EVAR Takes Root in Japan

Takao Ohki, MD, PhD, provides an overview of EVAR's emergence in Japan, including progress of the procedure to date and the advantages and disadvantages of the country's unique regulatory restrictions.

Japan is one of the most interesting international case studies for evaluating the emergence of an endovascular procedure. Although commercial EVAR devices were not approved in Japan until many years after regulatory approval in the United States (US) and many other countries, its acceptance after approval has been rather dramatic. As someone who practiced in Japan before EVAR, in the US during EVAR's emergence, and then back in Japan during the initial stages of approval and acceptance there, what have you learned about how EVAR can change the way a nation treats abdominal aortic aneurysms?

Dr. Ohki: The first endograft for the treatment of an abdominal aortic aneurysm (AAA) was approved in Japan in July 2006. Considering that European Union (EU) nations had approval in 1997 and the US received it in 1999, there is no question that there was a delay in Japan. But delays in approval are not all bad, and they do have some advantages. For example, no patients in Japan were treated with the first-generation endografts, which obviously weren't perfect. On the contrary, patients in the EU, which is known for its low regulatory hurdle, suffered from repairing and extracting hundreds of Vanguard stent grafts, which were later removed from the market due to high incidence of stent fractures and suture breakages.

The acceptance of EVAR in Japan has been quite fast and smooth, and the procedure did not meet too much resistance from the senior surgeons like we had experienced in the US in the late 1990s. By the time of the first launch in Japan, there were at least two randomized, controlled trials favoring EVAR compared to open repair, and the procedure had a much better track record with longer follow-up than we had in the US 10 years ago. The slower-than-expected acceptance was due to the presence of the rules set by the Japanese Committee for Stentgraft Management (JCSM). This committee consists of 10 delegates representing 10 different interventional/radiological and surgical societies. The JCSM has issued minimal requirements for both the hospital and the physician performing EVAR.

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What specifically is required of the hospitals and physicians?

Dr. Ohki: The requirements for the hospitals are: (1) that digital subtraction angiography permanently be installed in the facility; (2) 30 or more cases of vascular surgery or endovascular treatment per year, including at least 10 cases of AAAs; and (3) immediate support be available from a full-time surgeon who has experience with at least three cases of AAA rupture surgeries. The requirements for physicians wishing to perform EVAR are: (1) to have experience with 20 or more cases of endovascular treatment of the iliac artery and experience in 10 or more cases of treating aortoiliac aneurysms (surgery or stenting) as the operator or first assistant; (2) participation in a 2-day training program for the stent graft they wish to use; and (3) success in at least two or more EVAR cases under supervision of a proctoring physician. Many Japanese doctors have not yet cleared these hurdles, and some may not ever—particularly the first criterion. Performing 20 iliac angioplasties was tough for the surgeons, while experience with 10 AAAs

was difficult for the interventionists. The JCSM has the authority to approve or disapprove the institution as well as the individual physician. To date, more than 200 hospitals and 400 doctors have been approved in Japan, and we may be almost to the point of reaching a plateau.

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Another barrier for EVAR in Japan is the "high risk" restriction. Unlike in the EU or US, insurance will only cover EVAR in those patients who are deemed unfit for open repair. As a result of these strict hurdles and barriers, the penetration of EVAR has not been as fast as expected. In 2005, 1 year before EVAR was approved, almost all AAA cases were performed via open repair. During the last 4 years, the number of total AAA repair rose to 12,150, 12,700, 13,500, and 14,000 per year, respectively. The penetration of EVAR was rapid considering the strict regulations, and the endovascular percentage rates from 2006 to 2009 were 0.5%, 1%, 10%, and 19%, respectively. As a point of reference, the endovascular penetration rate in the US crossed the 50% mark in 2005.

The market share for the three approved devices in Japan is Zenith (Cook Medical, Bloomington, IN) 48%, Excluder (W. L. Gore & Associates, Flagstaff, AZ) 46%, and PowerLink (Endologix, Inc., Irvine, CA) 8%.

Although the restrictions set by the JCSM were a headache for many, I believe that this effort has been beneficial. One example of the benefit is that the death rate following EVAR in Japan thus far has been extremely low (< 1%). Also, JCSM restrictions have almost entirely prevented those interventional cardiologists who were not as dedicated to treating AAAs from joining this field because very few were able to clear the requirement of having experience in 10 or more cases of treating aortoiliac aneurysms (surgery or stenting) as the operator or first assistant.

When a new technology that is radically different from the traditional treatment becomes available, the Japanese system described above may be a reasonable approach in

reducing both the learning curve as well as reinventing the wheel. However, it does require a lot of effort and cost.

How does the pathway to approval differ from that of the US and Europe, and why did it take so long for EVAR devices to become approved for use in Japan?

Dr. Ohki: There are two reasons. First, Japan was previously seen as a small market for atherosclerotic disease and it was therefore not an attractive market for foreign device makers. Second, the regulatory hurdle was as high as that of the US Food and Drug Administration and required not only safety data (CE Mark), but as is the case in the US, the Japanese government also demanded efficacy data. So, in a nutshell, the EU market had a low barrier and a small market, the US had a high barrier and a large market, both of which resulted in a favorable expense-to-profit ratio, whereas the Japanese market's expense-to-profit ratio was not easily justifiable. The lack of appetite from the foreign device manufacturers definitely had an impact on the prolonged approval process.

However, things have changed quite dramatically over the last several years. Japan has the world's fastest-aging population, and along with the impact of a westernized diet becoming apparent in the baby boomers generation as it enters the atherosclerotic age, Japan has now become the world's second largest market for atherosclerosis, and the priority within the device manufacture has risen dramatically. In addition, the Japanese regulatory agency has become more flexible in accepting foreign data, and with more manpower, the turnaround speed has improved dramatically. Another factor that may push Japan up the priority list is favorable pricing. In Japan, most medical devices are traded by the price set by the government. The price for one EVAR device (main body and contralateral leg included, irrespective of manufacturer) is approximately $18,000, and the price for one thoracic endograft is $18,000, both of which are about 60% higher than the average selling price in the US. For these reasons, I remain optimistic and do not expect too much device lag in Japan in the future.

It has been 3 years since you have returned to your country. How is your own practice developing?

Dr. Ohki: Timing is everything, and I returned to Japan at an ideal point. The first endograft (Zenith) was approved in Japan only 2 weeks after my return home. I have been developing and using the endograft for more than a decade in the US, and when I returned to Japan, only a handful of physicians had used the Zenith. In addition, the Japanese mass media showed strong interest in my career when I returned to Japan. Storylines such as "A surgeon who has realized the American Dream comes back to Japan to help his countrymen" were very catchy, and since my return, I have been featured on over 20 national TV programs and in more than 50 newspaper and magazine articles. Because of my previous experience in endovascular procedures and the publicity I received, my practice was in the top gear from the beginning. Before I returned to Jikei University Hospital, Jikei was treating five or six aortic aneurysms per year. We are now treating more than 400 per year. Additionally, we have performed 45 fenestrated/branched endograft procedures for TAAAs. As a result of this performance, we now have three fixed flat-panel detectors and two mobile digital subtraction angiography machines in our operating rooms. I cannot complain about my practice, but scrubbing in for 800 arterial cases each year, managing a department of surgery that includes 235 surgeons, all while being paid about a tenth of what I used to receive in the US, does make me feel like an idiot once in a while. Fortunately, I love my job.

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What is one area in which currently available EVAR devices still need significant improvement?

Dr. Ohki: Poor access in some patients is a headache with currently available devices, which can still be bulky and stiff. However, this can be managed using a hybrid procedure of some kind. Short- and wide-neck aneurysms are also an issue, but these can usually be handled with either abdominal debranching plus abdominal/thoracic aortic endovascular repair or a fenestrated/branched endograft (such as the custom-made Zenith). We still don't have a solution for aneurysms with shaggy aortas and tortuous anatomies. Also, since fenestrated endografts can be technically challenging and cumbersome, I would love to see an endostapling device that cannot only enable but also simplify the treatment of pararenal aneurysms and distal arch aneurysms. ■

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