



# The Dawn of AAA Stenting in Japan

BY TAKAO OHKI, MD, PhD

Over the last 6 months, Japan is probably the country that saw the biggest change in the field of abdominal aortic aneurysm (AAA) therapy. This is because two industry-made devices were approved during this period. The Japanese media welcomed this news, and it has been introduced in a major way in the public press (Figure 1). The devices that won *shonin* (approval) from the Ministry of Health, Labor, and Welfare (MHLW) are the Zenith (Cook Medical, Bloomington, IN), which was approved on July 11, 2006, and the Excluder (Gore & Associates, Flagstaff, AZ), which was approved on January 22, 2007.

Approval of any industry-made AAA stent in Japan has trailed Europe by 9 years and the US by 7 years. One may wonder what was going on during this period in Japan.

Of note is that surgical codes (CPT codes for doctor's fees) for thoracic aortic aneurysm (TAA) stenting and AAA stenting were both approved and listed 5 years ago. Thus, for the last 5 years, Japanese physicians were placed in an awkward position: a patient may demand endovascular aneurysm repair (EVAR) because it is listed as an approved procedure, but there were no industry-made devices. For this reason, Japan—a country that has the second largest economy in the world and is known for its advanced technology—was using the world's largest number of “homemade” devices. The approval of the Zenith and Excluder devices has so far resolved the dilemma related to AAA therapy, but this awkward condition continues as far as TAA therapy is concerned. Gore & Associates Japan has recently submitted the paper-

work to the MHLW for the TAG *shonin*, and the Japanese Medical Association has requested that the agency approve the TAG without unnecessary delay. I am hopeful that the general public will have access to this promising technology by the end of 2008.

## DEVICE ACCESSIBILITY

The reason for the delay in AAA stent approval in Japan is probably due to the discrepancy between market size and the entry barrier.<sup>1</sup> In Japan, it is estimated that 10,000 AAA repairs are performed annually, and this is roughly one-sixth the number performed in the US. Approximately 100 EVARs (74 Zenith and some homemade devices) were performed nationally in 2006 (Figure 2). There are many countries around the world where the market size is much



Figure 1. Cover page of one of the nation's leading weekly magazines, *Yomiuri Weekly*, introducing the approval of EVAR in Japan.



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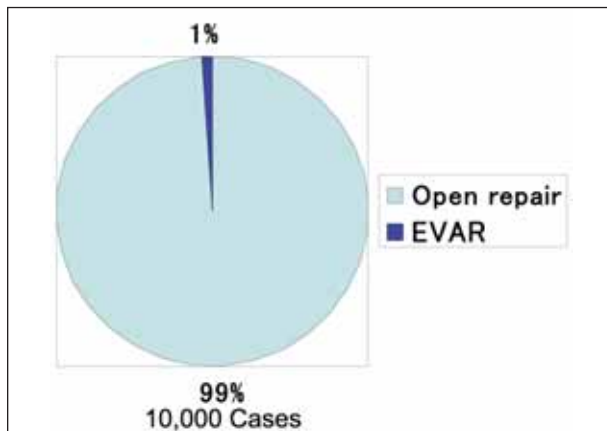


Figure 2. Ratio of open repair versus EVAR in Japan (2006 estimate).

smaller than Japan, but these countries have gained approval for AAA stenting much sooner. The new device-approval process in Japan is quite complex, and the regulatory hurdle is as high as it is in the US. Because the US market size is large, it is justifiable for the device companies to conduct expensive clinical trials upon the FDA's request. The Japanese market, however, is not large enough. Other smaller markets in the world had much lower entry barriers, which were low enough to justify their smaller market size. Some work needs to be done regarding this matter; otherwise, Japan will always be lagging by 4 to 7 years in terms of device accessibility. It is worth noting that Japan remains the only developed country that does not have approval for the Taxus coronary drug-eluting stent (Boston Scientific Corporation, Natick, MA).

Both the Zenith and the Excluder were approved based on the US pivotal trial results, although Cook also submitted its Japanese trial results to augment the US data. The Excluder was not being used officially at the time of this approval. In Japan, we are currently going through what the US did 7 years ago (ie, training doctors to use these devices appropriately and safely). Cook Japan and Gore & Associates Japan have each developed a training course for the launch of their devices.

### THE GOLD STANDARD

As I mentioned earlier, industry-made devices were approved just 7 months ago. Thus, the gold standard treatment remains open surgery. In general, the Japanese are fast in absorbing a new technology. This was the case with laparoscopic procedures and coronary stenting; 80% of cases are currently done with a drug-eluting stent. If the reimbursement issue mentioned subsequently does

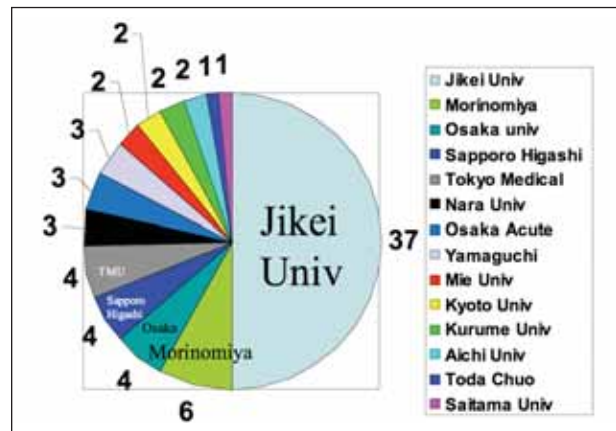


Figure 3. Breakdown of number and location of AAA stenting procedures using Zenith stents in Japan (July 2006 to January 2007).

not become a major problem, I believe that EVAR will soon become the gold standard treatment.

### RESTRICTIONS

The rules for performing EVAR in Japan are being developed even as I write this manuscript and are still unclear. However, several observations can be made. Unlike in the US, where the costs of stents and balloons are included as part of the diagnosis-related group (DRG) hospital fee (global fee), in Japan, the cost of the devices used is charged to the payer on a case-by-case basis. A recent document released by the Japanese MHLW clearly states that the hospital can charge the payer for the AAA stent only if the AAA patient is not a candidate for open surgery (ie, high-risk patients). Although it is similar to the US Center for Medicaid & Medicare Services document regarding carotid artery stenting payment, this document does not define high risk. It is left completely to the physician's discretion, but the physician in charge is mandated to record in the medical chart that the patient is not a good candidate for open surgery.

This is a significant blow to the industry, as well as the patient, and I believe that it will slow down the penetration rate significantly unless action is taken. This document is also not scientifically sound. The two devices that won the *shonin* in Japan used the US pivotal trial data for their approval. In both pivotal trials, the patients enrolled were good-risk patients. It is common sense that device labeling and reimbursement should reflect the patient population that was used to support the approval, and the Japanese MHLW's document goes against this. I am hopeful that this was an oversight, and that the agency will correct it in a timely manner. Until then, physicians will remain unwilling to make false documents in the medical



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chart and, thus, slow down the penetration. Since the *shonin* of the Zenith was introduced in a major way by the Japanese media, the patient's demand to receive an AAA stent is high, and the doctors are once again in an awkward position if a patient is not considered to be at high risk for open surgery (Figure 1).

### REGULATORY BARRIERS

As I mentioned earlier, the regulatory hurdle is as high in Japan as it is in the US, although the market size is much smaller. In addition, the hospital infrastructure that enables conduct of a reliable clinical trial is very poor. Very few hospitals in Japan possess a clinical research coordinator, and most of the data collection during a clinical trial is performed by doctors who are already overworked. One can easily imagine the quality of the data. Also, the industry lacks experienced regulatory personnel. I know of only a handful of competent regulatory/clinical personnel in Japan, most of whom have a pharmaceutical background because the clinical trial activities are much higher in the pharmaceutical market compared to the device industry. In summary, the agency, the hospitals, and the sponsors (industry) need to strengthen their teams in order to provide the latest technology to the Japanese patients without significant delay.

### RECENT EVAR DATA

The *shonin* of the Zenith and the Excluder came more than a year after the EVAR 1 and EVAR 2 results were published, and, therefore, it is difficult to determine the impact of these results. Also, my impression is that not too many Japanese cardiovascular doctors are aware of these trials. The EVAR 1 trial has shown that the 30-day mortality rate is reduced to roughly one-third with the stent procedure compared to open surgery. In addition, this survival advantage has been maintained up to 3 years in terms of aneurysm-related death. This would impact how people are treated, but if the doctors and the patients are not aware of the details, it will have little impact.

### DEVICES

The only approved devices in Japan are the Zenith and the Excluder. Five Excluder devices have been implanted in Japan as of this publication, and all were done at my hospital because I am currently the only approved user/instructor for the Excluder device in Japan. Gore & Associates is on the verge of training others around the country, and Jon Matsumura, MD, and I will be helping this process. Dr. Matsumura will come to Japan from March 5 to March 12, 2007, and visit five different hospitals, at which time it is hoped he will approve five doc-

tors to use the Excluder. I will also cover numerous hospitals to ensure the safe launch of this device in Japan.

Between July 11, 2006 (day of *shonin*) and January 31, 2007, 74 Zenith implants had been performed (Figure 3). These were performed at 14 different hospitals in Japan. Since Cook (Medicos Hirata, Inc.) conducted the confirmation clinical trials in Japan beginning in 1999, there are more instructors for the Zenith (11 instructors) than for the Excluder (one instructor).

The market share was 100% for the Zenith until March 1, 2007, when we performed the first EVAR using the Excluder. I believe that Cook Medical and Gore & Associates will be very competitive in Japan. The Excluder has the advantage for its simplicity in deployment, safety profile, and the ease of use. On the other hand, because many patients in Japan have short and wide common iliac arteries, compared to patients in the US, the lack of a flared bottom limb in Japan may hamper the Excluder's penetration. The wider range of sizes that are provided by the Zenith, along with its time-proven durability, are a significant plus in the Japanese market.

### REIMBURSEMENT

The health insurance company (payer) pays for the stent and the procedure. In Japan, there are approximately 5,000 different payers, and all have two things in common. First, all employees are mandated to participate in a health insurance plan. Secondly, the listed price of any medical service, product (eg, stent, balloon), and hospital and doctor fees are all controlled by the government. We have a nationwide uniform price, and it is non-negotiable. For example, the Zenith is listed at about \$15,000 USD in Japan (including all three pieces), the Equalizer balloon (Boston Scientific Corporation) is \$1,200 USD, and the Smart stent (Cordis Corporation, a Johnson & Johnson company, Miami, FL) is \$2,500 USD. As I mentioned earlier, if the patient is not determined to be at high risk for surgery, these items will not be reimbursed. The method and principle of billing and reimbursement for open surgery are the same.

### CARDIOVASCULAR SURGEONS, INTERVENTIONAL RADIOLOGISTS, AND INTERVENTIONAL CARDIOLOGISTS

Presently, EVAR is performed by cardiovascular surgeons (85%), interventional radiologists (10%), and interventional cardiologists (5%). Each group has unique strengths and weaknesses. Many cardiovascular surgeons currently lack sophisticated endovascular skills and imaging equipment, although they control the patients. Interventional radiologists may have the imaging equipment and the basic skills, but the knowledge regarding overall AAA therapy and



**TABLE 1. SOCIETAL GUIDELINES FOR PHYSICIANS**

**Requirement for the physician**

- Has attended a course conducted by the manufacturer
- Surgical/interventional experience
  - Has performed more than 20 iliac interventions
  - Has performed or assisted more than 10 AAA or iliac aneurysm cases (either surgical or interventional)
- Has performed at least two successful AAA stent cases under the supervision of an instructor

**TABLE 2. SOCIETAL GUIDELINES FOR INSTRUCTORS**

**Requirement for the instructor (device specific)**

- Has performed or assisted more than 30 AAA stenting procedures (including homemade devices)
- Has attended a course conducted by the manufacturer
- Has performed more than 10 cases using the stent he/she wishes to instruct
- Is board certified by one of the following professional societies:  
Japanese Society of Interventional Cardiology (JSIC), Japanese Association for Cardiovascular Catheterization Therapeutics (JACCT), Japanese Society of Interventional Radiology (JSIR), Japanese Society for Cardiovascular Surgery (JSCVS), Japanese Society for Surgery (If there is a physician certified by JSCVS in the same hospital)

access to patients are lacking. Interventional cardiologists, similar to the US, are the most powerful group in any given hospital. They will obviously take advantage of this, as well as their accessibility to high-end imaging equipment. Recently, a guideline was established that was a prerequisite for the *shonin* of AAA stents in Japan. This document was endorsed by 10 related professional societies in Japan, including the Japanese Circulation Society, Japanese Society of Interventional Cardiology, Japanese Association for Cardiovascular Catheterization Therapeutics, Japanese Society of Interventional Radiology, Japanese Society for Cardiovascular Surgery, Japanese Society for Vascular Surgery, Japanese Society for Artificial Organs, Japanese Society for Endovascular Interventions, Japanese Society of Phlebology, and the Japanese College of Angiology. According to this document, a physician must have performed (operator or assistant) more than 10 AAA or iliac aneurysm cases, including both open and EVAR cases, if he or she wishes to use an AAA stent (Table 1). This may be a significant hurdle for many interventional cardiologists who typically have not done any surgical or interventional therapy of AAAs.

**TABLE 3. SOCIETAL GUIDELINES FOR HOSPITALS**

**Hospital requirement**

- Possesses a fluoroscope
- Performs at least 30 vascular operations/interventions annually
  - Including at least 10 AAA therapy
- Possesses a full-time surgeon who has performed at least three surgical repairs of a ruptured AAA

The criteria to be an instructor for any given device has also been outlined (Table 2). The guidelines ask that the hospital should possess a C-arm (as opposed to leasing one on a case-by-case basis) and have good surgical back-up, etc. (Table 3).

## SURVEILLANCE

In addition to the societal guidelines mentioned, the manufacturer must perform postmarket surveillance (PMS), another prerequisite for *shonin*. Each company is mandated to follow the first 400 patients for up to 1 year. The protocol for this PMS is identical to the Society for Vascular Surgery guidelines related to EVAR. The protocol asks for 1-month, 6-month, and 12-month CT with intravenous contrast and abdominal x-ray films to check for fracture and migration. Although the PMS only mandates follow-up to 1 year, I believe many physicians will voluntarily follow their patients longer. Japanese patients do not feel burdened coming back to the hospital, and in fact, many feel good that they are given the attention. My recommendation for surveillance is to use the wireless pressure sensor more frequently, but this technology is not yet available in Japan.<sup>2</sup>

## FUTURE PROSPECT

EVAR is growing rapidly and will continue to do so in Japan. Both patients and physicians love advanced and minimally invasive technology. Because of the stable economy of Japan, we will probably be able to support new technology. ■

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