Robert M. Bersin, MD

The esteemed interventional cardiologist discusses the future of carotid stenting, the uptake of percutaneous EVAR, and treating the complete patient.

From your perspective, what does the future hold for carotid artery stenting? Do you believe there will be a certain subset of patients for whom CAS will consistently be the better option?

There is an undeniable role for carotid stenting, and there are a number of circumstances where it's essential—patients who are either very high risk or inoperable for either anatomic or clinical lesions. That was best demonstrated in the SAPPHIRE trial, where a team of operating surgeons and interventionists reviewed all the cases to determine eligibility for randomization, and only 43% of all patients screened were eligible for surgery.

What do you do with the other 57% who have a critical carotid stenosis, may even be at risk for stroke, and are not candidates for an operation? A stent should be placed. SAPPHIRE demonstrated that the patients actually do very well. Patients who are eligible for either treatment do better in the first year with a stent than with surgery, and beyond that, they are equal.

For the larger population of patients who are standard-risk candidates for surgery, the question becomes more clouded as to what's better to offer the patient. Studies were performed on standard-risk symptomatic patients in Europe and on both asymptomatic and symptomatic, standard-risk patients in the United States. CREST enrolled symptomatic and asymptomatic standard-risk patients; ACT-1 enrolled exclusively asymptomatic, standard-risk patients.

The trials performed in Europe on standard-risk, symptomatic patients suggested that surgery was superior to stenting in most situations. The problem with those trials, which has been pointed out many times, is that they were performed by operators with very limited stenting experience, and in many instances, the stent implants were performed without embolic protection with particularly poor results. Transferring those outcomes to what we have observed with experienced operators in the United States simply cannot be done but often is.

If you focus on the trials that are relevant to those of us practicing in the United States, you have two basic studies: SAPPHIRE in the increased-surgical-risk group and CREST in the standard-risk group. CREST showed absolute equivalence in the primary endpoint for increased and standard-risk patients going out to 4 years, which included risk of stroke, myocardial infarction, and death combined.

There is quibbling about the fact that there was a slightly greater risk of myocardial infarction with surgery (1.2%), and a slightly greater risk of stroke (1.8%), largely minor stroke, in the stent arm.

So, what's worse for the patient—a heart attack or a minor stroke? What are the outcomes of both of those events? If you look at the fates of those suffering minor stroke, the number of patients with residual neurologic deficits at 6 months was equal in both treatment groups (N = 7). On the other hand, myocardial infarction was a strong predictor of death, whether it was with surgery or stenting. Those who had a myocardial infarction had a 25% mortality rate at 4 years.

In the end, what's better for the patient? If you suffer a minor stroke, at 6 months your NIH stroke scale and your disability are equal either way you are treated. On the other hand, if you suffer a myocardial infarction, mortality is increased from 5% to 25%. Those data would say that the myocardial infarction is worse for the patient.

One caveat about these studies is that they were performed with filter embolic protection devices for carotid intervention. There is an excellent alternative method for cerebral protection: proximal occlusion. Two proximal occlusion devices have been cleared by the FDA: the Gore Flow Reversal system (FRS) (Gore & Associates, Flagstaff, AZ) and the Medtronic Mo.Ma (Minneapolis, MN).

When and how should proximal occlusion devices be used in carotid artery stenting? How do these devices compare to embolic protection devices in terms of adverse events?

There have been seven prospective trials and registries reported in the literature on proximal occlusion systems, including registries, IDE, and CE Mark trials for each device. The outcomes for these trials were consistently superior.

This observation led me to pursue a project to obtain all the original source data for the seven trials, which included the two US IDE trials, the two European CE Mark trials, and two other large-scale registries. Six of the seven had excellent electronic data that could be imported, but one of the older Italian trials did not have electronic data sufficiently intact to import and was excluded. The data were submitted to an independent third party, the Harvard Clinical Research Institute, to be merged and analyzed.

The aggregate database of the six trials was as large as CREST—2,397 patients. The analysis was striking. The risk

(Continued on page 89)

(Continued from page 90)

of stroke and death at 30 days was the lowest ever reported (2.25%)—lower than reported with endarterectomy in CREST. For the first time, the symptomatic status of the patient was not a risk predictor, which had been the case with all previous trials of endarterectomy and carotid intervention with embolic protection devices, typically with a twofold increased risk for symptomatic patients (3% for standard-risk asymptomatic patients and 6% for standard-risk symptomatic patients). These 3%/6% benchmarks for outcomes in standard-risk patients are still applied today. However, the outcomes using proximal occlusion devices in symptomatic and asymptomatic patients are equivalent, and that risk was under 3% in all subgroups. In other words, proximal occlusion devices neutralize the symptomatic status of the patient as a risk factor. We had suspected that might be the case, because proximal occlusion devices allow you to protect the artery before it is manipulated. The postmarket registries for carotid stenting have also consistently observed a higher risk of stroke and death in symptomatic individuals compared to asymptomatic patients who are treated with filter protection.

The open-ended question remains as to whether stenting could be superior to surgery if a proximal occlusion device was used instead of a filter device. Unfortunately, that study has not been performed. With 2,397 patients in the meta-analysis, those data cannot be ignored. For that reason, most operators are now thinking of using proximal protection first, and filter devices second.

What are your predictions for the uptake of percutaneous EVAR? Will this approach eventually be applicable to all AAA patients?

Percutaneous EVAR is definitely taking over. We know that as the delivery size of the device decreases, the risk of complications decreases. The proportion of patients eligible for percutaneous closure has increased. The next-generation EVAR devices coming onto the market that are in the 12- to 14-F range will routinely undergo percutaneous closure; there is no reason to do a cutdown on a 12-F device. Even if the closure device fails, it can be treated with hand pressure and/or a FemoStop (St. Jude Medical, Inc., St. Paul, MN), with the option to do a femoral artery repair later if needed.

In our institution, percutaneous EVAR is the default mode for vascular access. We do surgical exposure only when the vessel is not suitable for percutaneous access or when the percutaneous closure fails. That's becoming the case everywhere. As a result of this trend, there are a number of large-bore closure devices in development that may improve upon the reliability of the currently available suture-mediated ProGlide and ProStar closure devices (Abbott Vascular, Santa Clara, CA).

What is the latest update on the INSPIRATION trial, which you presented at ISET earlier this year?

The INSPIRATION trial is the IDE trial for the Incraft endograft (Cordis Corporation, Bridgewater, NJ) for the US and Japan, and finished enrollment in August, so it is now in follow-up. A year from now, we will have completion of the trial for analysis and submission to the FDA. This was one of the first joint US/Japan FDA IDE trials that will lead to eligibility for device approval in both countries. The early results were favorable, so we look forward to welcoming this low-profile (12-F sheath equivalent) device to the market soon.

You cover a variety of disease states. What advice do you have on managing the whole patient?

When a patient gets referred for a renal, carotid, or lower extremity problem, we don't just stop at that organ system. We may address the immediate problem initially, but when he or she comes in for follow-up, we look at the whole patient and say, "You are being followed up for renal artery disease, but have you ever been screened for carotid artery disease? Do you have any leg claudication? Have you ever had a lower extremity arterial duplex? What about your risk profile? Cholesterol status? Smoking history?" The whole patient is addressed, and risk factors are modified.

If patients come to me for evaluation of peripheral artery disease, they get carotid duplex ultrasound whether or not they have a bruit, because the risk of them having carotid stenosis is significantly higher in this population. However, performance of a lower extremity Doppler depends on the physical findings and whether the patient has symptoms.

Because they have established vascular disease in other organ beds, you already know they have an increased cardiovascular risk. The lower extremity duplex is more to define anatomy if you suspect significant lesions.

Another unanswered question is, when do you screen for coronary heart disease in patients with vascular disease and how do you do so? In the asymptomatic patient who is not a claudicant, a coronary calcium score may be the test to do. On the other hand, in a patient who is a claudicant and cannot walk enough to develop symptoms, you may want to do a pharmacologic stress test. It can vary, but some screening for coronary disease is appropriate in those who have advanced and/or previously intervened vascular disease. ■

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