Eric J. Dippel, MD, FACC

The esteemed interventional cardiologist and EXCITE ISR study PI shares his insights on restenosis treatments, peripheral embolic protection, and physician-industry partnerships.

Initial results of EXCITE ISR were published earlier this year, and 12-month results were presented at NCVH in May. What were some of the key findings?

EXCITE ISR is a landmark trial that begins to define the treatment strategy for in-stent restenosis (ISR). ISR is a major problem in the United States; there are probably over 100,000 cases a year. Even with the advent of drug-coated balloons (DCBs) and the possibility of stent use going down over time, there are millions of people who have had stents implanted, so this problem will not go away. We really need a more effective treatment strategy. Standard balloon angioplasty, as we know, is not effective.

The neointimal hyperplastic tissue that grows inside of stents is about 85% extracellular matrix and 15% cellular material, and it has a very high water content, so using a plain balloon simply squeezes the water out of the tissue—but the tissue rehydrates very quickly and the lesion comes right back. There needs to be a way to physically remove the tissue.

When we designed the EXCITE ISR study, we intended it to be a real-world study. I know that term gets thrown around a lot, but we didn't want to have an upper lesion length limit. If you look at a lot of the stent or DCB studies performed for the SFA and popliteal arteries, the typical lesion lengths are 6 to 10 cm. When you look at the baseline characteristics for EXCITE ISR, the average lesion length was 19 cm, which is longer than any other lesion studied to date in the periphery. A third of the lesions were total occlusions, and 20% were > 30 cm. That was an important point and something we wanted to establish up front—this is what operators see every day in the trenches.

EXCITE ISR was a randomized study that compared balloon plus laser to balloon alone. The study was designed to enroll 335 patients, but was halted after 250 were enrolled. The acute procedural success, 30-day safety outcomes, and 6-month efficacy outcomes were by far statistically superior in the balloon plus laser atherectomy arm versus the angioplasty-only arm.

We now have level-one evidence that a balloon should not be the default therapy for ISR to build on improving long-term outcomes. We have a baseline, and we can look into other therapy combinations for ISR.

What do you think needs to be prioritized in terms of the next course of study for optimal ISR treatment?

The next logical step to me is combining laser atherectomy and DCB and see where that takes us. They are currently enrolling studies of this in Europe, including the PHOTOPAC study, which is evaluating laser etherectomy plus DCB for ISR.

We know how laser plus a plain balloon behaves, so if we add a DCB, will that give us better results? There are some small studies with only DCB for ISR (the FAIR trial, for example) coming out, but those lesion lengths were relatively short (around 8 cm). We'll need to know how a DCB will behave in real-world lesions. There are many remaining questions, but we now have a starting point with EXCITE ISR.

As devices increase in sophistication, they aren't necessarily becoming more cost effective. How do you decide when it's most necessary to use a more expensive option? How do you rationalize costly procedural add-ons?

There are two separate costs that we talk about: the cost to the patient for individual cases—what they have to pay out of pocket or what insurance carriers have to pay— and the cost to the hospital in terms of equipment used and the cost of the procedure. You would think that these two different costs would be harmonious in wanting the same thing, but there are situations in which hospitals benefit financially by patients coming back frequently. Patients, however, certainly don't want to come back frequently. It may be more cost effective to spend more upfront to keep patients out of the hospital for a longer period of time.

Physicians need to be in line with hospitals for the most part—we have to respect the cost of the case. I think most physicians practice relatively economically, and not necessarily less efficaciously. When we start getting into ISR cases, these patients tend to come back over and over again. They get frustrated with their health care when they have to return to the hospital. It gets to the point where spending more money up front for one individual procedure to keep the patient out of the hospital longer is better for everyone. I don't think we're at a stage where we're curing anyone of ISR. The ideal scenario is that we do one procedure and wave our hands and they're cured, but every procedure has some degree of failure, so we need to strive for a better option.

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How necessary is embolic protection? Which disease presentations or therapy options precipitate the need for it?

Embolic protection is something I've been very interested in for nearly 15 years, and I have been involved in almost every filter developed. My strategy has been to try to use them as often as possible. The cost argument comes up often—filters in general cost around $1,500, and it's not a reimbursable item, so hospitals don't get paid for that filter. So why would operators use them? The cost of one case having severe embolization skyrockets, so it comes to using filters prophylactically. We've looked at cost effectiveness of filters and there is a significant cost benefit of using them on a routine basis.

Using them selectively, as some physicians advocate, is the equivalent of only using your seatbelt on the highway, but not using it when you're driving around the city. Some people say they are only going to use it on the high-risk cases, but every case has the potential to embolize. Every time we dilate arteries with balloons, we crack atherosclerotic plaque—it's the same as breaking a saltine cracker 6 inches above the table and being surprised by seeing crumbs fall down.

Patients who end up with major amputations have a mortality rate at 1 year that approaches 20%. It's not a benign process to amputate someone's leg if you cause a severe complication. Filters are something you hope you don't need, but you're sure happy you used one if you get into a bad situation. Current filter devices are not perfect and have limitations, but I think they are clearly better than not using a filter.

What needs to occur to trigger a paradigm change in filter usage?

Educating physicians on the complications of embolization. The problem with embolization is that its incidence depends on how you look for it. If you use angiographic criteria, the incidence is very low, 2% or less. We did a study close to 10 years ago (the PROTECT registry), where I had the idea of putting a filter down for every case regardless of the type of procedure. The embolization rate ranged from 40% to 80%. However, if you look at Doppler, the rate is 100%, no matter what kind of artery. Most operators who say they don't have embolization aren't looking for it. It's like closing your eyes and saying you don't see it. Low-volume operators don't use filters because they think the filters are too complex, and high-volume operators don't use them because they think they don't need to. They think they don't have complications.

If you end up having an amputation, that's a devastating outcome. The attitude should be, "Why am I not using a filter here?" rather than "Should I use a filter here?"

What is at the top of your device wish list when it comes to treating peripheral arterial disease?

In no particular order, I would like a peripherally dedicated filter. The ones we use right now are designed for carotid arteries, saphenous vein bypass grafts, or coronary arteries, not the periphery.

I also don't think we've defined the optimal treatment strategy for heavily calcified lesions. These are very hard to treat, no pun intended, both in terms of acute procedural success and long-term patency.

Also, antirestenotic therapy for tibial arteries. It's very frustrating to see what is available in Europe and know that we are at least 5 years behind in the United States.

In the era of the Sunshine Act, what do you think the ideal physician partnership with industry looks like?

Physicians have to partner with industry, and industry has to partner with physicians. Physicians have invented at least 80% of all medical devices, regardless of the field. Physicians are on the front line of developing new products, so there has to be a relationship. The Sunshine Act is trying to prevent biased care decisions by making the physician/industry relationship transparent. I'm not convinced that publicly making this information available is the right way to deal with the issue. I think the way the government has gone about it is wrong, despite good intentions. The way it's been executed has been wrong, and the data that are published on the CMS website are inaccurate. Publishing erroneous data on a public website simply inappropriately vilifies physicians. In the long run, I think it will slow the growth of medical progress. There will be physicians who become reluctant to work with industry out of concern that the general public will perceive them in a negative way. Overall, it will have a negative impact.

As a related example, the state of New York has mandatory outcome reporting. If you look at the data, the incidence of complex PCI cases in the state of New York has dropped dramatically compared to states that don't have mandatory outcomes reporting. Physicians in New York are afraid of doing complex procedures on patients that have potentially higher mortality. So, rather than doing procedures to save lives on critically ill patients, the unintended consequence is that sick patients aren't treated. In the same analogous way, the Sunshine Act is designed for one goal, but the unintended consequence is that it will make physicians less likely to work with industry. ■

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