

A two-year experience with a rapid access, self-sealing, polycarbonate urethane nanofiber vascular access graft for hemodialysis

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ABSTRACT

We present our experience with AVflo™, a nanofiber, electrospun, self-sealing, early-access graft for hemodialysis (HD).

Objective: Evaluating the safety and efficacy of the AVflo™ graft in terms of patency and complications (early and late) over 2 years.

Materials and methods: Twelve end-stage renal disease (ESRD) patients (age: mean 68.5 ± 10 years) were followed up for a mean period of 946 ± 570 days after receiving an implantation of the graft for HD. The grafts were implanted at the lower arm (loop configuration), upper arm (straight configuration) and the thigh (loop configuration). First dialysis was performed at day 7 (3-21) following implantation.

Results and discussion: After a mean follow up of 24 months, the primary patency was 56% and the secondary patency was 82%. In this group, AVflo™ shows similar if not superior efficacy and safety to that of available grafts in terms of safety, complications, and long-term patency.

Keywords: AV-graft, Early access, Hemodialysis, Long-term patency, Nanofibers

Introduction

Since the days of Brescia et al (1) the issue of creating and maintaining a functional vascular access for patients undergoing hemodialysis (HD) has not been satisfactorily solved. The Fistula First Initiative (2) launched in 2003 in the USA spread meanwhile to the entire globe and its recommendations are considered the gold standard of therapy. Yet, many studies demonstrated some of the clinical and economical drawbacks of the Fistula First recommendations. In 2006, Lok et al (3) detected that up to 70% of native fistulas never reach maturation, thus exposing the patient to repeated access surgery and to a central venous catheter (CVC), in order to keep a patent access for their treatment over the fistula's maturation period. Although easy to insert and use, CVCs carry with

them a high burden of complications, mainly infections and thromboses (3). More than that, every insertion of a foreign object into a central vein is associated with an increase in the chances for a stenosis occurring in the central vein chosen (4).

Investigators from National Kidney Foundation - Kidney Disease Outcomes Quality Initiative (NKF-KDOQI), Dialysis Outcomes and Practice Patterns Study (DOPPS) and others, have attempted to construct an algorithm for predicting the odds of a fistula to mature in each patient group, using different parameters (age, morbidity leading to end-stage renal disease [ESRD], body mass index [BMI], previous interventions in the venous system, etc.) available to the physician. None have yet reached a conclusion.

Early access grafts may propose a suitable alternative for arteriovenous fistulae (AVFs) in patients whose chances of developing a mature AVF according to the proposed algorithms are rather low.

The current article describes our experience with AVflo™, an early-access arteriovenous graft (AVG) that may be cannulated 24-48 hours after implantation, over the period of two years.

Materials and methods

Between 2011 and 2012, AVflo™ was implanted in 12 patients (7 males, 5 females; mean age: 68.5 ± 10 years) with ESRD treated by HD. Five grafts of the straight configuration

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TABLE I - Patients' characteristics

| | |
|-------------------------------------|------------|
| Patients (n) | 12 |
| Gender (m/f) | 7/5 |
| Age (years) | 68.5 ± 10 |
| Previous access procedures | 9/12 (75%) |
| Previous radiological procedures | 5/12 (40%) |
| Permanent CVC | 9/12 (75%) |
| Implantation site and configuration | |
| Upper arm | 5 |
| Lower arm | 4 |
| Thigh | 3 |

CVC = central venous catheter.

were implanted in the upper arm, four grafts in the loop configuration in the lower arm, and three further loop grafts were implanted in the thigh. Of all patients, nine (75%) had at least one previous access procedure, five (40%) had at least one previous radiological access graft-rescue procedure and nine reached operation with an indwelling permanent CVC (Tab. I).

All patients received an AVflo™ vascular access graft (NICAST, Lod, Israel), which is made of electrospun, non-woven polycarbonate-urethane nanofibers. It provides self-sealing features that prevent hematoma or seroma formation and allows early HD puncturing (Fig. 1). The specific nanotechnology employed for this graft, allows obtaining a nanofabric resembling ultrastructurally the extra-cellular matrix of human tissue (Fig. 2). This physical feature underlies the unique self-sealing capability of AVflo™. Although published clinical experience with this graft is still limited (5-8), it has been implanted in over 2000 patients in the four years since its market introduction. To date AVflo™ is regularly implanted in Europe and Asia.

Endpoints

The primary endpoints of the study were the primary and the secondary patency rates according to the most recent definitions for HD access (9). Surgery censored patency rates according to NKF-KDOQI (10) were also calculated. Secondary endpoint was adverse events at 12 and 24 months. Complication rate was obtained by dividing the number of observed complication by cumulative follow-up days × 1000.

Standard descriptive statistics were used to assess demographics and clinical characteristics of patients. Survival analyses were performed using the Kaplan-Meier estimator (SPSS ver. 15).

Results

Results are summarized in Table II. The mean follow-up time was 946 ± 570 days. The first cannulation of the graft

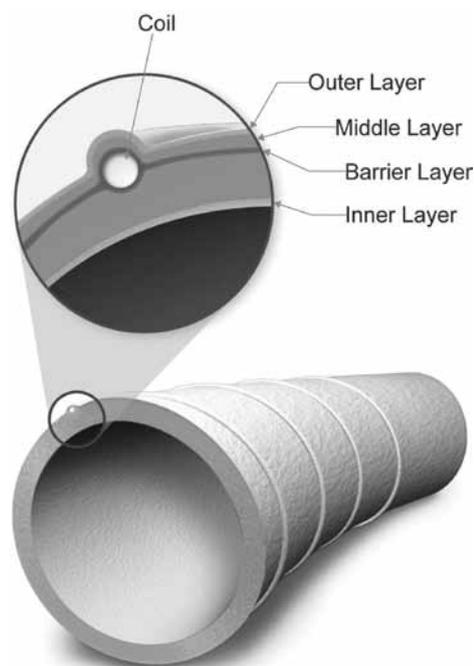


Fig. 1 - Structure of the AVflo™ nanofiber made graft (source Nicast Ltd).

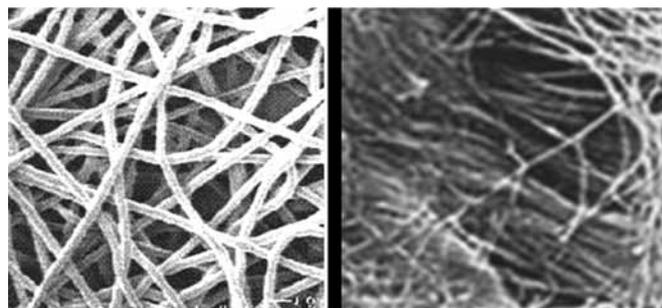


Fig. 2 - Comparison between AVflo™ nanofibers (left panel) and human extra cellular matrix (right panel) (×500; source Nicast Ltd).

TABLE II - Follow up

| | |
|---|-----------|
| Follow-up time (days) | 946 ± 570 |
| Median time to first cannulation (days) | 7 (3-21) |
| Early complications | |
| Thrombosis | 2 |
| Kinking | 1 |
| Thrombotic rate | 0.92 |
| Drop-outs | |
| Recurrent thrombosis ^a | 1 (149) |
| Chronic hypotension ^b | 1 (144) |
| Death ^c | 1 (126) |

^a Patient known to have a hyperactive coagulation system. Graft related: maybe.

^b Cause unknown. Graft related: no.

^c Cause of death: lung cancer. Graft related: no.

Parentheses in column two denote post-operative days.

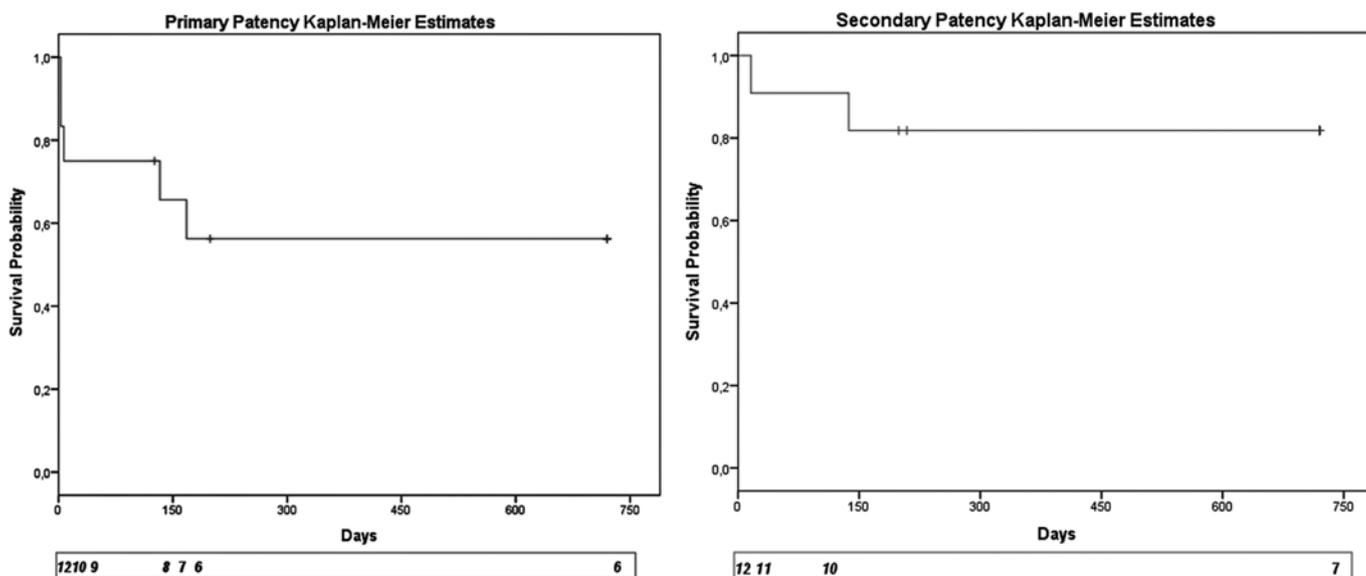


Fig. 3 - Two years patency rates (Kaplan-Meier estimator plots). Censor and drop-out patients are listed in bold at the bottom of the graph.

was done 7 (range: 3-21) days after the implantation. Two early thromboses were observed in two patients following an incorrect puncture of the graft which caused significant bleeding in the subcutaneous tunnel. In both patients, the nurses punctured the graft with the force used by expanded polytetrafluoroethylene (ePTFE) grafts, so that the opposite wall of the graft was punctured as well. Both were successfully treated by a surgical thrombectomy and returned to function. The graft's manufacturer provided instruction material for the dialysis nurses and after training this failure did not recur. This training material is now being placed in packaging of every graft. One kink of the graft causing high dialyses pressures was detected by an angiogram on post-implantation day 7. The graft was surgically revised.

Three patients did not complete the study. One because of a hypercoagulable state causing recurrent thrombosis, the second developed chronic hypotension and the third died of lung cancer. All three withdrawals were considered not graft related and omitted from the calculations of the patency rates.

The primary patency rate was 56.3%. The secondary patency was 81.8%. Both of them remained steady after 12 months and 24 months from the day of implantation (Fig. 3). The NKF-KDOQI guidelines (10) require the exclusion of any graft malfunction occurring in the first 30 days after implantation from the patency calculation, since they are not considered device related. Complying with this requirement, we recalculated our primary patency rate and found it to be 75%.

No infections or thromboses occurred as late complications. We did observe two patients, who developed on post-implantation day 149 and 209, respectively, a stenosis of the venous outlet of the graft, which was found to be neointimal hyperplasia. This was treated by endovascular balloon dilatation and the grafts continued to function well and are still used for performing dialysis.

Discussion

An optimal solution for an AV access for ESRD patients on hemodialysis is not yet available. The existing guidelines on the treatment for ESRD with hemodialysis can be condensed into the recommendations for an "ideal graft":

- Long period of functionality (patency)
- Early-access (within 24-48 hours after implantation)
- Self-sealing (to minimize bleeding from needle insertion)
- Non-weeping (to prevent seepage of serum through the graft wall thus reducing the risk of infection)
- Good tissue integration (to eliminate the formation of a peri-graft space, thus minimizing the risk of infections)
- Easy and reliable handling during implantation and dialysis.

Comparing the results of several leading grafts in terms of patency and complications with our own experience (Tab. III) (5, 11-16) shows that AVflo™ displays comparable if not better patency rates than all other compared grafts.

The review done by Al Shakarchi et al (17) summarizes the published experience with the novel "rapid access" grafts. These grafts may be accessed for HD within 72 hours after implantation, dramatically reducing the current long maturation times needed for conventional grafts and the exposure of HD patients to a central venous line and its negative effects, while providing long patency periods.

Also, Maytham et al (18) stress the usefulness of a rapid-access graft in reducing the need for creating a temporary access through a central venous line while awaiting maturation. The one-year patency rates reported by the authors (46% primary patency and 61% secondary patency) may be comparable to other ePTFE grafts, but cannot be considered as satisfactory. Also the infection rate of 16% is in the higher level of the reported studies (see Tab. III).

TABLE III - Literature comparison

| Author | Graft | Primary patency (1 year) | Secondary patency (1 year) | Infection rate | Days to 1 st dialysis |
|----------------------------|------------------|--------------------------|----------------------------|----------------|----------------------------------|
| Glickman (11) | PU | 51% | 85% | 5.6% | 3-14 |
| Matsuda (12) | PU | 44% | 79% | 4.34% | 2.4 |
| Scher (13) | ePTFE | 58% | 79% | - | - |
| Schild (14) | ePTFE (Flixene™) | 49% | - | 6.06% | 1-3 |
| Chiang (15) | ePTFE (Flixene™) | 34% | 51% | 20.2% | 3 |
| Aitken (16) | ePTFE (Acuseal™) | 32.4% | 40.5% | 16.2% | 1 |
| Karatepe (5) | Avflo™ | 50% | 75% | 4.16% | 1 |
| Ferraresso (present study) | AVflo™ | 56% | 81% | 0% | 7 |

Furthermore, we accept that foreign bodies introduced into humans are a potential risk for the development of an infection. Yet, in our series and in the previously cited series (1-3), AVflo™ showed an extremely low incidence of infections. This might be attributed to the specific nanofibrous structure of this graft, which highly resembles the ultrastructure of the extracellular matrix of human tissue.

The structure of the AVflo™ wall contains a thin layer of densely packed nanofibers, preventing large molecules from seeping through the wall into the peri-graft space while carrying other serum molecules with them to create a seroma.

The nanofibers also create a very comfortable scaffold for cells in the peri-graft area to migrate and anchor the graft into the tissue. This rapid procedure may not only attribute to the absence of a peri-graft space, the prerequisite for the formation of seromas which may be infected easily, but also to the stability of the graft inside the tissue, allowing for early cannulation.

Conclusions

AVflo™ is a specifically developed AVG presenting many features demanded by international bodies for this specific kind of intervention, such as early cannulation and self-sealing. In our experience, the handling of the graft during surgery is good, the feedback from the nephrologists as well as the nurses and technicians in the dialysis units is also positive.

Most of the complications (thrombosis) were experienced in the early post-implantation phase. The vigilance of the team in treating thrombosis, reopening the graft and further usage of it for dialysis purposes, has in turn resulted in a high patency rate over a long period of time (ca. 2 years).

The low rate of infections is very rare in vascular implantations and may be attributed to the fibrous nature of the graft and its rapid integration into the surrounding tissues, avoiding phenomena like seromas or hematomas, which usually serve as a predisposition for infections.

We conclude that AVflo™ presents today a reasonable alternative for patients in need of a vascular access for HD,

especially those in urgent need of dialysis due to a failure of a previous access.

Disclosures

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