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One of the world's pre-eminent vascular surgeons shares his viewpoints on the EVAR and DREAM trials and Charing Cross 2006.

During the past several months, the EVAR and DREAM trials have received disparate interpretations by speakers at medical conferences and authors in both medical journals and the mainstream media. What is your interpretation of the design and implementation of these two trials? The EVAR trials are the first randomized trials for assessing the value of endovascular surgery for abdominal aortic aneurysms. EVAR I was a comparison of endovascular repair against open repair in patients who were otherwise fit for open repair, but suitable for endovascular surgery. EVAR II was a separate population of patients who were unfit for open repair, but suitable for endovascular surgery; these patients were randomized between best medical treatment and EVAR against best medical treatment alone.

Subsequently, the DREAM trial used a very similar protocol to EVAR I, but with a smaller number of patients. EVAR I is fully and properly powered using the right number of patients to expect an evaluable result. The DREAM Trial was always powered on the basis of 30-day mortality and nothing else, and therefore the numbers involved in DREAM are significantly smaller. The value of DREAM is mainly that the findings do not conflict with EVAR I, but, on a stand-alone basis, it is hardly strong enough or large enough to be able to have a distinct message.

What is your interpretation of the data from the EVAR and DREAM trials? The messages of the EVAR trials are quite stark. When the results were analyzed, EVAR II failed to show any mortality benefits in patients who underwent endovascular repair, in whom the anatomy was suitable for endovascular repair. We had modeled and expected that a group of patients who were unfit for open repair would have a 50% mortality rate over 2 years. We also expected a larger number of ruptures than we observed. We found that in patients who were suitable for endovascular repair, there was something in their anatomy that conferred a lower rupture rate than was anticipated.

A crystal clear finding of the EVAR trials was that there should be a change in focus—instead of doing early EVAR, the emphasis should be on getting the patients to their fittest state rather than early intervention. I, for one, will alter my approach to EVAR in that type of patient. I will be very reluctant to offer EVAR in the very sick patient. Where, in the past, I would be inclined to use EVAR straight away because I thought that the cause of death was likely to be a ruptured aneurysm, I now know that the cause of death is not essentially always a ruptured aneurysm, and it is very important to get the patient to be more fit.

As far as EVAR I is concerned, there is no difference in all cause mortality. But, we were able to show-I think more clearly in EVAR I than in DREAM-that the aneurysm-related mortality is significantly better at the mid-point of the trial: there is a 3% aneurysm-related mortality benefit for EVAR in the mid-term, and there is a 3% benefit from the operative mortality. In other words, the 3% operative mortality benefit, which was significant, is maintained and is significant in the EVAR trial. All we can say about the DREAM trial is that the data are in line with the EVAR trial, but they could not on their own make the conclusion either for or against EVAR in the mid-term because the numbers are not large enough to do that. But, it is supportive of EVAR I.

You have been an outspoken critic of the PIVOTAL and CAESAR small aneurysm trials. What is the basis of your criticism, and do you see any benefit to determining whether earlier intervention will improve outcome? I am proud to have been the Principal Investigator the UK Small Aneurysm Trial. I find great difficulty in the comparisons I see being made by some distinguished colleagues. For example, they are using the follow-up arm of the UK Small Aneurysm Trial, in one continent, in one decade, to compare to endovascular repair in another continent, in another decade, and then claim to show the benefit of EVAR in small aneurysms as a justification for intervention. I have spoken against EVAR intervention in small aneurysms for the simple reason that in the UK Small Aneurysm Trial, we set up the trial because we were certain that it was obviously sensible to offer surgery to a smaller aneurysm in a fitter patient (who is a younger patient) than to wait for the

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aneurysm to get bigger and more difficult in an older patient who is less fit. It was so obvious that we decided to put it to the test.

To my surprise, we were proved wrong. The basis on which we set up the UK Small Aneurysm Trial was blown sky high. The protocol we used was not surveillance, as some people say, but a protocol of awaiting either the aneurysm reaching 5.5 cm, the aneurysm growing more than 1 cm per year, or the aneurysm becoming tender. That protocol was the starting point of the EVAR trials and was the starting point of intervention of the follow-up arm of the not-immediate intervention group in the UK Small Aneurysm Trial. The difference between the two arms of the UK Small Aneurysm Trial is that one had early surgery, and the other had surgery if and when the patient reached one of those protocol points. The outcome was such that there was no benefit from earlier intervention against our expectation.

Imagine performing EVAR after a period of using the protocol, and instead of a mortality rate in the delayed group of 7.1%, it is 1.7%, which is the 30-day mortality for EVAR. The expected mortality of a 5.5-cm aneurysm, or one that has become tender, or one that has grown fast, will be 1.7% by EVAR. Imagine what that will do to the comparison with early surgery. What is the possibility that early surgery can beat that (in the UK Small Aneurysm Trial, 1% rupture rate per year; in the ADAM Trial, 0.5% rupture rate per year)? The possibility of early intervention beating that is so small as to make the two proposed trials supported by two great industrial concerns of dubious benefit to the patient. Imagine what the clinician and the companies are going to have to say to the patients when the patients learn that they have had a procedure recommended for a condition, which in the US has a 0.5% rupture rate per year, and the expectation of natural history after EVAR is about the same. "Why on earth," they will say, "did you give me this operation when the natural history is not significantly better? You have put a device inside me which means that I've got the complications of that as well." Will they thank you for that?

I have said to the companies that I would prefer them to use their ingenuity to develop innovative techniques to grow their business at the other end of the market-to learn how to treat more of the large aneurysms by endovascular means, the ones with the difficult branches and the stent graft systems. I'd like the fenestration and the branch graft systems to become available to many regional centers, and for companies to be developing graft systems rather than trying to encourage surgeons to feel comfortable at intervening in the very small aneurysms. The trials are a technique or a mechanism to give a comfort zone to those surgeons who are being encouraged to do what I consider to be the wrong procedure at the wrong time.

Are there any other additional trials that you would like to see take place regarding other endovascular therapies? Yes, I am currently Principal Investigator of the MIMIC Trial (MIld to Moderate Intermittent Claudication) and I am anxious to establish if angioplasty is of proven benefit in patients with claudication, given that supervised exercise is of benefit. I am leading that investigation, and I would like to be able to come up with a clear algorithm of management of intermittent claudication.

What can we expect will be the main topics of discussion at the next Charing Cross meeting, and what will be the big controversies? We are picking up from the very successful 2005 meeting where there were more than 1,500 participants from over 50 countries. At next year's Charing Cross we will combine showcasing of the latest innovations in the Global Endovascular Forum with a close examination of the evidence in a series of debates on controversies that were identified in this year's consensus discussions. Above all we always hope to achieve a balance between radiological input and vascular surgical input for endovascular matters and vascular matters. Sometimes, I think I have been criticized for going too far over to the endovascular, but this is not because I am an endovascular megalomaniac. This is because the Charing Cross stands for both innovation and evidence. If there are a large number of new procedures in the vascular field, then I want to be the first to both show and scrutinize them. The reality is that many of the new, intricate procedures are endovascular and, therefore, I cannot find a good reason for not showing and scrutinizing them. Above all Charing Cross allows us to look at the evidence as to whether something works and we always allow plenty of time for discussion involving both the faculty and an expert audience, most of whom are senior vascular specialists. And so alongside innovation, the Charing Cross always focuses on the major controversies, challenges the available evidence in order to reach consensus after what can be a heated discussion. I look forward to seeing many of my colleagues next year in London's Imperial College for the 28th Charing Cross International Symposium on April 8-11, 2006. ■