Tomorrow's Gold Standard?

The scrutiny faced by carotid artery stenting (CAS) and the individuals and organizations who sought to see it approved in the US may be the most intense ever levied upon a new procedure. However, rather than being frustrated by this distinction, Jay S. Yadav, MD, inventor of the first embolic protection device and designer of the landmark SAPPHIRE Trial, appreciates and welcomes it. In this interview, Dr. Yadav discusses why in order for a new therapy to be adopted to address a disease that is already treated with a proven procedure, the results with that therapy must be undeniably proven, and all related issues must be addressed. Dr. Yadav also describes the invention of the AngioGuard device and its role in making CAS adoption possible.

Endovascular Today: Endarterectomy has long been a procedure performed every day by thousands of physicians, with proven short- and long-term data. And stenting, while gaining popularity in other vascular beds, was considered taboo in the carotids during the mid-1990s. What were some of the barriers you faced as one of the early proponents of the procedure that would challenge the "gold standard"?

Jay Yadav, MD: The traditional wisdom was that the carotid artery would be the one vessel that would not lend itself to endovascular treatment because of the risk of embolization and the vulnerability of the brain to embolization. That was the dogma at the time, but I started working on addressing the issue of embolization, really as an attempt to treat acute stroke, as we were treating acute myocardial infarctions using angioplasty. I developed a porcine carotid artery thrombosis model, in which I began performing angioplasty. What I found was that angioplasty worked fairly well, but that embolization of the brain did occur, only the strokes were not as big as one might have thought. That led us to some work in developing an IRB protocol for carotid angioplasty in high-risk patients who were not good surgical candidates. Once our protocol was approved with the IRB, we actually began to have a lot of patients referred to us who were poor surgical candidates.

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EVT: How did your specific concept for embolic protection come to you?

Dr. Yadav: It became pretty clear after we had performed some carotid angioplasty and stenting that simply improving upon technique was not an adequate treatment for the incidence of embolization and stroke. We kept having a certain fixed stroke rate that really wasn't acceptable. I felt that we did need emboli protection.

We really wanted to maintain perfusion. I thought that was very important because it is one of the great advantages of endovascular treatment versus carotid surgery, that we would not be occluding the artery for very long. I didn't want to sacrifice that advantage, so I didn't think balloon occlusion methods were ideal. In order to maintain perfusion, a filter is really the only viable option. At that time,

however, the consensus was that a filter couldn't be made small enough that could go into an artery, go through a lesion, and be retrievable. Remember, nitinol had not really been used in any related capacity at this point.

EVT: What time period was this process initially taking place?

Dr. Yadav: I began thinking about this problem in 1996, and we made the first prototype in 1997. The first use in a patient occurred in 1998; it took about a year to go from being a prototype to being used in a patient.

EVT: What was the development process with industry?

Dr. Yadav: Initially, I took the idea to some large companies, and they didn't feel there was a need for it. The people they consulted did not feel that embolization occurred that frequently or was that significant of a problem. Then I talked to some people who told me that it wouldn't be possible to make such a device, so the response was negative regarding both the need and the feasibility. I was forced to go out and start my own company, which I didn't really want to do because I didn't have any money. I scraped together some funds and got an engineer to work on the project part-time in Minneapolis, and we were able to construct the prototype. Once we made the prototype, we were able to generate some more excitement and also get some money from angel investors. The company never had anything more than angel investors.

EVT: What year did Cordis become interested?

Dr. Yadav: Cordis became interested in 1998, and purchased it in 1999.

EVT: Which physicians were helpful in developing AngioGuard?

Dr. Yadav: I basically worked alone in developing AngioGuard, but the people who were helpful in testing it were Hugo Londero, MD, from Buenos Aries, and Eberhard Grube, MD, in Siegburg, Germany. These gentlemen were the people who, along with myself, performed the initial procedures.

EVT: On a larger scale, how would you say that AngioGuard facilitated the acceptance of carotid stenting as a viable treatment option?

Dr. Yadav: I don't think it would have been possible without AngioGuard because embolization was the Achilles' heel of the procedure. Before AngioGuard, whenever we did the procedure, it was always a game of Russian Roulette; we never knew whether the patient was going to have a stroke or not. And, when they did have strokes, they were often significant.

I think AngioGuard showed that embolic protection was feasible for CAS, and that it could be done easily. What has happened since then is that people are actually very comfortable doing the procedure. When we perform CAS today, we are very comfortable, we're not nervous, and we're pretty confident that the patient will not have a significant stroke. SAPPHIRE showed that there were no major ipsilateral strokes in patients treated with AngioGuard and Precise stents, which is pretty remarkable. There were a few minor strokes, but there were no major strokes. And that is what I believe embolic protection can do for you—it doesn't completely eliminate all strokes, but it does get rid of the big strokes. Most patients can recover from small strokes fairly well.

"My primary intent was not to get a device to market. It was really to change the treatment of a disease—in this instance, carotid disease."

EVT: How did you come to design the SAPPHIRE trial, and why was its specific design necessary for this procedure?

Dr. Yadav: My primary intent was not to get a device to market. It was really to change the treatment of a disease—in this instance, carotid disease. That was the goal because I felt, certainly in high-risk patients, that surgery was not an ideal treatment, and there was enough anecdotal evidence to support that contention. But, I knew that to change practice patterns would require data randomized against the established standard.

We probably could have gotten AngioGuard to market much more quickly by simply conducting a registry, but that wasn't what we were after. We did want to get AngioGuard to market, but more importantly, we wanted to see if CAS was the right treatment for these patients. We would never have known that without a randomized trial. I have to applaud Cordis and Johnson & Johnson for being supportive of that goal, because it really wasn't easy to sell industry on that idea. Industry generally takes the fastest path to market, and their primary mission isn't to conduct good science. But, in this instance, I think Cordis really did agree to do good science, and without their support, we could not have done the study.

EVT: Do you think the type of scrutiny that CAS and SAPPHIRE underwent will become the norm?

Dr. Yadav: I don't think so. I think this was special because

a specialty—vascular surgery—had a procedure that they were very vested in. They had done a very good job of developing it and testing it in multiple randomized trials, and it is the major operation of their specialty. They would not change their practice patterns without randomized data. And I think their position is absolutely reasonable. If there is that much data supporting endarterectomy, there had better be some good data to change the focus away from that procedure. So, I think this is a special instance in which you are really changing an entire procedure—this really isn't about a device. The device facilitates and allows the change. Most devices do not change a procedure, they augment it.

EVT: So, only in the sense that the standard of care might be completely changed would this level of scrutiny be undertaken?

Dr. Yadav: Absolutely. The key is that in this case, we are talking about changing the standard of care. It is about much more than just the device, it is about the whole procedure. The device is integral to the procedure, and you wouldn't have the procedure without the device, but it is more than that. There's training, reimbursement, and all types of other issues that are involved. But if you are just introducing a new way to do angioplasty, or a new type of catheter, the level of scrutiny is much less.

EVT: What devices or inventions were spawned by the AngioGuard?

Dr. Yadav: It spawned the whole embolic protection industry. I don't know how many types of filters are out there now, but there are at least seven or eight. It has really catalyzed a lot of activity. It has also led to a lot of nonfilter devices that target the same goal. There are now a lot of combination thrombectomy/embolic protection devices. It has also spawned recognition of the occurrence of embolization. The AngioGuard provided the smoking gun evidence that embolization occurred because it showed us the particles. I think the AngioGuard proved that embolization occurs in essentially every endovascular procedure that we do; it is more significant in some than in others.

EVT: What improvements do you see being made in embolic protection during the next 5 to 10 years? In which other vascular beds do you think it will have a significant impact?

Dr. Yadav: I think devices will keep getting smaller and easier to use. It clearly has a role in saphenous vein graft intervention in the heart. There will be some role in acute myocardial infarction, but that has not yet been worked out. There will definitely be a significant role in renal intervention. There's also a role in thrombolysis of the lower extremities to prevent distal embolization. ■