

# Hiroyoshi Yokoi, MD

An experienced endovascular interventionist from Japan shares his thoughts on the Harmonization by Doing Initiative and explains how difficult lesions are treated at his institution with high rates of success.

**What has your experience been with the Harmonization by Doing (HBD) Initiative? Do you think this initiative will eventually serve as a model for regulatory collaboration worldwide?**

My first experience with HBD was attending a town hall meeting (THM) at the Transcatheter Cardiovascular Therapeutics meeting in 2003. This was before coronary drug-eluting stents (DES) were approved in Japan. I remember being surprised to see physicians, government, and industry working together for the benefit of patients—this sort of collaboration did not occur in Japan. I also recall thinking that having such a system here would surely result in more rapid approvals and a resolution of Japan's device lag as well. The following year, Dr. Shigeru Saito of Shonan Kamakura Hospital led the effort to arrange Japan's first HBD meeting at the Japan Circulatory Society conference. This was attended by Dr. Mitch Krucoff, as well as key US Food and Drug Administration representatives.

Through HBD, we learned about the setup of United States THMs, and many subsequent Japanese medical society meetings (Kokura Live, Kamakura Live, Meeting of the Japanese Association of Cardiovascular Intervention and Therapeutics, etc.) featured THMs. This was most effective in bringing physicians, government, and industry closer together and making it clear that we are all on the same side. Subsequently, we ran HBD programs for two coronary drug-eluting stents (Endeavor [Medtronic, Inc., Minneapolis, MN] and Xience [Abbott Vascular, Santa Clara, CA]) and one lower limb DES (Zilver PTX, Cook Medical, Bloomington, IN).

In addition to resolving the device lag, participation in these trials also served to improve the quality of clinical settings in participating hospitals. These programs also gave us the opportunity to learn more

about the differences between medical practices in Japan and the United States. I served as Co-Chair of the HBD's WG 1 project in October 2011, and I will continue to support HBD projects in the future as well. Any country wishing to provide its citizens with better medical treatment as quickly as possible would be well advised to look to HBD as an effective model for making this happen. I will add that if a given country's systems are already established and mature, new framework may be necessary.

**How might this type of collaboration affect industry and device innovation, as well as patient care?**

Relationships among physicians, government, and industry would be strengthened; devices would be developed more rapidly; and safe, effective treatment would be available to patients sooner.

**Are there any updates regarding the status of the OSPREY trial?**

Japan is taking part in this global trial, based on an HBD project. Enrollment of 100 patients has been completed, and we are in the follow-up period. We have applied for approval for a superficial femoral artery (SFA) bailout indication, based on 30-day post-procedure results.

**How would you describe the adoption of endovascular techniques in Japan during the past 10 years? The past 5 years? Which factors have contributed to these trends?**

Up until 10 years ago, endovascular treatments were mainly performed by radiologists and vascular surgeons; it was only approximately 10 years ago that cardiologists began performing these procedures. We cardiologists learned that many patients with coro-

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nary vascular disease tend to have vascular problems elsewhere. We also saw that these problems adversely affected treatment outcomes, and this led to our interest in endovascular treatment. Cardiologists' entry into this sphere has increased the number of endovascular cases. Five years ago, we saw the first reports of long-term outcomes of stenting in Japanese patients, which resulted in increased stent usage. Lately, we are seeing increasing referrals of critical limb ischemia patients from nephrologists, diabetic internists, and orthopedic surgeons, and this has led to an increase in below-the-knee endovascular treatments.

**What treatment techniques do you most often employ when facing complex SFA and/or below-the-knee cases?**

With multiple guidewires designed specifically for use in chronic total occlusion (CTO) lesions (Treasure and Astato tapered wires, Asahi Intecc, Nagoya, Japan) available in Japan, our success rates are high (generally > 90%). We often use stents in the SFA, and for TASC C and C-type lesions 15 cm or longer, we are comparing stenting versus bypass surgery to determine the best indication.

Below-the-knee lesions are treated with balloons only, no stenting; thus, the advent of long balloons that are 20 cm or more are especially useful, as they allow for longer inflation times. There are no atherectomy devices approved for use in Japan, but I think we would find them useful in treating nonstenting zones. We also frequently use intravascular ultrasound when treating CTO lesions.

**What is your protocol for medical management to prevent SFA restenosis in high-risk patients?**

Here in Japan, there are reports that cilostazol is effective in preventing restenosis, so when stenting in the SFA, we begin dosing 200 mg/d prior to the procedure and continue this as long as possible. For the first month poststenting, we administer aspirin and clopidogrel, then continue with aspirin and cilostazol thereafter. If the patient cannot tolerate 200 mg/d of cilostazol, we reduce this to 100 mg/d. If there is sufficient vessel diameter, we treat long CTO lesions with a combination of a long covered stent and a DES that is implanted proximal to the covered stent.

**How might one predict which patients will be the best candidates for successful SFA stenting?**

An analysis of 1,000 SFA stented patients indicates that restenosis predictors are female sex, ankle-brachial index < 0.6, TASC II C/D lesions, stent fracture, lack of cilostazol, and vessel diameter.

**Which facet of SFA occlusive disease treatment most requires urgent study?**

I am interested in researching whether there is any difference in long-term patency between subintimal stenting and intraluminal stenting. I would also like to know whether the use of DES or drug-eluting balloons in the subintimal space would be efficacious as a way of preventing restenosis. Furthermore, I would like to investigate what length of long-term patency might be achieved through the use of atherectomy devices and drug-eluting balloons.

**Considering that many patients who present with coronary artery disease also have some type of peripheral disease, does your hospital use any type of preemptive screening tests for patients who present only with symptoms of heart disease?**

We measured ankle-brachial index and performed full-body blood sonography on 2,108 percutaneous coronary intervention patients. We found that 549 patients (26%) also had polyvascular disease. Among the polyvascular cases, 379 patients (18%) had peripheral artery disease, 97 patients (4.6%) had carotid stenosis, 99 patients (4.7%) had renal stenosis, and 122 patients (5.8%) had abdominal aortic aneurysms. The rate of major adverse cardiac and cerebrovascular events at 1 year for the polyvascular disease patients was 6.5%, which is significantly higher ( $P < .001$ ) than the coronary artery disease-only patients (2.3%).

**To what do you attribute the high success rates associated with endovascular procedures at your hospital?**

Extensive experience with percutaneous coronary intervention to treat complex lesions, including CTO cases, contributes to the high procedural success rate at our hospital. Devices specifically created for CTO lesions, such as Treasure, Astato, and X-treme (Asahi Intecc) guidewires and microcatheters such as Corsair (Asahi Intecc), also contribute to our success rates. Our frequent use of diagnostic imaging technologies, such as surface sonography and intravascular ultrasound, also helps us maintain high success rates. The most important factor is simply always taking on these complex lesions, gaining experience, and improving technique. ■

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