

Analyzing the Impact of INSTEAD at 5 Years

Matt M. Thompson, MD, FRCS, discusses the long-term results of INSTEAD with Principal Investigator, Christoph A. Nienaber, MD, and their influence on treatment protocols for aortic dissection.



Prof. Thompson: What were the original design and goals of the INSTEAD trial?

Prof. Nienaber: This was the first randomized trial to compare best medical therapy (BMT) with stent graft placement in addition to BMT. It was designed to compare and evaluate the impact of stent graft placement on type B aortic dissection in patients who were traditionally conservatively managed with

drugs alone. Patients were selected in the subacute phase after they survived a type B aortic dissection.

The initial study period was planned for 2 years of follow-up; those results were published in 2009 and did not show a significant difference in outcomes (survival, vascular survival, and progression) between groups.

However, aortic remodeling and stability were seen in 90% of cases that involved elective stenting in addition to BMT. There was a 20% crossover rate to stenting or surgery in the BMT group due to false lumen expansion and late complications.

INSTEAD-XL was the amended follow-up study to INSTEAD, extending the follow-up to 5 years. This long-term follow-up study showed that the BMT group experienced further ongoing late complications and fatalities, whereas the initially stented group had a rather stable long-term course, with no late fatalities up to 5 years.

Prof. Thompson: What were the key observations from the extended follow-up?

Prof. Nienaber: The so-called uncomplicated type B dissection is in fact not uncomplicated; between 2 and

5 years after dissection, the BMT group revealed sudden fatalities, further expansion of the false lumen, rupture, and other late complications. Those adverse events were not seen or rarely seen in the stent graft group, which obviously benefitted from induced remodeling. Only cases with evidence of remodeling guaranteed a stable, uneventful long-term course.

Prof. Thompson: As with any long-term study, technology has continued to evolve since the inception of INSTEAD. How would you address challenges to INSTEAD's continued relevance? To what degree does it withstand the tests of time, namely new technology and increased operator experience?

Prof. Nienaber: With long-term follow-up, we see the beneficial effects of upfront scaffolding in so-called uncomplicated dissection, even though a first-generation stent graft was utilized. Nevertheless, such relatively primitive technology was able to show the advantage of scaffolding and induced remodeling of the aorta. I expect that with more modern contemporary stent graft technology and more operator expertise, the results would be strikingly better today than in those early days with first-generation stent grafts. Moreover, the manufacturers are beginning to work on dissection-specific devices, a concept that did not exist in the early days at the inception of INSTEAD.

Prof. Thompson: There was a considerable number of deaths in the BMT group at

longer follow-up. What were the causes of these deaths?

Prof. Nienaber: Those deaths usually occurred suddenly, which is suggestive of aortic rupture. Some patients were identified as having an enlarged false lumen awaiting repair (which is difficult in the very chronic phase of dissection), and others were not identified in the surveillance period but obviously ruptured suddenly as well. Conversely, scaffolded patients had a stable long-term outcome, suggesting that even a surveillance program with repeat CT angiography may not identify conservatively treated patients who will eventually rupture.

Prof. Thompson: Do the deaths in the BMT group imply that standard surveillance protocols are unsafe?

Prof. Nienaber: To some degree, it became clear that even a subcritical dimension or diameter of the aorta in the BMT group is not a signal of safety. We are searching for other and better parameters to identify patients who are at risk of rupture with subcritical dimensions; this will become increasingly important. Nevertheless, the numbers are small, and not all patients had undergone recent imaging before they died. It is still a bit speculative to dismiss surveillance in nonstented patients. I still believe that surveillance and blood pressure control are important, but I also understand that most patients (if not all anatomically suitable ones) might benefit from scaffolding to stabilize and remodel their aortas.

Prof. Thompson: Can you relate the aortic remodeling in the INSTEAD study to clinical outcomes?

Prof. Nienaber: Yes, it seems that successful remodeling is key to stabilizing the previously dissected aorta and inducing healing and realignment of those aortic wall layers; in particular, in the thoracic aspects of the aorta. Death only occurred in patients without evidence of remodeling. We see this morphologic event of remodeling now in other observational studies as the major reason for stable long-term behavior of the dissected aorta.

Prof. Thompson: What are the implications of the study on the treatment of patients with uncomplicated type B dissection? Should all patients be treated? What determines an uncomplicated dissection, given recent data?

Prof. Nienaber: The community recognized the long-term benefits of an early interventional approach

to so-called stable, uncomplicated dissection, as we have learned that those patients have no long-term stable course and develop late complications that are usually fatal. The conclusion of those new long-term data is that a dissection is never safe under BMT, and an early investment of stent grafting will take longer to pay off in patients with complicated dissections but will eventually pay off beyond 2 years of follow-up. Thus, with modern dissection-specific technology, and with increasing expertise, almost every patient with dissection will eventually benefit from active treatment.

With this being said, a truly uncomplicated type B dissection is hard to imagine. In addition, there are new and very interesting factors on the horizon that seem to identify hidden dangers and impending complications and will eventually help to create an individual risk profile for any given patient with dissection.

Prof. Thompson: If you were going to treat a patient with an uncomplicated acute type B dissection, what timescale would you follow for thoracic endovascular aneurysm repair?

Prof. Nienaber: It is clear that patients with obvious complications or ongoing symptoms of pain require a timely intervention using the contemporary stent graft technology or stent grafts in combination with open stents. For the other candidates that seem to embark on a stable course (so-called uncomplicated type B dissection), I suggest using a window of plasticity of 3 months after impact of dissection for stenting. This window allows the opportunity to successfully realign the aortic layers and enable remodeling. Any later time would introduce the problem of increasing stiffness of aortic tissue and lamella and add additional technical difficulty to successful stent grafting. ■

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