The EVAR Revolution

Juan Carlos Parodi, MD, discusses what led him to develop the world's first endograft for the treatment of abdominal aortic aneurysms, how he surmounted early obstacles, and his perspectives on the philosophy of minimally invasive options to open surgery. Working alone and with fellow innovators such as Julio Palmaz, MD, Dr. Parodi invented a technology that offered new therapeutic options for patients who previously had none; in fact, one such patient, at the request of the President of Argentina, became the first person ever treated. Today, EVAR is one of the most predictable and universally successful life-saving procedures in medicine, and this therapy would not have come so far without the early and continued work of Dr. Parodi.

Endovascular Today: What was the standard of care prior to your invention of the endograft?

Juan Parodi, MD: Until we started using endografts, the standard of care was just to do the open operation. The first report of open resection of an abdominal aortic aneurysm and replacement with a homograft was in 1951. Dubost from Paris performed it through an extraperitoneal approach. Later, in New York, Voorees introduced the use of a fabric graft. Aortic replacement is a proven and very effective operation, but the magnitude of it restricts its use in very sick and debilitated patients. In addition, mortality and morbidity in patients fit for open surgery is still significant today. This was the main reason behind designing a less-aggressive, minimally invasive procedure as an alternative to the effective, but very traumatic open operation.

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EVT: Your inspiration was that it might be possible to use a minimally invasive technique to spare patients the trauma of surgery, but also to broaden the number of patients who would be accessible to this surgery?

Dr. Parodi: Yes, absolutely. Many patients could not undergo surgery because of the high risk. There are many examples of patients dying because nobody

wanted to take care of them due to their comorbid conditions. In addition, the mortality rate of surgery performed for ruptured aneurysms exceeds 50% in most series and has not changed in the last 20 years.

When I first conceived this idea, I was a resident at the Cleveland Clinic in 1976. I thought perhaps we could take advantage of the size of the arteries and enter in a retrograde fashion from the femoral artery, compressing the graft into a tube, and then releasing it inside of the aneurysm, excluding the area of the dilatation with a kind of covered metal component that I called a "cage." That cage was made of two zigs of elastic stainless steel joined by two bridges of the same material welded and covered with a Dacron graft. That was the initial prototype I designed in 1976.

EVT: What was the next step in the development process?

Dr. Parodi: After I produced the prototype, I began doing some animal studies. These were very crude experiences and prototypes because I was building the grafts in the research department using pieces of metal and welding them with materials and devices borrowed from the engineering department.

The initial experiments didn't work very well because I was not using an over-the-wire system, and also because I didn't have a nosecone for this tube. At least the idea was there, and I knew that it was feasible. Obviously, I needed more technical support and better kinds of prototypes.

EVT: How did you acquire more advanced materials?

Dr. Parodi: At the 1988 TCT meeting, I met Julio Palmaz, who presented his initial results with stents in animals. I did not know Julio at that time, but I approached him and learned that he too was from Argentina. I explained to him that I was trying to develop an endograft to treat aneurysms and that I was using a different kind of metal and a different kind of shape. I thought that it could be interesting to use his design for this purpose—just adapting his stent to a fabric graft instead of using the self-expandable, spring-loaded design. Julio was very kind and he gave me a couple of stents. I went back to Buenos Aires and tried them in animals, and it worked very, very well.

I then went to see an engineer back home who was working with missiles. I worked to convince him to get involved with the medical industry, and he accepted. He had very sophisticated equipment, and finally he started to produce stents. I had redesigned the Palmaz stent to make it larger and to have the ability to open up to 40 mm. We then got in touch with Johnson & Johnson and asked permission to produce these devices because they were based on J&J products.

EVT: How long was it before you were able to begin trials in humans?

Dr. Parodi: In 1990, the President of Argentina asked me to take care of one of his friends who had an aneurysm but could not undergo surgery. This patient was in very bad shape. He was having back pain, and he was concerned about his aneurysm. I had to explain to him and his family that we had done only 43 experiments in dogs. Together with his family, he accepted and signed a consent letter. I invited Julio Palmaz to be part of the first treatment because he was very kind in helping me. In September 1990, we performed the first case, which went amazingly well for being the first of its kind. The patient was having dinner after 2 hours and was walking the next day. Even for us, it was a big surprise.

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EVT: How long did that patient survive after the initial implant?

Dr. Parodi: That patient survived for 9 years, although we needed to perform a secondary procedure on him. Initially, we were using an aorto-aortic graft. In this case, the patient developed a distal neck dilatation, and we put the second system inside. He died 9 years later of pancreatic cancer. After this initial case, we did many others and finally published our experience in the *Annals of Vascular Surgery* in 1991.

EVT: What are some other devices or inventions that were spawned by your invention of the endograft?

Dr. Parodi: From the beginning, there were many people learning that this was a very attractive way to treat patients. The initial device that received FDA approval was the Ancure, which was developed by Endovascular Therapies Company. Other companies, such as Boston Scientific Corporation, Cook, Gore, and Medtronic, all developed their own products.

The endograft concept was used to reline arteries after balloon angioplasty, to treat trauma cases, and

was also used to prevent restenosis after TIPS. Probably the most important impact this development had was to alert the vascular surgeons that a new trend in vascular therapies was ongoing and that vascular surgeons could be part of these new developments. Iliac stenting was performed by radiologists and went unnoticed or rejected by surgeons. The perspective of losing aneurysms acted as a revulsive over the vascular surgeons.

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EVT: It was 14 years between the initial conceptualization of the device and the first procedure, and it has been another 14 years since the first procedure. Have we gone as far as we can go with the endograft?

Dr. Parodi: I believe that we are getting closer. As with any new idea, it takes time for people to understand it and for the industry to understand the impact that it could have. Also, this is not a very simple matter. I always compare this with the development of artificial cardiac valves. The environment in which a cardiac valve is implanted is so aggressive in terms of mechanical stress that in order to achieve the acceptable cardiac valve, we have seen nine earlier generations, which means that we needed to understand the failures and then to overcome the problems. I think these last 14 years were very, very important because we learned a great deal, and I think we are very close now to developing the ideal device.

EVT: What should the ideal device do or be?

Dr. Parodi: The ideal device should have a very low profile, it should be very flexible and durable, and all vascular specialists should easily apply it. Sometimes, when a new technique emerges, there are only one or two people in the world who can do it. Such procedures are not going to be applicable. We understood that the method should be simplified and made accessible to everybody. What we have also learned in the last few years is that the main issue pertaining to endografts is durability; material fatigue and the lack of adaptation to the remodeling of the artery after excluding the aneurysm are the big issues that need to be resolved.

Also, there are certain anatomies that require special designs. I would say probably 70% of cases can be covered with available systems, but in other cases you need special combinations of systems or a specific custom-made device specifically designed for a particular patient. Devices with fenestrations and branches have been developed during the last 4 or 5 years. There are other new developments, such as endosutures, which will likely be available soon. Endosutures perform like a stapler being applied from inside the lumen to attach the graft and better prevent migration.

EVT: What are some of the developments that will shape the future of endovascular therapy for the treatment of aneurysms?

Dr. Parodi: I've recently been working with a combination mechanical and pharmaceutical treatment for aneurysms, which we will probably see in the near future to treat small aneurysms, or patients with large aneurysms with unfavorable anatomy. We have been working with growth factors, inhibitors of the elastase, and other MMP inhibitors.

EVT: The goal, again, being that endovascular treatment should be equal to open surgery with regard to efficacy, but with less trauma to the patient?

Dr. Parodi: I believe that there are many studies now proving that is the case. There are at least three studies. One is the Lifeline Registry data that Chris Zarins presented at the last meeting of the Society of Vascular Surgery. He proved that the results are equivalent, at least for the projection of 6 years, and that the procedure provides the advantage of being less aggressive while offering less mortality and less morbidity. There were also two studies recently published in the *Lancet* and in the *New England Journal of Medicine*, also proving that the results are comparable, with less morbidity and mortality, at least in the short-term.

We still lack prospective randomized studies showing comparable results in the long run. In June, the EVAR 2 trial will report a long-term comparison between open and endovascular treatments.

EVT: Do you envision a day when the efficacy of this endovascular procedure could be proven in the long-term and stand up against open surgery?

Dr. Parodi: I think that time is going to come. I think that in 5 years, standard open surgery mostly is going to be a thing of the past, like open cholecystectomy.

EVT: For all patient populations?

Dr. Parodi: Yes, all patient populations. ■