER REGULATORY CHALLENGES

In 1999, the FDA published the Guidance for Cardiovascular Intravascular Filter 510(k) Submissions to

document the preclinical and clinical testing needed to comply with the requirement of special controls for class II devices. The guidance identifies specific labeled indications for use for IVC filters (ie, prevention of recurrent pulmonary embolism [PE]) and described the types of data needed to demonstrate substantial equivalence to a predicate device.

The design and clinical use of IVC filters has evolved significantly since this guidance was published. Optional (retrievable) filters are now on the market, and physicians are implanting filters in patients without documented PE. For example, according to reports in the literature, optional filters have been placed prophylactically in trauma patients who cannot be anticoagulated due to the need for surgery, and have been retrieved later after the perceived risk of PE is gone. Although use of optional filters may offer an important clinical benefit to patients requiring only short-term protection from PE, new failure modes and risks associated with the design and use of these filters have been identified. This problem, combined with a better understanding of the physiological environment of the vena cava and filter placement, has required the FDA to re-evaluate the standard of evidence needed to determine that IVC filters are as safe and effective as devices currently on the market.

PVDB IVC FILTER INITIATIVE

The PVDB is working to revise the current guidance document to include optional filters and to update the FDA's recommendations regarding preclinical and clinical testing of IVC filters. The PVDB is also considering including other indications for use in the guidance, such as an indication for prophylactic placement. A summary of some of the likely modifications to be included in the updated guidance document follows.

Bench Testing

Given the identification of new failure modes and risks associated with filter placement and retrieval, additional and more rigorous bench testing is needed to better characterize a filter's clinical performance. Both radial fatigue and flat plate testing should be conducted to best simulate the forces an IVC filter is experiencing *in vivo*. In addition, the testing parameters, such as the number of cycles and displacement, need to be clinically relevant (eg, related to respiration). Interpretation of results should also be correlated to other relevant analyses, such as a Goodman analysis or finite element analysis. For novel device designs, multiple or alternative methods for demonstrating migration resistance and clot trapping ability may also be needed. All bench testing should be conducted using worst case conditions and test sample sizes and acceptance criteria should be statistically justified.

Animal Studies

In the past, animal studies have been used to assess fixation, healing, and histopathology of implanted filters. For optional filters, *in vivo* studies should also be conducted to evaluate the simulated retrieval of a filter. Such studies are important to demonstrate that the filter can be safely retrieved prior to initiation of a clinical study. Indwelling time (ie, time of filter implantation prior to retrieval) and healing time (ie, time to sacrifice after retrieval) should be prespecified and based on the anticipated clinical use of the filter.

Clinical Studies

Clinical evaluation of IVC filters continues to be very important and is needed to fully assess the safety and effectiveness of both permanent and optional filters premarket. A multicenter, single-arm registry study of 50 to 100 patients may be appropriate, depending on the device design and indication, as long as acceptable study endpoints and follow-up time points are prospectively identified. Study endpoints should be clinically meaningful and related to the objective of the study. For example, if the objective of the clinical study is to assess the safe removal of the filter, technical success and clinical success for retrieval should be evaluated. However, if the objective of the study is to assess the prevention of PE using a permanent filter, freedom from recurrent PE, IVC occlusion, and filter embolization should be evaluated. Follow-up time points are dependent on the device design and prior clinical experience with the filter. Evaluations should include appropriate imaging to adequately assess complications and filter performance. The number, severity, and causality of adverse events should be reported.

SUMMARY

The current FDA recommendations regarding IVC filters have been drafted internally and will ultimately be published as an official guidance document. This guidance document will likely form the basis for ISO 25539-Part 3, an international standard for these devices. Especially before this guidance is available, we would like to encourage manufacturers wishing to market an IVC filter in the US to interact with the FDA early and often. ■

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