The polymer-based concept in abdominal aortic aneurysms endovascular therapy

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The endovascular era has completely changed the traditional approach to abdominal aortic aneurysms repair. The possibility of substituting the aneurysmal dilatation by endograft with minimal (or no) invasiveness has opened new horizons to surgeons and patients.

Remote (mainly femoral) control of intrabdominal manoeuvres has been one of the first challenges in endovascular surgery, rapidly followed by the need for a safe, effective, and durable proximal securing of the aortic graft into the native aorta. Short, angulated, large, non-cylindrical, or highly thrombotic or calcific aortic necks are recognized as risk factors potentially leading to EVAR failure. Indeed, effectively anchoring the new graft substituting the native wall with a prosthetic one has long been the main issue in EVAR. To accomplish this important goal different mechanisms have been advocated and employed with good results and progressive improvement over time.

Radial force exerted by the endograft on the aortic neck has been one of the first features studied and used in EVAR. The pressure of the fabric on the vascular wall generated and supported by the metallic struts is the simplest and immediate way of securing the graft to the arterial wall and this concept was at the base of the first employed endografts in the past. The AneuRx and Talent devices (Medtronic Corporation, Santa Rosa, CA, USA) did not employ active suprarenal fixation and relied completely for attachment on graft oversizing.

Oversizing longly employed in aneurysmal correction ensures that radial force is always maintained over time. Despite a distinction must be made between fixation and seal, radial force exerted on the aortic wall by the calculated oversizing is able to accomplish both goals. Materials used to form the skeleton has progressively moved in most cases from stainless steel to nickel titanium alloy (nitinol) or cobalt chromium alloy. The first has the advantage of more elasticity since it follows the deformation characteristics of the various tissues of the living body but it can be responsible for continuous radial pressure on the aortic neck wall.

This exerted pressure has been advocated as involved in the aortic wall remodeling and its possible role in the occurrence of complications such as graft migration, endoleaks, and sac expansion.

Aortic neck dilatation is a common phenomenon after both EVAR and open repair, and has been investigated in numerous series. Dilatation of the aortic neck in aneurysmal pathology is, of course, due to the progression of atherosclerosis and progressive impairment of the native wall and some authors have reported that it can be enhanced by the apposition of the endograft and by its radial force. Nevertheless, some authors have indicated as endograft effect on aortic neck dilatation can be considered independent on the diameter of the native aorta. Dating back to 2002 Lee et al. have pointed out as changes in aneurysm remodeling over time are quite similar in EVAR patients with large infrarenal necks or with more favourable neck criteria. They concluded that EVAR in patients with large perirenal necks and challenging morphology did not increase the risk of migration nor affected the change in aortic remodeling. However, at the time of the study (1998-2001), patients with short or wide necks were mainly excluded from endovascular treatment by infrarenal fixation, so that the effect of the endograft pressure on very diseased aortic wall couldn’t be correctly investigated.

The possible consequence of this pressure, mainly the aortic neck dilatation, has been indicated as one
of the main causes of EVAR failure, because of possible endoleak occurrence or endograft migration. Tsilimparis et al. have found as oversizing of the endograft can be considered responsible for rapid neck change within the first postoperative month but it didn’t positively correlate with aortic neck expansion in the long-term. Nevertheless, other authors have shown a correlation between oversizing and neck dilatation on late follow-up, while Malas et al. have reported absence of proximal neck dilatation and graft migration after EVAR when using balloon-expandable stent-based endografts.

To minimize the possible enlarging effect of the endograft on the aortic wall and to maintain a secure fixation, active fixation by hooks and barbs has been tested and employed since many years. The Ancure device, one of the first to be designed with an active fixation by hooks at all attachment points, has been extensively studied and tested so that its clinical trials have prompted redesigning and refinements of new generation endografts. Hooks improve active fixation to the aortic neck and so they have the advantage of reducing possible complications due to inadequate proximal sealing. Today the vast majority of abdominal aortic endografts have some kind of hooks to secure the graft to the aortic wall. Results of major series reporting on the use of active fixation by those adjuncts have shown few or no effect on aortic neck remodeling.

Active fixation is able to secure durable results in EVAR irrespective of the suprarenal or infrarenal area used even in patients with challenging proximal neck characteristics, as demonstrated by a recently published single-center series on 340 patients treated by Gore Excluder (W. L. Gore & Associates, Flagstaff, AZ, USA) or Medtronic Endurant (Medtronic Vascular, Santa Rosa, CA, USA) devices.

Moving cranially, suprarenal flares or stents can surely improve stability by constituting a whole more or less rigid body with the graft to be implanted into the aorta. The straightening effect of suprarenal adjuncts can possibly enhance complete adhesion of the endograft to the aortic wall. Indeed, suprarenal fixation has the possibility not only of increasing fixation, but also of remodeling the entire neck zone. Surely, the straightening of the neck area has the possible advantage of decreasing the flow turbulence and so, possibly, of reducing the pressure on the aortic wall. Different devices have shown their efficacy in excluding the aneurysmatic wall by suprarenal fixation.

The Talent device (Medtronic Corporation, Santa Rosa, CA, USA) was one of the first developed utilizing a Nitinol frame and thin-walled polyester fabric and it had a suprarenal frame that allowed placement close to the renal ostia.

The ENGAGE trial has evaluated results in patients treated by Endurant Stent Graft System (Medtronic Vascular, Santa Rosa, CA, USA) that has a suprarenal fixation configuration. In this multicenter real-world experience early and 1-year follow-up results showed no significant differences in type-IA rate between patients with regular, intermediate, or challenging neck anatomies.

Adherence to the aortic wall can be enhanced by anchors. They have been more recently developed and employed to increase proximal fixation and sealing. The Aneurysm Treatment using the Heli-FX Aortic Securement System Global Registry (ANCHOR) study has evaluated clinical and imaging outcomes after EVAR with EndoAnchors, deploying EndoAnchors prophylactically at the time of primary EVAR or therapeutically when proximal neck complications arose immediately after endograft deployment or over long-term follow-up, demonstrating satisfactory results in terms of freedom from type I endoleak and aneurysmal sac regression or expansion at 1 year follow-up.

Nevertheless, the real fate of the aortic neck in aneurysmal disease is quite impossible to predict with certainty. This is why to treat the aortic neck by the use of malleable and adaptive plastic material can enhance the possibility of prevent complications of aortic neck changes over time.

Polymer use has completely changed the idea at the base of fixation and sealing, leaving to a plastic rubbery material the task of sealing the graft to the wall and maintain the seal over time. This goal can be pursued by the combination of different features in the Ovation stent graft (Endologix, Irvine, CA, USA; Figure 1.1). In this endograft a new kind of polymer is injected in liquid form as a 2-part solution that turns solid in around 14 minutes at normal body temperature. The Ovation endograft is a new-concept device that separates fixation from sealing; fixation is guaranteed by suprarenal stent and anchors, while sealing is ensured by inflatable rings filled with a low-viscosity, non-embolic, radiopaque fill polymer. The presence of the polymer-filled proximal sealing...
endograft onward, different polymer-base platforms have been developed and tested with an extensive use of it in some of them.

Sure enough, the polymer cannot be considered the only and final solution to AAA treatment, as demonstrated by recent series on the relatively new Nellix endograft (Endologix, Irvine, CA, USA), the only at the moment on the market to maintain the way that the solution to aneurysmal disease can be the aneurysm sealing (EVAS) instead of aneurysm repair or substitution. Despite encouraging and shocking early and mid-term results, late results on this kind of concept and endografts have demonstrated alarmingly high rates of failure of EVAS when compared to traditional EVAR design and concept (42% freedom from graft failure in patients treated for primary AAA at 4 year23). Maybe the final answer to AAA treatment can be in the place and dose of polymer used to treat this degenerating pathology, where the use of the polymer/filling rubber can be winning when dealing with proximal neck fixation and sealing, while it is not able to cure and stand the evolving degeneration of aneurysmal sac.

Technology is continuing to evolve and new solutions for aneurysmal disease are on the way. Only time can prove that the polymer has a role and is effective in aneurysms treatment, and if its amount must be carefully dosed in order to prevent late failures, bearing in mind the old saying “the dose makes the poison”.

REFERENCES
Since Parodi’s initial experience of endovascular exclusion of the abdominal aortic aneurysm (AAA), it was important to have appropriate vascular access to deliver the aortic stent graft (ASG).

There are still complications related to the access site, such as dissections, arterial ruptures and hematomas, even in case of percutaneous approaches. Reduced access site complications and lower overall procedural mortality rates have been reported after EVAR, with the use of new lower-profile endograft systems. The disadvantage of reducing the profile is the possible loss of proximal sealing, which can compromise the overall performance and durability of the device. For this purpose, not only were different anchoring systems introduced, but also prostheses with greater free-flow. The Ovation ASG (Endologix, Irvine, CA, USA) addresses these dual problems by combining a large free-flow with hooks, with an inflatable ring beginning 10 mm below the top of the covered part of the graft.

The Ovation ASG uniquely separates fixation and seal, with fixation achieved through suprarenal stent anchors and seal achieved through polymer-filled inflatable sealing rings.

By eliminating the need for a metallic endoframe entirely, the Ovation can keep a lower profile while achieving good proximal sealing and probably good durability over time. Having received the CE Mark on September 17th, 2010, the low-profile Ovation ASG system (14 Fr) was available for use with selected AAAs with relatively challenging necks or small and tortuous iliac vessels. The Ovation platform is a tri-modular, two-docking limb device system with the aortic body delivered via a flexible hydrophilic-coated catheter, as well as the contralateral limb.

**TECHNICAL FEATURES**

The most important characteristics are listed below.

1. A suprarenal nitinol stent, 35 mm in length, made of a proximal crown with anchors to achieve active fixation to the aortic wall and a mid-crown, without anchors, to achieve the accommodation of the ASG to the aortic wall. At the inferior border of the free-flow there are eight markers for identifying the proximal edge of the textile (Figure 2.1).

2. The aortic body is 80 mm in length and the textile is a low permeability PTFE graft. The graft has a fill port that connects the polymer network of the aortic body graft to the delivery catheter.

**FIGURE 2.1.** Mid crown (arrow); proximal crown and anchors (double arrow); free-flow markers (arrow-head).
To seal the proximal aortic neck, the graft body contains two inflatable rings, with a diameter ranging from 20 mm to 34 mm, 6 mm in height, that are filled with a liquid polymer that solidifies during the deployment procedure.

3. The center of the upper first sealing ring is located at 13 mm from the proximal markers and allows the circumferential sealing to the aortic wall. The center of the lower secondary ring is located at 20 mm and accommodates the aortic body to the aortic neck anatomy (Figure 2.2).

4. The Ovation ASG body has two-docking limbs, 9 mm or 11 mm in internal diameter, with four polymer-filled rings for each one. These rings, connected with the sealing rings, assure the limb support and visualization necessary for both limb cannulation and overlapping (Figure 2.3).

5. Contralateral gate access can be achieved by retrograde cannulation as usual or by antegrade cannulation through a 0.14 or 0.18 integrated cross-over lumen system (Figure 2.4).

6. The iliac limbs have a range of diameters from 10 mm to 28 mm and are made of a low permeability PTFE graft with a scaffold of nitinol stents. The iliac limbs are overlapped into the leg sections of the aortic body. Two radiopaque markers enable the physician to visualize the appropriate iliac limb-aortic body overlap (Figure 2.5) or iliac extension-iliac limb overlap during a catheter-based deployment. Stent radial force provides both the fixation and sealing of the interface between the aortic body and each iliac limb, between the iliac limb and iliac extension, and between the iliac limb/extension and its landing zone in the iliac artery (Figures 2.7-2.9). According to the IFU from Endologix, the fill polymer is composed of three components that are mixed prior to injection. After mixing and injection into the graft, the components form a radiopaque polymer that fills the channels of the sealing rings in the wall of the aortic graft. It is emphasized in the contraindication section, that the implant should be avoided in patients with known sensitivities or allergies to the device materials, including polyethylene glycol (PEG)-based polymers.

7. In contrast to nitinol-supported bimodular ASG, the lack of a nitinol skeleton from the fabric material in the Ovation ASG enables significantly smaller catheter profiles (14 Fr outer diameter) for the main body, and the implantation of 12-15 Fr conformable iliac limbs completes the procedural process.

**OVATION IFU ANATOMICAL CRITERIA**

The main criteria are reported below.

- Adequate iliac/femoral access compatible with vascular access techniques (femoral cut-down or percutaneous), devices, and/or accessories.
Abdominal aortic endograft ultra-low profile polymer-filled stent graft

This patient-specific treatment is a direct result of the polymer-enabled, flexible design of the Ovation ASG System.

DISCUSSION

EVAR modality is hampered by the fact that a favorable anatomy is a necessary prerequisite and not all patients are considered suitable to undergo EVAR. Risk factors for type Ia endoleaks are related both to the patient's anatomy and to the graft characteristics, assuming that the endograft is properly positioned. Patient-related risk factors depend on aortic neck anatomy. A hostile neck anatomy is typically defined as a short (<15 mm) and/or wide (>28 mm) neck, increased neck angulation (>60°), calcification at the landing zones, and thrombi. Previous reports indicate that only 32% of men and 12% of women are suitable candidates for EVAR.

DEPLOYMENT

The suprarenal stent is deployed in distinct stages allowing for precise orientation of the graft to the patient prior to fixation. The deployment of mid-crown allows: 1) the ASG to center within the aorta; 2) the visualization of the radiopaque markers, that are positioned to the desired orientation in relation to the renal arteries before the proximal crown is deployed and fixed in place. This sequential staged delivery of the suprarenal stent facilitates a precise alignment to the anatomy of the individual patient. Previous to the polymer injection it is necessary to retract the stiff aortic body in order to avoid a wire biased aortic body accommodation. When the fixated Ovation main body is injected with liquid polymer, the device forms a customized conforming seal (Figure 2.6).
women met all three criteria of the neck (diameter between 18 mm and 32 mm, length >15 mm, angulation <60°) and had iliac lumen diameters >6 mm, and most people have at least one anatomic index that did not fall under the current requirements for the available stent-grafts.

Some authors have reported promising results since their initial experiences with this low-profile device. The first multicenter trial with the Ovation ASG on 33 patients with AAA obtained a 100% technical success rate without any conversion to open surgery, aneurysm enlargement, rupture, fracture or migration. No type I, III or IV endoleaks were observed. The hospitalization death rate was 0%, and the postoperative mortality rate was 0%, with no major complications.

Graft-related risk factors involve the fixation and sealing systems. Stress tests have established that endografts that rely only on radial force for fixation are more prone to migration and subsequent type Ia endoleaks than devices with active fixation mechanisms.

The characteristic technical feature of the Ovation ASG involves the idea of uncoupling the level of stent graft fixation and sealing during the procedure. In the Ovation endograft platform, stent and fabric are not competing for the same space within the delivery system and an ultra-low-profile delivery can be achieved without complications. With such a low-profile delivery catheter, approximately 90% of men and 70% of women with abdominal aortic aneurysm have access vessel diameters suitable for endovascular repair.

Ioannou et al. conducted a single-center retrospective study including 66 patients who underwent EVAR using the Ovation ASG. Patients were submitted to a median follow-up of 13 months. Technical success was 95%, and immediate and midterm mortality rate was 0%. No type I, III, IV endoleak or stent migration were observed.

Mangialardi et al. in their single-center experience of Ovation ASG, with totally percutaneous endovascular access on 35 patients, reported a similar technical success rate (97.5%) although one type Ia endoleak was identified on final angiography, which was treated with an extension cuff. One type Ia endoleak was identified at the 12-month follow-up, resolved with a Palmaz balloon expandable stent. No type II, III, or IV endoleaks were identified. Metha et al., in a prospective, multicenter, single-arm trial conducted on 161 patients with a complete 1-year follow-up, reported 100% technical success. At one year, AAA-related and all-cause mortality were 0.6% and 2.5%, respectively. The one-year treatment success rate was 99.3%.

Nano et al. reported an 89.2% primary success rate for their 37 patients treated with Ovation ASG, and neither deaths or major complications during the procedure or the follow-up were reported, nor type I, III, or IV endoleaks, AAA enlargements, AAA ruptures, stent fractures, migrations, or endovascular or surgical reinterventions.

Another interesting element involves aortic neck dilation after EVAR with self-expanding devices. It has been suggested that as the Ovation ASG does not exert the chronic outward force that is normally seen with other stent-grafts achieving proximal sealing through the radial force of the stent portion of the device, it could avoid the neck dilation that potentially occurs over time.

An Italian multicenter registry of 161 patients treated with Ovation ASG, carried out for a mean period of 32 months, reported 95.1% primary clinical success at two years, defined as an absence of aneurysm-related death, type I or type III endoleak, graft infection or thrombosis, aneurysm expansion >5 mm, aneurysm rupture, or conversion to open repair. The assisted primary clinical success was 100%. No graft migration, barb detachment nor