

Early experience with a newly developed electrospun polycarbonate-urethane vascular graft for hemodialysis access

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ABSTRACT

Purpose: In this pilot study, we tested a newly developed electrospun multilayered, self-sealing graft, AVflo™, specifically designed for early hemodialysis access.

Methods: Ten eligible consenting patients had a polycarbonate-urethane graft (AVflo™) implanted and were followed up prospectively for at least six months. Performance measures included graft patency, complications and time to first cannulation. Mean age of the patients was 66.7 ± 10 years. Chronic glomerulonephritis was the most common cause of renal failure. A total of 70% of the patients had a history of previous vascular access and 40% history of minimally invasive radiologic procedures for patency maintenance. In 40% of the cases the need for AV graft implantation was because of recurrent infections from permanent catheter for dialysis. Seven grafts were placed in the upper arm and three in the thigh. Mean follow up was 230 ± 75 days.

Results: There were no systemic or local reactions to the graft and we did not report any graft infections. Two grafts thrombosed because of severe bleeding post-cannulation due to an incorrect needle puncture. Both grafts were successfully thrombectomized. Primary and secondary patency rates at six months were 60% and 78%, respectively. These patency rates were comparable to those reported for other polyether-urethane and ePTFE grafts. Median time to first cannulation was seven days (3-21) and all puncture sites sealed in less than five minutes.

Conclusions: This newly developed electrospun polycarbonate-urethane graft is safe in humans, permits early access obviating the need for venous catheters, and has equivalent patency as other prosthetic grafts.

Key words: Early vascular access, Electrospun, Hemodialysis, Polyurethane graft

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INTRODUCTION

The preferred method of hemodialysis access uses an autogenous fistula (1,2). Unfortunately, the patient population with end-stage renal disease has significantly increased in age and their life expectancy has also improved (3). Therefore, the superficial vessels become less suitable for the construction of an autogenous fistula and a synthetic arteriovenous graft becomes necessary. Among the artificial graft used, ePTFE is the most widely used (4). However, several multicenter, randomized, controlled trials show a one-year patency rate ranging from 40% to 70% (5-7) and large registry data indicate that prosthetic grafts have a 40% increased risk of primary failure when compared to autologous access (8). Problems with ePTFE include thrombosis following use, poor resealing qualities after puncture and intimal hyperplasia at the venous site leading to stenosis. Polyurethanes have been used as an

alternative to ePTFE because of their ability to self-seal at the puncture site (9). This intrinsic property of the material could provide early cannulation of the graft avoiding the need to implant large-bore central venous catheters which present a myriad of possible complications (10). In addition, several reports suggested that polyurethanes also reduce thrombosis and platelets adhesion and intimal hyperplasia (11-14). However, long-term patency and safety of polyurethane vascular access in dialysis patients has not been completely established. A new AV graft using polycarbonate-urethane and silicone copolymers and electrospinning technology to produce ultrafine fibers in a non-woven fashion was designed to spontaneously and rapidly seal puncture after needle withdrawal. We report our early experience with this new AV graft for hemodialysis which represents to the best of our knowledge the second report in humans and the largest Italian study with this new device.

MATERIALS AND METHODS

From October 2011 to March 2012, 10 patients received AVflo™ arteriovenous access implantation. Informed consent was obtained from all of the patients enrolled. This new AV graft with polycarbonate-urethane and silicone copolymers and electrospinning technology (AVflo™; Nicast Ltd, Israel) enables controlling the size, density, diameter and orientation of the fibers, giving the final product distinct mechanical properties such as post-puncturing spontaneous sealing, flexibility and radial pulsatility. The graft features a self-bonded, four-layer design (Fig. 1). The self-sealing middle layer is highly flexible and imparts elastic properties that mimic those of the natural blood vessel. A third layer operates as barrier to prevent the diffusion of large molecules and provides strength and elasticity to the graft's structure. The nanofiber fourth outer layer adds onto the self-sealing properties of the device and permits ingrowth of surrounding tissue. The decision to use AVflo™ graft was taken only when the construction of an autogenous fistula was impossible. Patient demographics are reported in Table I. All but three patients had a history of previous vascular access and four out of ten patients underwent minimally invasive radiologic procedure for patency maintenance. Eight out of ten patients bore a permanent central venous catheter at the time of referral. In 40% of the cases the need for an AV graft implantation was because of recurrent infection episodes from a permanent catheter for dialyses. All grafts were placed by the same skilful surgeon. Four were forearm loop grafts, three were upper-arm straight graft and three were thigh loop grafts. The 6 mm AVflo™ graft was laid subcutaneously using a tunneler and vascular end-to-side anastomosis using a 6-0 polypropylene suture. A single intravenous bolus of Ceftazidime (2 g) and 2500 U of unfractionated heparin were administered during implantation. Graft patency was assessed according to standard practice (15). Primary patency was defined as uninterrupted patency and graft use without surgical or angiographic intervention. If a graft required surgical thrombectomy or thrombolysis or percutaneous angioplasty for inadequate flow, the graft was con-

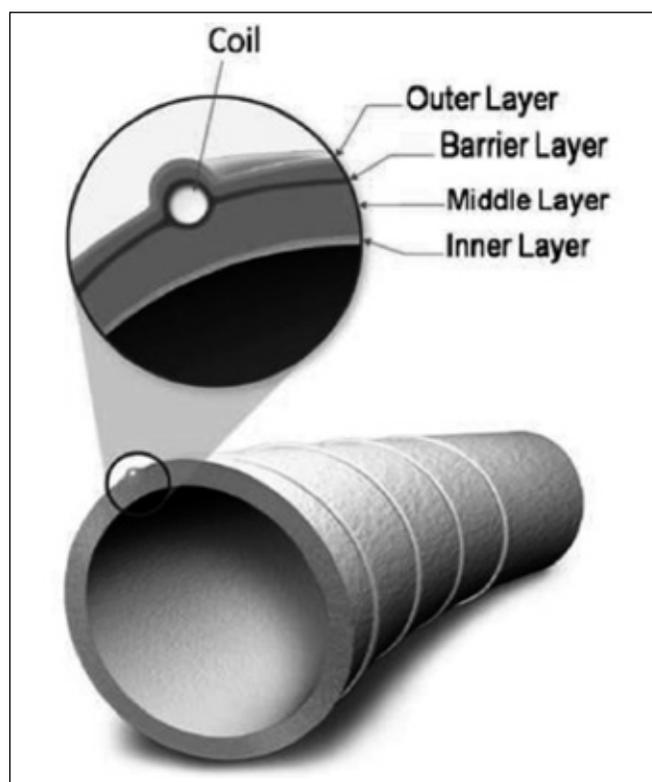


Fig. 1 - The four layers design of AVflo™.

sidered failed. Grafts salvaged in this way were combined with those in the unassisted patency group to determine the secondary patency. Graft patency was calculated with the Kaplan-Meier method. Graft complications not affecting patency but requiring medical therapy were recorded. The time of the first hemodialysis after graft implantation was recorded and the time for hemostasis after first decannulation was assessed. IRB/Ethics Committee decided approval was not required for this study.

RESULTS

All the implanted grafts were used and achieved a flow rate of at least 700 mL/min. All functioning grafts were observed for at least six months with a mean follow-up of 230 ± 75 days. Median time to first cannulation was seven days ranging from 3 to 21 days post-implantation. All of the first punctures of the graft had sealed off in less than five minutes. Primary and secondary patency rates from the date of the implant up to the sixth month post-procedure are illustrated in Figure 2. Two grafts thrombosed for severe bleeding post-early cannulation on post-operative day (POD)#3. Both were salvaged upon surgical thrombectomy. A third graft occluded on POD7 secondary to a kinking. A surgical revision of the graft facilitated recovery of the access. On POD#149 one patient under-

TABLE I - BASELINE PATIENT DEMOGRAPHICS

Patients (N)	10
Male/Female	7/3
Age	66.6 \pm 10
Cause of renal failure	
Glomerulonephritis	5
Diabetes	4
Hypertensive nephrosclerosis	1
Previous access procedure	7/10
Permanent venous catheter	8/10

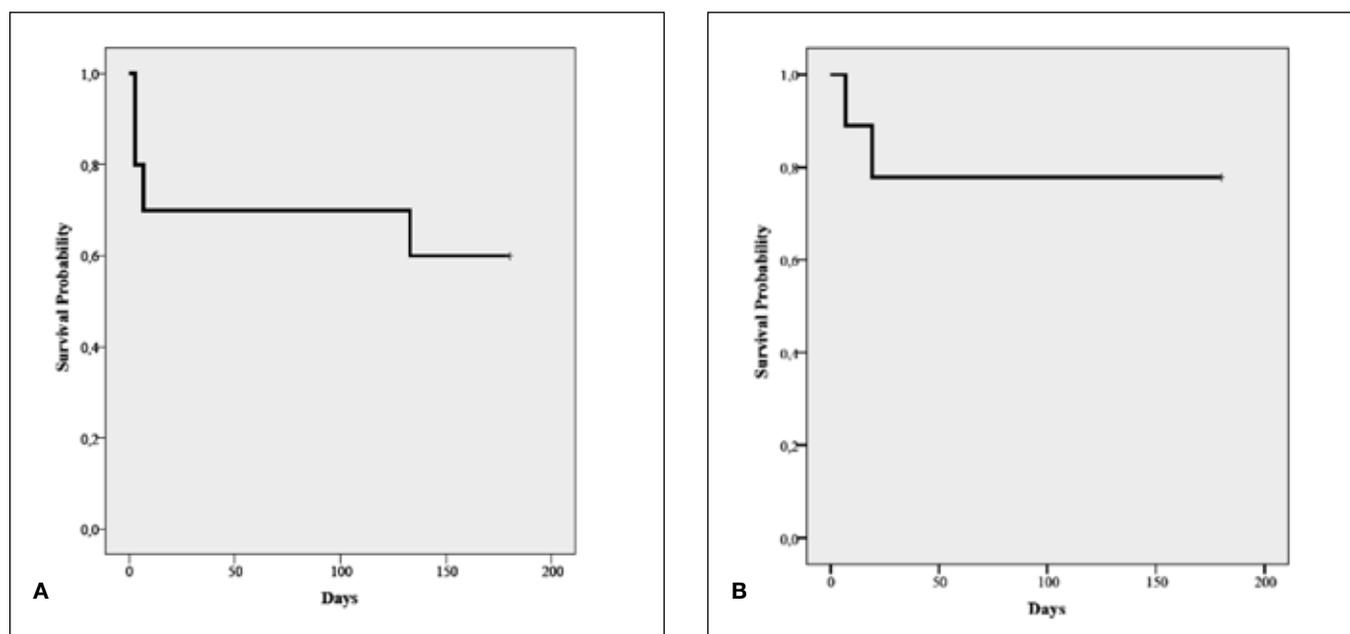


Fig.2 - Kaplan-Meier survival from implant to end of primary patency (left panel) and from implant to end of secondary patency (right panel)

went angioplasty of the subclavian vein ipsilateral to the forearm graft for chronic obstruction causing recirculation on high percent access. Despite revision, two of the grafts were lost: one because of recurrent thrombosis and one because of persistent hypotension during dialysis. We did not observe any reported graft-related complications such as seroma, pseudo-aneurysm or infection. One patient died with a functioning graft for underlying medical complication (lung cancer) unrelated to the device.

DISCUSSION

The overall outcomes of this early experience show that this new polycarbonate-urethane graft is safe and no unanticipated graft-related complication occurred during a six month observation period. Primary and secondary patency rates were 60% and 78%, respectively, in compliance with those reported by other authors. Using a polyether-urethane-urea graft (Vectra®), Glickman et al. reported an unassisted patency rate at six months of 51% and an assisted patency rate of 85% (16). Comparable results were reported for the same period by other groups with another polyurethane graft (Thorate®VAG) (17-19). Interestingly, Wijeyaratne et al. in their first clinical report in man with AVflo™, reported primary and secondary patency rates at six months after implantation of 70% and 81%, respectively (20). Those patency rates are in line with those reported for conventional ePTFE grafts (16,17, 21-23). Polyurethanes have recently been proposed as an alternative to ePTFE because of their ability to self-seal at

the puncture site thus preventing the formation of peri-graft hematomas. This would theoretically enable an early cannulation of the graft which is seldom applied because of their potential for complications. In our experience AVflo™, thanks to the particular texture of the polycarbonate-urethane fibers, enables cannulation of 60% of the graft within 10 days post implantation with a time-to-hemostasis after needle removal of less than five minutes. However, two grafts thrombosed on POD#3 because of a massive tunnel hematoma caused by an incorrect needle positioning (posterior puncture). Both grafts were salvaged upon drainage of the hematoma and surgical thrombectomy but after this experience we recommended a one-week delay before using the graft and until now we did not report similar complications. A negative effect of polyurethanes is their elasticity that, together with the minimal tissue adhesion, is responsible for the kinking of the graft (24,25). This specific problem of the polyurethane grafts is to enhance the loop configuration that reaches an incidence up to 8% (16,18). In our experience one kinking of the graft occurred in the mid-portion of a straight graft as documented by intra-operative angiogram performed during surgical thrombectomy. That was clearly a technical error because in the presence of a relatively short patient's arm, we thought it would have been better to position the graft with the tunneler with a two step procedure performing a small transverse midline incision. In this way, axial elongation of the graft was neither controlled nor prevented. After this case, proper attention to the placement procedures has removed this graft-related complication in our series. Infection is another worrisome complication

with polyurethane grafts and is related to early graft cannulation. This maneuver, before complete surgical healing carries a theoretic risk of introducing an infection into the graft. The complication rate ranges from 3% to 30% according to different published series (9,17,18,26,27) and it increases when polyurethane grafts are placed in the thigh (19). In our series such a complication was not observed and this might be accounted for by the fact that all the grafts were placed by the same trained surgeon and treated with a two-week broad spectrum antibiotic prophylaxis upon discharge. On the other hand, our limited observation may underestimate this complication.

The study has some limitations which include a relatively small patient sample from a single institution and a limited observation period. However, this might be compensated by the fact that the patients chosen for this sample were at high risk for complications considering that only three of them had their primary access with this new device. For this purpose large multicenter trials have to be designed to reinforce our promising results.

In conclusion, AVflo™ polycarbonate-urethane graft is a valid alternative to other prosthetic grafts for hemodialytic access in patients where autogenous fistula cannot be established.

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