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Single-centre experience of an early cannulation graft for haemodialysis access

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Abstract

Introduction: As the demographics of the population changes, increasing challenges are being faced in providing reliable access for dialysis. This article reports on the outcomes from the largest series to date using the early cannulation graft Flixene in a single centre.

Methods: Between May 2012 and March 2018, 141 Flixene grafts were placed for dialysis access. The outcomes of the arteriovenous grafts were reviewed retrospectively from electronically held records and imaging.

Results: In 75 patients, placement of Flixene graft was performed on an emergency basis and in 66 patients on a planned elective list. The 12-month primary, assisted primary and secondary patency rates were 48.7%, 56.6% and 83.6%, respectively. Eight (5.7%) patients developed infections of the graft during the follow-up period.

Conclusion: In our experience, we have found the use of the early cannulation graft Flixene to be safe with a low complication rate and favourable patency rates. We believe these early cannulation grafts provide a useful addition for vascular access surgeons preventing the use of tunnelled lines and providing more flexibility in the timing of placing a graft for dialysis.

Keywords

Dialysis access, prosthetic grafts, arteriovenous access, Flixene, early cannulation graft

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Introduction

There has been a push towards the creation of native arteriovenous fistulas (AVFs) over arteriovenous grafts (AVGs) and central venous catheters for dialysis access through initiatives such as 'Fistula First Breakthrough Initiative' which has evolved to 'Fistula First, Catheter Last (FFCL) Workgroup Coalition'.[1] This is due to the historic literature reporting AVFs having superior primary and long-term patency, requiring fewer interventions to maintain, being cheaper and lower rates of complications.[2,3] To create functional AVF, patients need vessels with diameters of at least 2 mm and referred 6 months prior to needing renal replacement therapy to a vascular access surgeon to allow for maturation and any interventions that may be required to establish usable access.[4]

Native AVFs are increasingly difficult to obtain due to several factors. In the United Kingdom, at least a third of patients present less than 6 months prior to commencing renal replacement therapy.[5] Patients requiring renal replacement therapy are increasingly co-morbid, elderly and obese.[6] Increasingly, complex health care requires frequent venepuncture, and cannulation of peripheral veins results in damage, scarring and thrombosis of these veins, reducing native access options.[7] There has also been an increased use of peripherally inserted central venous catheters (PICC) which are associated with up to a 50% rate of thrombosis[8] and 7.5% incidence of central venous stenosis or occlusion.[9] Central venous catheters can result in changes in less than 2 weeks to the central veins with injury to the endothelium and formation of thrombus that then progresses on to thickening and scarring of the vein leading to stenosis that increases with duration.[8] The combination of these factors creates significant challenges for vascular access surgeons aiming to create dialysis access

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with enough time to mature and function while avoiding central lines for dialysis with their associated impact upon central veins, in particular stenosis.

AVG is an alternative when no suitable native options are available to create functional access for dialysis. Another role for AVGs is when managing existing access where complications have developed. AVG can be placed in the region of the existing access, for example, to remove aneurysmal or stenotic segments, without moving to the contralateral limb, thus preserving future options. Traditionally, AVGs are composed of expanded polytetrafluoroethylene (ePTFE) which does have some drawbacks. Similar to AVFs, AVGs cannot be used immediately to allow them to incorporate into the surrounding tissue before needling, which takes a minimum of 2 weeks. Needling early may be difficult due to swelling and bruising. The potential space perigraft can fill with seroma or haematoma which is then at risk of becoming infected. They are also associated with complications such as thrombosis, stenosis and the formation of aneurysms with a resultant average of 1.5–3 interventions per year to retain patency.[10] Newer AVGs have come on to the market, which report the ability to needle early compared to traditional ePTFE AVG. These early cannulation AVGs include Acuseal (W.L Gore and Associates, Inc., USA), Flixene™ (Maquet, Germany), AVflo™ (Nicast Limited, Israel) and Rapidax™ (Vascutek – Terumo, Scotland). They differ from ePTFE in that they are generally multilaminar AVGs with an outer layer designed to achieve quicker incorporation into the surrounding tissues, a middle self-sealing layer to minimise weeping and bleeding from the AVG and an inner smooth surface to minimise platelet attachment. AVflo differs in that it is a polycarbonate urethane nanofiber AVG.

In 2012, the use of Flixene grafts was introduced in our unit for patients requiring urgent vascular access to minimise the use of bridging central catheters. The objective of this case series is to detail patency rates, outcomes and complications of these AVGs.

Methods

Study design and setting

This study is a retrospective review of all patients who underwent insertion of a Flixene graft in Oxford University Hospitals NHS Trust between May 2012 and March 2018. The follow-up period was up to March 2019. Procedure-specific information and data on demographics, interventions and complications of patients who had Flixene grafts for haemodialysis access were collected from a prospectively maintained database. Electronically held data for these patients were retrospectively reviewed on patient electronic records, renal proton system (Clinical Computing Ltd, UK) and radiology picture archiving and communication systems (PACS).

Patients in the study were followed up according to local protocols, which included routine access surveillance and efficacy of dialysis measurements. Access flows were monitored every 3 months using Transonic® Hemodialysis Monitor (Transonic Systems, Inc., USA) and if a reduction of ⩾25% was observed the test was repeated. If the reduction in flow measurement was sustained, then a venogram was performed. Patients were discussed at a multidisciplinary team (MDT) meeting with radiology, nephrology, haemodialysis nurse specialists and surgeons. Stenosis was treated when there was more than 50% narrowing or physiological evidence of poor function. Treatment was either endovascular or surgical and was based on the type of stenosis. Any AVG thrombosis was treated surgically as there was no radiological thrombectomy service available.

Population and indications

The indication for a Flixene graft in our centre was the absence of useable vascular access in any patient requiring renal replacement therapy within 2 weeks. The population was divided into two groups that consisted of an elective group who could be placed on the next elective vascular access operating list within 2 weeks and an emergency group who could not.

Relative contraindications for a Flixene graft were considered the same as for a conventional ePTFE graft and included vein diameter ⩽3 mm, arterial diameter ⩽3 mm and cardiac ejection fraction ⩽20%.

One patient was excluded from the analysis who had placement of an early cannulation AVG to facilitate multivisceral transplant and not for dialysis use.

Operative procedure

The surgical procedure was partially standardised with Teicoplanin 800 mg at induction, the use of chlorhexidine–alcohol skin preparation and use of the Slider Easy Glide System (Maquet, Germany) for tunnelling. However, the choice of whether the AVG was configured as a loop, straight or interposition, the anastomosis technique and type of AVG was surgeon specific. Three different AVG types were used and included straight, trumpet and graduated. For patients with central stenosis, the Hemodialysis Reliable Outflow (HeRO) grafts (Merit Medical Systems, Inc., USA) system was deployed with venous outflow component located in the right atrium and the Flixene graft anastomosed from the brachial artery in a straight configuration on to the venous component connector.

Outcome and definitions

Primary patency (unassisted patency) was defined as the interval from AVG insertion to the first intervention to maintain or re-establish patency. Assisted primary patency

Table 1. Demographics of patients receiving Flixene early cannulation graft.

	n	%
Gender		
Male	58	41.1
Female	83	58.9
Age (years)		
Median	61	
Range	25–88	
Diabetic status		
Diabetic	65	46.1
Not diabetic	76	53.9
On dialysis at the time of insertion of graft		
Yes	104	73.8
No (pre-dialysis)	37	26.2
Median days of follow-up	435	

was defined as the interval from AVG insertion to first thrombosis requiring intervention to re-establish patency. Secondary patency was defined as the interval from AVG insertion to AVG abandonment or a censored event was reached.[11,12] Events that were censored for include death, transplantation and end of study period.

Other endpoints included infection, which resulted in removal of AVG, and confirmed with positive microbiology results from culture of the AVG or presence of positive wound swabs from around the AVG; steal syndrome, which included patients with ischaemic pain distal to the AVG that occurred on exercise, on dialysis or at rest (no patients had tissue loss); wound complications (seroma, dehiscence, lymphocele); and the need for intervention.

Statistics

Kaplan–Meier survival statistics were performed using RStudio Team (2015) (RStudio, Inc., USA), on an intention-to-treat basis. All other statistics were performed using GraphPad Prism version 6 for Windows (GraphPad Software, USA). Categorical data were compared using Fisher's exact test.

Results

Between May 2012 and March 2018, 141 AVGs were performed using a Flixene graft. The demographics of the patients are shown in Table 1.

Patients receiving Flixene grafts were divided into two groups, emergency and elective. In the emergency group, 16 patients had AVG placed after 'crash-landing', requiring dialysis with no suitable upper-arm veins for autologous AVF and to avoid placement of tunnelled lines. Three patients had AVG placed following rapidly failing transplants while being inpatients. Four patients prior to placement of AVG were on peritoneal dialysis and had developed peritonitis that necessitated the removal of the peritoneal dialysis catheter. In order to maintain them free of tunnelled central venous catheters, they had Flixene grafts placed to allow them to transition immediately to haemodialysis. There were six patients with complications from their central venous catheters who had Flixene grafts placed. The remainder of patients consisted of those with existing access that had clotted (37 patients), presented with bleeding (3 patients) or aneurysmal with either imminent threat to the skin or pseudoaneurysm (6 patients).

Sixty-six patients had Flixene grafts placed on planned elective operating lists, the indications for which are summarised in Figure 1. Although two patients had options for native fistulas, an individualised approach was taken due to their comorbidities. A conscious decision was made to only list them when dialysis was inevitable. Twelve patients had central stenosis and thus, as part of placing HeRO grafts to traverse these stenoses had Flixene placed for inflow allowing early use.

The placements of the Flixene grafts consisted of 3 adductor thigh leg loops, 19 forearm loops, 13 forearm straight and the remainder in the upper arm in a straight configuration.

In total, 94% of the Flixene grafts placed, excluding the two AVG that never functioned, were used within 2 weeks. Eight patients who did not use the AVG within the first 2 weeks of placement were in the elective groups and it was decided after placement that they could hold off dialysis to a future date.

Early complications

Five patients had early complications within the first 30 days of AVG placement. Three patients had steal syndrome requiring surgical intervention and one patient developed a haematoma from a bleed from the arterial anastomosis which was re-fashioned. One patient developed a seroma which was managed conservatively. Two patients had Flixene grafts that never functioned, however, have been included in all the survival analysis on the intention-to-treat basis.

Infections

There were no AVG infections in the first 90 post-operative days. However, nine patients had AVG removed due to infection over the course of the first year following placement. Two of these patients had secondary infections from other sources than the AVG. The first patient had recurrent episodes of cholecystitis together with bacteraemia. The second patient had been treated over the preceding months for septic arthritis of the hip and shoulder. One patient had an AVG removed due to suspected infection following a positron emission tomography (PET) scan in the early post-operative period; however, at surgery it was found to be well incorporated with no signs of infection, and microbiology swabs and cultures of the prosthesis and wound were all sterile.

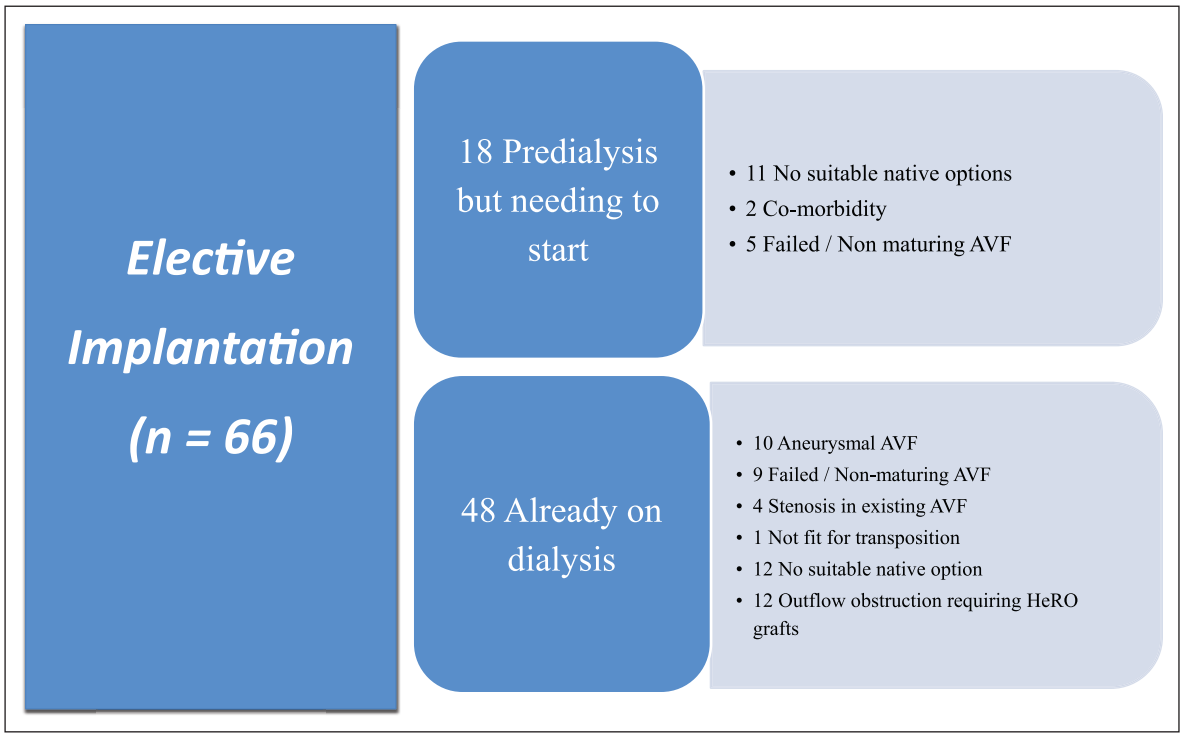

Figure 1. Indication for elective insertion of Flixene graft.

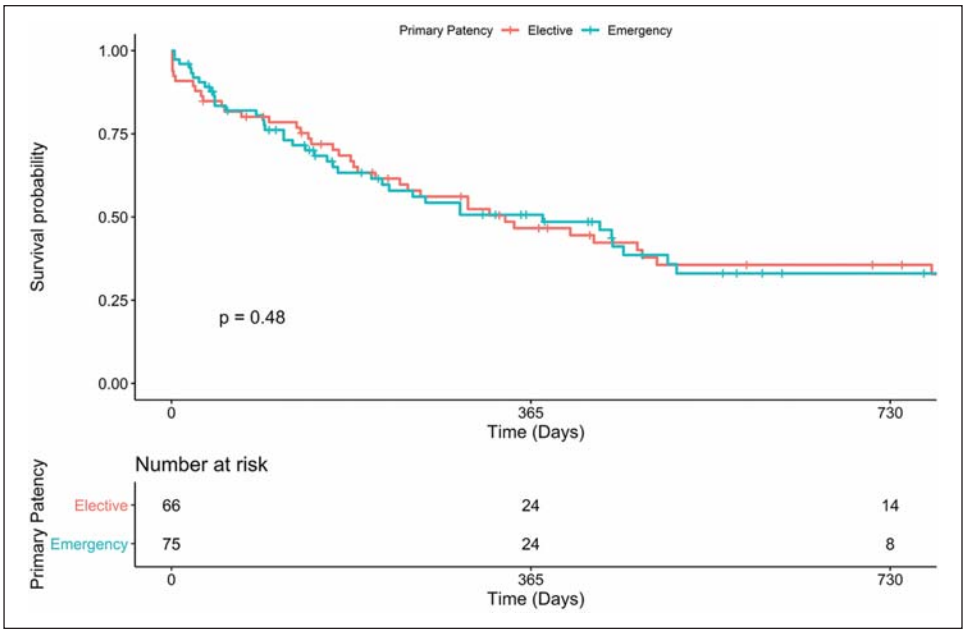

Figure 2. Primary patency of Flixene grafts.

Patency rates

The primary, assisted primary and secondary patency rates were compared between the elective and emergency-placed Flixene grafts as displayed in Figures 2, 3 and 4, respectively. There were no significant differences between the patency rates between these two groups.

In the first year, 16 AVGs were lost other than due to patient death or transplantation. The reasons for which are summarised in Figure 5. Nine of these were due to infection as described above. Two patients developed central venous stenosis over the study period and had placement of HeRO graft during which the Flixene component was replaced. Eight patients had thrombosis of

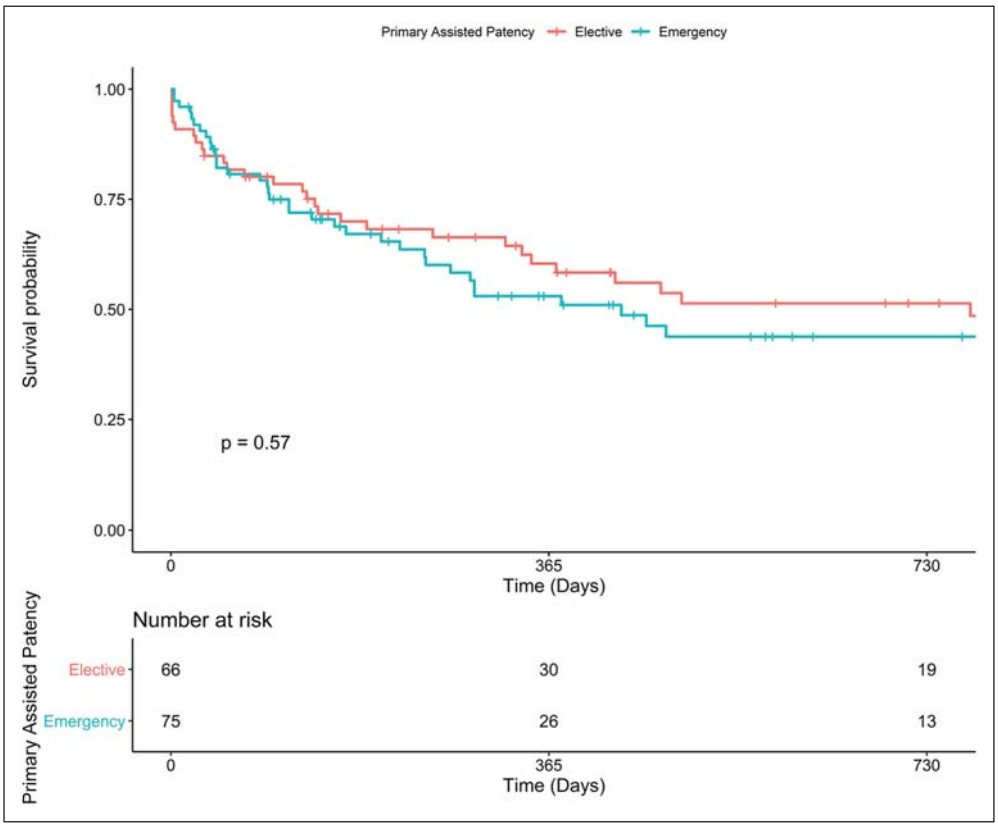

Figure 3. Assisted primary patency of Flixene grafts.

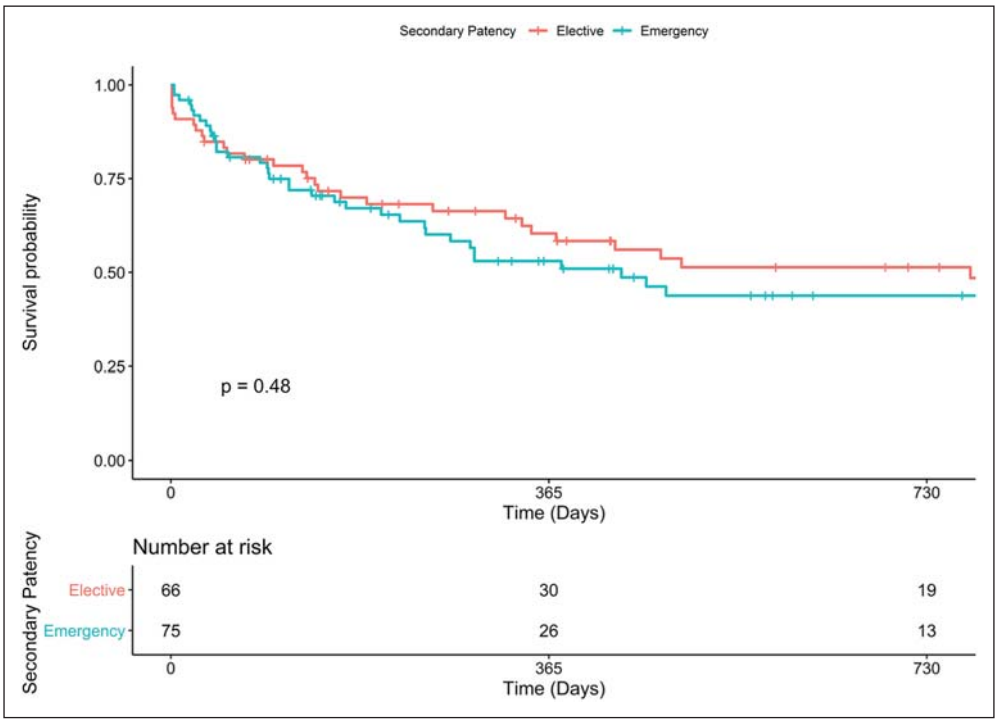

Figure 4. Secondary patency of Flixene grafts.

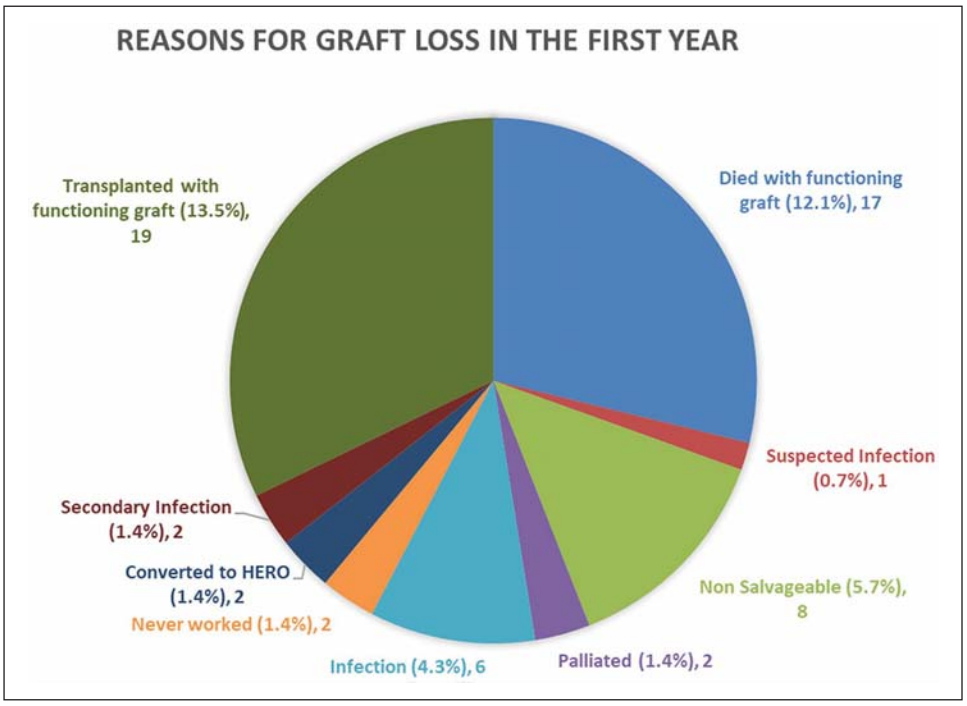

Figure 5. Reasons for loss of graft in the first 12 months following insertion.

Table 2. The 12-month outcomes of patients having had Flixene graft placement.

Outcome	Elective (%)	Emergency (%)	*p* value
Primary patency	46.6	50.7	0.68
Assisted primary patency	60.4	53.0	0.57
Secondary patency	83.4	83.5	0.48
Transplanted with functioning grafts (n)	6	13	0.22
Died with functioning grafts (n)	7	10	0.80
Abandoned/non-salvageable (n)	4	4	1.00
Palliated (n)	1	1	1.00
Infection (n)	4	5	1.00
Never worked (n)	2	0	0.22
Converted to HeRO graft (n)	1	1	1.00
Patent (n)	41	41	0.40

their AVG and flow could not be re-established to maintain dialysis.

The 12-month outcomes are summarised in Table 2.

The combined patency outcomes for the two groups are shown in Figure 6. Overall, the 12-month primary, assisted primary and secondary patency rates were 48.7%, 56.6% and 83.6%, respectively.

Discussion

Although native vein fistulas are often considered the best option for the purposes of haemodialysis access, circumstances still necessitate the need to use AVG. There is an increasingly elderly, frail and obese population who are presenting on a background of previous lines and access surgery using up vascular real estate. One of the purported benefits of AVFs is their patency rates based on historic studies. However, a 2014 meta-analysis of AVF reported at 1-year primary patency rate of 60% and secondary patency of 71%.[13] Furthermore, the reported benefits of AVF compared to AVG for the need for intervention, thrombosis and risk of infection only start to become apparent after 18 months or more.[14,15] Immediate-access AVG provide comparable patency to standard AVG, with fewer reinterventions and catheter-related complication.[16] We do not know with the newer generation of AVG whether these differences will persist and at what time point they diverge which may be much further down the line compared to the standard AVG.

The presence of an option for creating an AVF is not always in the patient's best interest. Those with a poor prognosis may be better served with having one definitive procedure, if required, that results in functional vascular access closer to the time for the need for dialysis. This reduces the risks from AVF with an unknown maturation time and the possible need for further uncomfortable and potentially distressing interventions that may be unsuccessful in someone with a limited life expectancy.

Taking the above into consideration, our unit, in line with others, aims to be patient-centred and tailor access.[17] We create around 250–300 native AVFs a year in our unit. However, some of our patients may have potential native

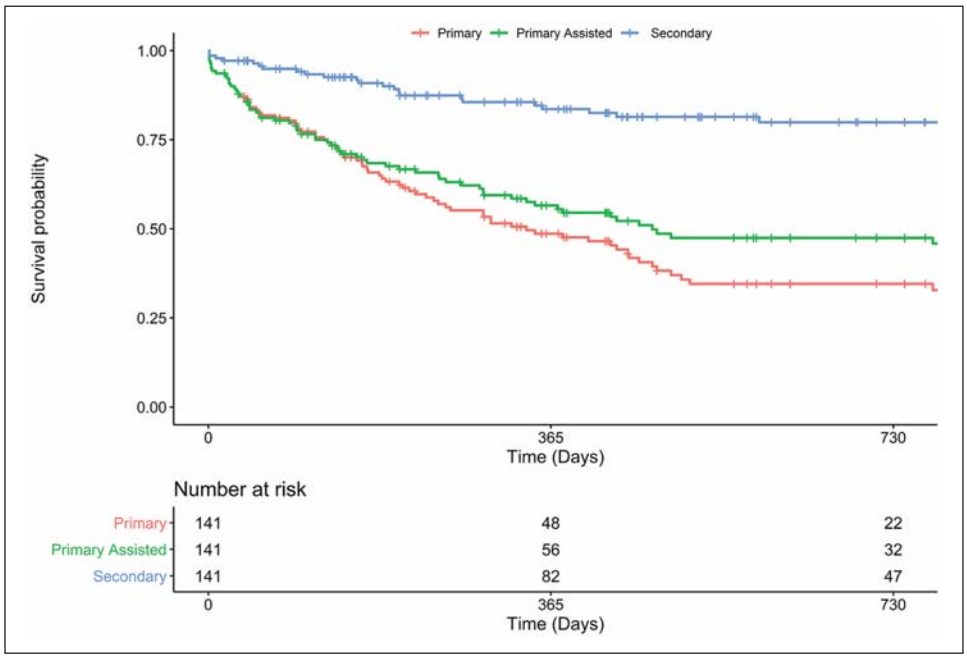

Figure 6. Patency of all Flixene grafts inserted.

Table 3. Comparison of current series with other studies.

Study	Number of grafts	Infection (%)	Primary patency (%)	Assisted primary patency (%)	Secondary patency (%)
Lioupis et al.[19]	48	6	30 (12 months)	53 (12 months)	73 (12 months)
Schild et al.[20]	33	6	49 (6 months)	80 (6 months)	N/A
Chemla et al.[21]	10		66	N/R	83.5
Scarritt et al.[22]	78	9	54 (12 months)	N/R	77 (12 months)
Chiang et al.[23]	45	11	44 (12 months)	45 (12 months)	63 (12 months)
Berard et al.[24]	46	4	44 (12 months)	56 (12 months)	86 (12 months)
Hinojosa et al.[25]	24	8	25 (12 months)	N/R	55 (12 months)
Current study	141	5.7	48.7 (12 months)	56.6 (12 months)	83.6 (12 months)

N/R: not reported.

options and we believe that AVGs still have a role in them, by providing immediately usable vascular access. Reported mean time to use of AVF is 3.5 months and around 20% of AVFs created are not used.[18] In our patient cohort, 52 (36.9%) died during the follow-up period with 23 (16.3%) in the first year of AVG placement showing their frailty, and that relentlessly pursuing the creation of native fistula is not always appropriate with the required time for maturation and uncertainty whether it will be useable.

Unfortunately, the timing for when access may be required cannot always be anticipated. Some patients require access urgently or as an emergency with clotted and/or problematic existing fistulas and AVG. In our emergency group of patients who presented with complications of existing access, the use of Flixene allowed us to maintain access without resorting to the use of central tunnelled lines and preserve valuable venous options for future use if required.

In our case series with the use of the Flixene early cannulation graft, the 12-month primary, assisted primary and secondary patency rates were 48.7%, 56.6% and 83.6%, respectively. Within our series, two patients had immediate failures of their AVG and have been included in our analysis. Our outcomes are in line with other published series using Flixene as shown in Table 3.

In another large series of using an alternative early cannulation AVG, Accuseal, the secondary patency was 79% at 1 year with a primary patency rate of 35%.[26]

Our group of patients had a very low rate of infection, with no primary wound infections in the first 90 days, despite being an elderly and significantly diabetic population. The Flixene graft with its low friction polyethylene sheath together with its associated tunneller and a 6-mm tip causes less trauma to the surrounding tissues, bruising and oedema.[27] Therefore, the graft could be identified immediately and safely, rather than waiting for any

swelling to go down. The protective sheath also allowed for less direct handling of the actual AVG. Furthermore, our routine use of Teicoplanin which has a long half-life provides cover not only for surgery but also for the first needling.[28] To date, we have not had any patients who have developed pseudoaneurysms or other perigraft haematoma that may predispose to infections.

In our practice, we have found the use of the early cannulation graft Flixene to be safe with a low complication rate and favourable patency rates. We believe this AVG provides a useful addition for vascular access surgeons and minimises the use of catheters.

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Author contributions

R.S. contributed to data collection; data analysis and interpretation; and manuscript preparation. J.A.G. contributed to design of study; data collection; data analysis and interpretation; and manuscript preparation.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Statement of ethics

This piece of work would be defined by Oxford University Hospitals NHS Foundation Trust as Practice/Service Evaluation and Development; thus, ethical approval was not required. The governance requirements of the Oxford University Hospitals were followed.

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