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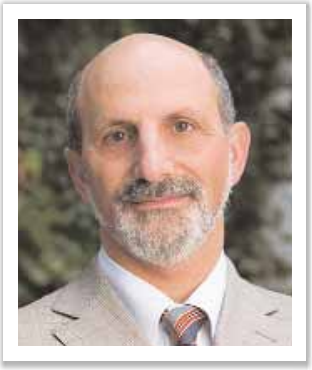
An expert asserts the importance of trials and registries, reflecting on lessons learned from his own experience, and discusses this year's VIVA meeting.

What are the key components to achieving "global vascular" management of peripheral vascular disease?

Global vascular management entails several key elements. First, the provider must consider all of the patient's vascular issues—not just the one that is the most noticeable or bothersome, or the primary reason for which the patient was referred. For example, if a patient is referred for evaluation of severe bilateral renal artery stenosis, it is important to use the opportunity to determine whether the patient suffers from intermittent claudication; has carotid bruits or TIA symptoms; or has angina, congestive heart failure (CHF), or other symptoms indicative of cardiovascular disease.



Second, in any given patient, the clinician must appreciate the interaction of the vascular disease in different territories. For example, the patient with left ventricular hypertrophy (LVH) or CHF might have renovascular disease as the cause; alternatively, the patient with angina after coronary artery bypass grafting (CABG) might have a left subclavian stenosis resulting in a "coronary-steal" phenomenon. Finally, the patient whose hip is bothering him during post-CABG rehabilitation may have an iliac stenosis.

Third, the provider should evaluate the impact of the vascular pathology on the patient's general well-being. This requires having an appreciation for the patient's lifestyle, emotional state, social and living situation, and expected longevity. Fourth, global vascular management implies that risk factors are being addressed, and that the clinician is not just thinking about the current visit or interaction.

In summary, the point of global management is to avoid the temptation of "tunnel vision," or focusing only on a single vascular problem. Instead, assessment and therapeutic decision making regarding vascular disease should occur in the context of the patient's overall health and well-being.

What have you learned as the National Co-Principal Investigator of the ACT I trial?

ACT I is a landmark trial comparing the outcomes of carotid artery stenting (CAS) and carotid endarterectomy (CEA) in patients who are at standard risk for CEA. The trial is designed and powered to detect whether CAS is "noninferior" (eg, equivalent) to CEA in prevention of stroke, death, and myocardial infarction (MI). Enrollment criteria are strict: only those with a stenosis severe enough to warrant revascularization can be included. Of note, the very important, NIH-sponsored CREST trial combines both asymptomatic and symptomatic patients. ACT I is the first trial to focus on only standard-risk asymptomatic patients. Because this represents the largest cohort of patients that undergo endarterectomy each year in this country, it is particularly important to determine whether CAS produces the same outcomes. If such is the case, then this will provide many more patients with the option of CAS for revascularization to prevent stroke.

Jon S. Matsumura, MD, my Co-Principal Investigator, and I played a large role (along with other key physicians, including Drs. William Gray, Michael Dake, Jim Zidar, Mahmoud Razavi, and the late Don Schwarten) in convincing Abbott Vascular (Santa Clara, CA) to undertake ACT I. It is an industry-sponsored trial, but Abbott has always respected the importance of staying at arm's length from certain operational aspects so as to minimize conflict and maintain the scientific integrity of ACT I.

Dr. Matsumura and I have been "hands-on" national principle investigators. We are involved in every aspect of ACT I and thus have learned a tremendous amount about the logistics of conducting a large, multicenter, national trial. We appreciated early on, by reviewing the results from other trials, the importance of selecting appropriately trained investigators, who would enable balanced and fair comparison between the two study groups. We therefore created formal Interventional and Surgical Management Committees (IMC and SMC, respectively) to select participating interventionists and surgeons who are highly experienced and talented individuals, dedicated to their craft and to choosing the proper patients to randomize in ACT I. We have also learned the value of giving our investigators a sense that they are part of a team, with a shared mission: to answer important scientific questions. Finally, we have learned first hand the importance, in the current era, of conducting a trial with the highest integrity and standards, so as to maintain scientific validity.

What are the goals of the CARE registry?

CARE is one of several registries within the "family" of the National Cardiovascular Data Registry (NCDR); it was created about 2 years ago with the intent of collecting

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outcomes data for carotid revascularization procedures including both stenting and endarterectomy.

The goals of CARE are many. One primary goal is to enable interventionists and surgeons to assess their own results and allow comparisons to their colleagues' results both locally and nationally (eg, to enable "benchmarking"). This might enable a local practitioner or hospital to identify and resolve problems early on so as to optimize outcomes. Another goal of the registry is to accumulate a large body of data on carotid revascularization procedures, both stenting and endarterectomy, and to use that data to inform our decisions about what is appropriate versus inappropriate care. We might find, for example, that patients with a certain profile do more poorly with one therapy and better with another. Likewise, the registry will eventually become robust enough to enable true risk adjustment. Ultimately, CARE is going to be a very important tool for physicians, hospitals, payers, government agencies, and (last but certainly not least) patients to assess quality of care, to determine best practices, and to improve outcomes.

I was very involved with the inception of the CARE Registry. Ralph Brindis, MD, who is the head of NCDR, was visionary to push the concept and obtain the support of the NCDR Management Board. The subsequent effort that went into the actual creation of the Registry was enormous and involved the collaborative efforts of a dedicated group of cardiologists, vascular surgeons, neurologists, vascular medicine specialists, neuroradiologists, radiologists, and NCDR staff. Each and every proposed data element was carefully scrutinized; once selected, a formal definition was created for that element. The elements were then assembled into a unified data collection tool, which was codified and put online.

One unique aspect of CARE—setting it apart from the other NCDR registries—has been the involvement of many disciplines in the Steering Committee. It was structured this way to acknowledge the many stakeholders in carotid artery therapy. Chris White, MD, in his role as Chairperson of the CARE Steering Committee, has done a masterful job of coordinating the input from multiple specialists, keeping us all on the same page, and maintaining the forward momentum.

To date, there are already more than 6,000 entries of individual patient procedures, approximately two-thirds CAS and one-third CEA. As these data are accumulating, the role of the Research and Publications (R&P) Committee, for which I have the privilege of serving as chair, will become more important. Proposals for research projects and manuscripts based on analysis of the data will be considered at regular intervals throughout the year using a formal review process. Those projects deemed to be meritorious will be supported, and access to the relevant data will be provided. Mid-America Heart and Vascular Institute (MAHI), designated as the CARE data analysis center, will work with the investigators and the R&P Committee to complete the analysis and publication. We anticipate many analyses and publications will emanate from CARE.

Individual physicians and hospitals will be able to benchmark using CARE; in addition, CMS and other payers are going to be very interested in the data that are generated. But, ultimately, CARE is designed to improve the outcomes and quality of care for patients. I believe it is essential for hospitals that are performing carotid stenting to join the CARE registry. This is very important in terms of moving this therapy forward.

What can the CREST trial tell us so far?

The CREST trial is another landmark trial that will be important in identifying the role of carotid artery stenting versus endarterectomy. There are those who claim that neither strategy is appropriate, and that in the current era, revascularization should be reserved only for those who desperately need it, and that medical therapy for asymptomatic patients has greatly improved. While this is true to an extent, trial after trial over the past 25 years has shown us the benefits of revascularization over medical therapy in both symptomatic and asymptomatic patients, so long as the stenosis is high grade enough and the patient is going to live long enough to benefit from the procedure. That said, CREST and ACT I are going to be important, even though neither has a randomized arm to medical therapy. Such a trial (TACIT trial)—with three arms: medical therapy versus CAS versus CEA—has been proposed. Although this would provide important scientific information, it might require creative strategies to enroll. Patients, once they are aware they have a critical stenosis, often want the artery opened, even with the attendant risk of stroke.

There is one conundrum that both CREST and ACT I have faced. As is true with CEA, the optimal patients for carotid stenting may be those under the age of 65, who are young and otherwise healthy. Unfortunately, many third-party payers have not agreed to pay for hospitalization of members enrolled in a clinical trial; therefore, this ideal population does not have access to these important studies. Ultimately, it will be important to evaluate results in this younger population, especially because those older (especially >80 years) and more infirm patients seem not to do as well with either mode of revascularization—CAS or CEA. Nonetheless, CREST will provide a tremendous amount of data about carotid

artery disease and the management thereof. It will hopefully give us level I evidence regarding the utility of CAS versus CEA. It is worth noting that Robert W. Hobson II, MD, who was the Principal Investigator and initiator of the CREST Trial, sadly passed away prematurely and will not get to see the fruits of his labor. CREST will be a lasting legacy to Dr. Hobson, without whose persistence it would not have been consummated and continued. Thomas G. Brott, MD, another force behind the trial, has assumed the role of National Principal Investigator. Dr. Brott is a brilliant neurologist, scientifically driven, and very fair-minded. I am pleased that CREST will continue to be led by someone so distinguished, who has a balanced perspective.

What improvements and developments would you like to see in distal protection devices used in carotid artery stenting?

Distal protection is the single most important advance that allowed us to achieve acceptable, if not excellent, outcomes in carotid stenting. Without it, we would not be where we are now. The devices that are presently on the market are quite good, but we want perfection. We need filters that have perfect apposition to the wall of the vessel beyond the lesion, that are easily delivered, ultra-low profile, that do not disrupt the plaque as the interventionist delivers them. We need proximal occlusion devices that are 100% effective in removing debris.

It is unlikely that there will be just one type of embolic protection that will be perfect for all patients. The important thing is going to be discerning which type of protection device is appropriate for each specific patient.

Incidentally, this is another role that the CARE registry might play; it will enable accumulation of real-world information about device use that will hopefully inform us which patients fare better with each type of device. In addition, CARE may enable us to evaluate the role of novel approaches to embolic protection that we have not yet considered. Perhaps some combination of devices will work best. My friend and CAS maven, Jay Yadav, MD, has shown a case wherein he used two serial filters. The distal filter caught debris missed by the first filter. That kind of "outside-of-the-box" thinking is what will enable us to achieve a higher level of safety in performance of CAS. We must not allow ourselves to be constrained by current techniques and devices; rather, we need to be creative and develop new paradigms. I firmly believe that CAS will ultimately provide unprecedented safe and effective revascularization and stroke prevention for the vast majority of patients. When that time comes, there will still be a role for CEA, but it will be much more limited. I would estimate that, in another 5 or 10 years, after all the political and economic issues are settled, most patients requiring revascularization will undergo carotid stenting.

Is VIVA Physicians Inc. currently working to develop any new clinical studies or guidelines?

Clinical research is a major focus of VIVA. Krishna Rocha-Singh, MD, has done a phenomenal job of spearheading the research effort within the organization. He is passionate and tireless about this. We have developed a clinical trials program that is increasingly robust. VIVA is interested in targeting the areas that are the most interesting and the most relevant—where there are gaps in our knowledge base. For example, the VIVA EXCEL trial deals with infrapopliteal stenting for critical limb ischemia.

VIVA is also interested in developing practice guidelines and working with other entities to move our field forward. We see it as our duty to increase the evidence base in endovascular therapies.

Finally, as you may be aware, VIVA has been fortunate enough, primarily through the efforts of Michael Jaff, DO, Krishna Rocha-Singh, MD, and Gary Ansel, MD, to work with the FDA to develop reasonable performance criteria for obtaining approval of stents in the superficial femoral artery/popliteal artery. This type of collaboration helps our field, and we are proud to be a part of it.

What will be different this year at VIVA '08?

It has always been our intent with VIVA to create a conference that was focused primarily on education and not unduly influenced by current trends or our own biases and relationships. We have always aspired to find the best ways to deliver that educational content, such as Laptop Learning. The format at VIVA provides attendees with an unmatched level of communication directly with faculty.

We do have some changes and additions to the agenda this year at VIVA '08. First, we have moved VIVA to a spectacular new venue—the Wynn Las Vegas. The Wynn provides a more intimate and higher-quality location. In our ongoing quest to find the best ways to deliver educational content, we have developed some new sessions that make VIVA distinct. Last year, we added VIVA Dialog Sessions, which were wildly popular. This year, we have added another intimate session called *Chalk Talks*. The purpose of these sessions is to have faculty members explain how they approach patients with different conditions and how they actually do procedures. The format is interactive and encourages attendee participation. Dialogs and Chalk Talks provide an opportunity to interface closely with our distinguished faculty. I am encouraging people to sign up early because we already have an unprecedented number of people registered for this year's VIVA. ■