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Rerouting in vascular access infections using a biosynthetic vascular graft (Omniflow® II)

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Abstract

Background: Surgical treatment of infected arteriovenous grafts (AVG) while preserving the hemodialysis access remains a challenge. Partial graft excision (PGE) directly followed by interposition grafting (IG) is an established method but is associated with a high rate of local reinfection. This retrospective study investigated the technique of rerouting using a biosynthetic vascular graft (Omniflow® II).

Methods: This was a retrospective analysis of all patients at a tertiary referral center undergoing surgical treatment for AVG infections using PGE and IG with the rerouting technique using Omniflow® II between January 2009 and December 2018. Follow-up data were collected until May 2021.

Results: Fifteen patients (53% male, median age 62 years [range 49-81]) were identified for further analysis, thereof twelve received an Omniflow® II vascular graft. Eleven patients had positive local microbial cultures, with *Staphylococcus aureus* being the most frequently identified pathogen (9 cases). Mortality and reoperation rates within 30 days were both 0%. Median follow-up was 32 months (range 2–101 months) with a median follow-up index of 0.92 (range 0.18–1). During follow-up a surgical intervention for reinfection was necessary in 3 patients with Omniflow® II at a median of 304 days (range 298–485 days).

Conclusion: Partial graft excision and direct interposition grafting using a biosynthetic Omniflow® II vascular graft is a valid treatment option in selected patients with AVG infections when total graft excision can be avoided. Using a careful rerouting technique, while preserving clinically noninfected graft sections the risk of early reinfection can be minimized and the dialysis access maintained.

Keywords
Renal dialysis · Arteriovenous graft · *Staphylococcus aureus* · Reoperation · Treatment outcome

Introduction

Vascular access (VA) complications in patients with end-stage renal disease (ESRD) are common and often require interventions. Although loss of patency is by far the most common reason for a surgical intervention, vascular access infections (VAI) are a relevant complication, associated with morbidity and mortality due to sepsis [12]. The VAI are more frequent in arteriovenous grafts (AVG) using polytetrafluoroethylene (PTFE) than in native arteriovenous fistulas (AVF). Infection rates as high as 9% per year have been reported for AVG in comparison to AVF with 4.1% [5, 17]. The VAI may occur as an early complication of VA creation or VA revision for another reason or, in the longer term due to repeated puncture for hemodialysis (puncture site infection) or secondarily due to a systemic infection.

Treatment of VAI usually includes systemic antibiotic therapy and surgical intervention. In early AVG infections, total graft explantation is usually necessary. In cases of late AVF and AVG infections, mostly related to puncture site infections, the surgi-

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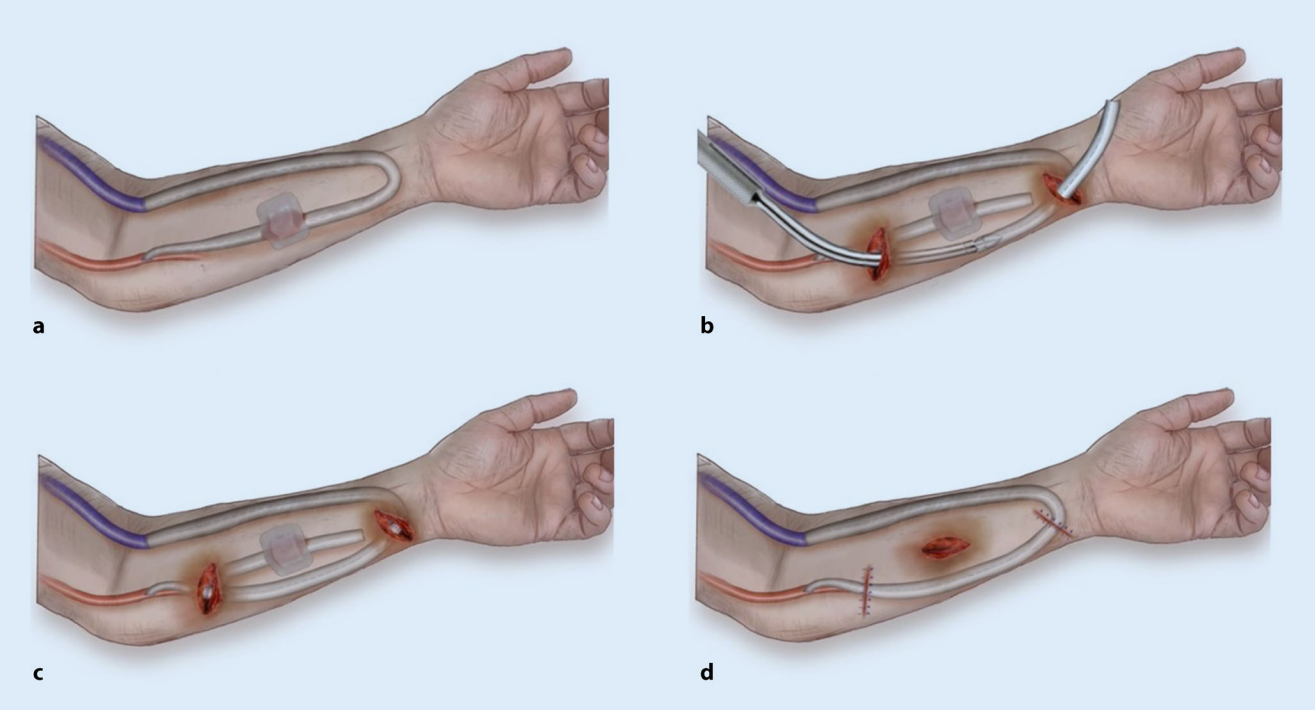

Fig. 1 ▲ Sketch of partial AVG replacement using the rerouting technique. **a** The infected wound is covered to keep the operating field as sterile as possible. **b** Two incisions are made at a distance from the infected area where the AVG is well-incorporated. **c** After short resection of the AVG towards the infected area with closure of the fatty tissue in that direction, a new AVG is placed more laterally in a healthy zone. **d** After closure of the sterile incisions the partially infected graft is explanted, followed by open wound treatment (reprint with permission © A. Zdoroveac. All rights reserved)

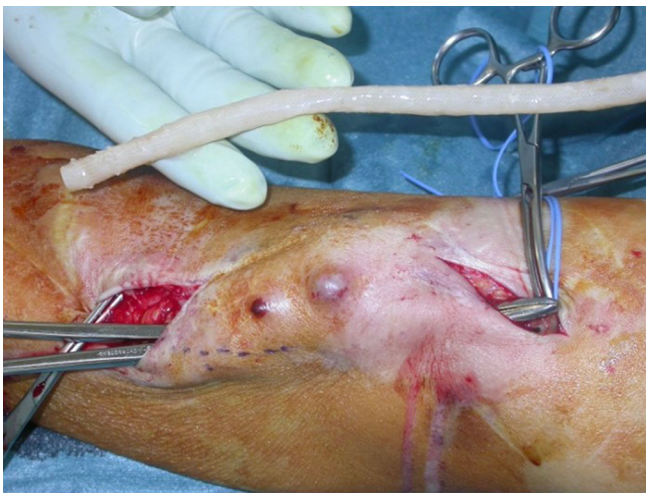

Fig. 2 ◀ Rerouting with an Omniflow® II graft in a patient with an infected false aneurysm of an upper arm PTFE AVG

cal options range from local debridement of infected and necrotic tissue to partial graft excision with interposition grafting (PGE), or total graft excision (TGE) with in situ reconstruction or rerouting with an interposition graft (IG). ◘ **Figure 1** shows the technique how PGE and IG can be performed with rerouting in a safe manner [20].

The chosen surgical treatment largely depends on the extent of VAI, the patient's condition and the surgeon's clinical evaluation and preference. Clinical practice guidelines, such as those of the European Society of Vascular Surgery [18] and The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative [13] may help in decision making but are mostly based on expert opinions.

Older studies have shown acceptable infection control while preserving vascular access using PGE and IG, although the rate of local reinfection requiring further intervention was up to 35% [15]. PTFE was usually used for IG [11, 16], although alternative materials, such as autologous veins, xenografts or biosynthetic grafts have been considered [2].

In this study, PGE and IG is the favored surgical approach for the treatment of infected AVG. To further reduce the risk of recurrent infection, Omniflow® II was routinely used for IG. Omniflow® II is a biosynthetic vascular prosthesis, which is a composite of cross-linked ovine collagen with a polyester mesh endoskeleton (LeMaitre Vascular Inc., Burlington, MA, USA; ◘ **Fig. 2**). This product is mainly available in Europe, Canada and Australia but it is not approved by the U.S. Food and Drug Administration (FDA). Whenever possible, rerouting the graft should be done in healthy tissue. The aim of this study was to investigate all VAI cases at a tertiary center over a 10-year period, then identify and evaluate the outcomes of cases where Omniflow® II was used for IG after PGE in AVG infections.

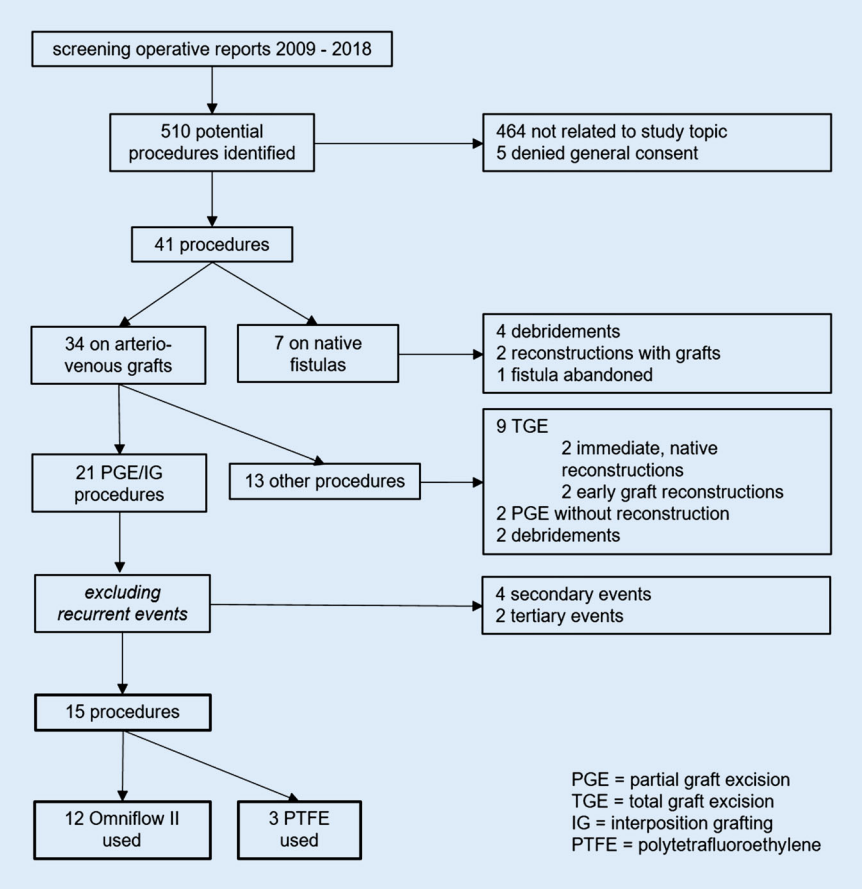

Fig. 3 ▲ Flow chart of patient identification for vascular access infections (VAI) and treatment with Omniflow® II

Methods

This is a retrospective analysis of all patients who underwent surgical revision of VAI between January 2009 and December 2018 at a single tertiary referral center. Follow-up data were gathered until the end of May 2021. The local ethics committee approved the study and waived the requirement for written informed consent for patients who were missing documentation (decision number 2019-01677). Patients who had refused informed consent for the use of their health-related data in the context of research, were excluded. A full text search for the terms fistula or shunt and infection was performed on all operative reports of our vascular unit registered between January 2009 and December 2018. The resulting reports were manually screened for eligibility. Preoperative, procedural and postoperative data were collected from surgical and anethesia reports and electronic medical records. Data were stored in a secured REDcap database (Research Electronic Data Capture, Vanderbilt University, Nashville, TN, USA). Follow-up data were collected from nephrological records at our institution. The VA was classified as infected if the attending vascular surgeon considered an infection as highly likely due to clinical presentation (e.g., erythema, swelling, purulent liquid near site), local microbial cultures proved bacterial infection or the patient had positive blood cultures in the absence of another more likely focus. The attending surgeon indicated the time of operation and technique of surgery. Intraoperative swabs or tissue samples were cultivated for bacterial growth. Further PCR testing for specific pathogens and sonification of graft parts were not routinely performed. The PGE and IG was performed if deemed feasible. New grafts were rerouted through noninfected tissue. The choice of graft material was at the surgeon's discretion. Antibiotic protocols were not standardized. Empirical treatment was administered in all cases and later adjusted according to the microbiological results. The duration of antibiotic treatment was determined on an individual basis, in collaboration with attending nephrologists and infectiologists.

For the statistical analysis the R statistics program version 4.1.3 was used (R Foundation for Statistical Computing, Vienna, Austria). Categorical variables are presented as absolute numbers and percentages. Continuous data are presented as median values and ranges.

Completeness of follow-up was examined using a follow-up index [23].

Results

The patient identification process is illustrated in **Fig. 3**. The surgical approach to treat VAI varied greatly, emphasizing the need for tailored approaches to different extents of infection and different patient situations. Patients in need of multiple PGE and IG procedures over the years were only included with the first event. Demographic data, patient characteristics and clinical aspects at presentation are shown in **Table 1**.

A total of 15 rerouting PGE and IG procedures were found, of which 12 cases were reconstructed with Omniflow® II (3 cases were reconstructed with PTFE). In all these cases microbial cultures were obtained. *Staphylococcus aureus* was by far the most common pathogen (nine cases, including all cases that underwent reconstruction with PTFE); coagulase-negative *Staphylococci* and *Streptococci* were identified once each. No microbial growth occurred in four cases despite a clinical suspicion of infection. All of these had been preoperatively treated with antibiotics. The infection necessitating the surgical procedure occurred between 2 and 43 months after the AVG creation. Early postoperative outcomes were favorable, with freedom from local infection at discharge in all cases, without the need of secondary interventions. There was no in-hospital mortality. The duration of systemic antibiotic therapy varied greatly between 1 week and 4 months. During long-term follow-up, a surgical intervention for reinfection was necessary in 4 cases, between 298 and

Table 1 Demographic characteristics of the patients included in the study

Group	IG with Omniflow II	IG with PTFE
Number of patients, n	12	3
Age (years), median (range)	66 (49–81)	61 (60–62)
Male, n (%)	6 (50)	2 (67)
Body mass index, median (range)	25 (19–33)	19 (18–22)
Months since current fistula creation, median (range)	12 (2–43)	9 (4–10)
Comorbidities, n (%)		
Hypertension	11 (92)	3 (100)
Diabetes mellitus	4 (33)	0
Dyslipidemia	7 (58)	1 (33)
Current smoker	2 (17)	1 (33)
Coronary heart disease	4 (33)	1 (33)
Occlusive peripheral artery disease	4 (33)	1 (33)
Chronic obstructive pulmonary disease	0	0
Clinical presentation, n (%)		
Blood cultures taken	9 (75)	3 (100)
Blood cultures positive	9 (100)	2 (66)
Systemic infection signs	7 (58)	3 (100)
Local inflammation signs	9 (75)	1 (33)
Fluid collection	5 (42)	2 (67)
Open wound	3 (25)	0
ABT established before operation	11 (92)	3 (100)

ABT antibiotic treatment, *IG* interposition grafting, *PTFE* polytetrafluoroethylene

Table 2 Perioperative and outcome data of all patients included in the study

Group	IG with Omniflow II	IG with PTFE
Number of cases, n	12	3
Microbiological sample taken, *n* (%)	12 (100)	3 (100)
Microbiological sample positive, *n* (%)	8 (67)	3 (100)
Days of ABT, median (range)	41 (6–124)	27 (15–42)
In-hospital death, *n*	0	0
Local reinfection after 30 days, *n*	0	0
Follow-up		
Cause of death known, *n* (%)	5 (63)	1 (50)
Cause of death related to fistula infection, *n*	0	0
Reoperation for loss of patency, *n* (%)	6 (50)	2 (67)
Time to reoperation for loss of patency, days (range)	149 (65–2088)	485 (473–497)

IG interposition grafting, *ABT* antibiotic treatment, *PTFE* polytetrafluoroethylene

515 days after the PGE and IG procedure. Of these, three reinfections occurred in the Omniflow® II group and one in the PTFE group. At the time of reinfection all patients presented with local signs of infection and three also had systemic symptoms. *Staphylococcus aureus* was found in two cases, the others showed no microbial growth. The PGE and IG was performed again in three of these cases and in all of them Omniflow® II was used. One Omniflow® II with a new infection was treated with local debridement and reconstruction using a xenopericardial graft (as the resulting defect was small). The time to reoperation for reinfection in the Omniflow® II group is depicted in ◘ **Fig. 4** and 2 tertiary infections occurred in the Omniflow® II group after 4 and 15 months. *Staphylococcus aureus* was again found in the first mentioned patient, who was on home hemodialysis and PGE/IG was performed again in both cases. Loss of patency was more common and a surgical intervention for this reason was necessary eight times. Only five patients were alive at the end of data collection (including one PTFE rerouting case). No death appeared to be related to an AVG infection (◘ **Table 2**). The median follow-up was 32 months (range 2–101 months) with a median follow-up index of 0.92 (range 0.18–1).

Discussion

Infections related to vascular access in patients with ESRD are not infrequent and different strategies are established to resolve this problem. In the case of an early AVG infection, total graft excision is usually unavoidable. In situations with late infections related to puncture sites, where the graft has areas of complete soft tissue integration, or in cases of a potentially infected false aneurysm, a partial graft replacement, as described by Raju in 1987 [15] is a good treatment option. In this study two thirds of all identified patients with AVG infections were treated by this method. The median times of 12 months (for Omniflow® II) and 9 months (for PTFE) until the first manifestation of reinfection suggest that the VAI was related to a complication of cannulation.

In the guidelines for the management of vascular graft and endograft infections different classifications are presented [7]. The MAGIC classification was developed for aortic graft infections but with some exceptions this concept is also suitable for AVG and AVF infections for vascular access patients because, as in this case series, not all criteria (clinical or surgical signs, radiology and laboratory with the subclasses major versus minor) were present all the time [14]. During data analysis a certain lack of correct identification and description of an infected situation was encountered, especially if local microbial cultures or blood cultures were missing or inconclusive. This might lead to faulty decision-making regarding PGE and IG, as in the clinical practice it should be offered to selected patients with localized infections, where such a procedure can be safely performed with low risk of reinfection. As in the analysis of the US Renal Data System, with more than 870,000 patients with AVF, AVG or catheters by Locham [12], *Staphylococcus aureus* was the most common microorganism found in this population

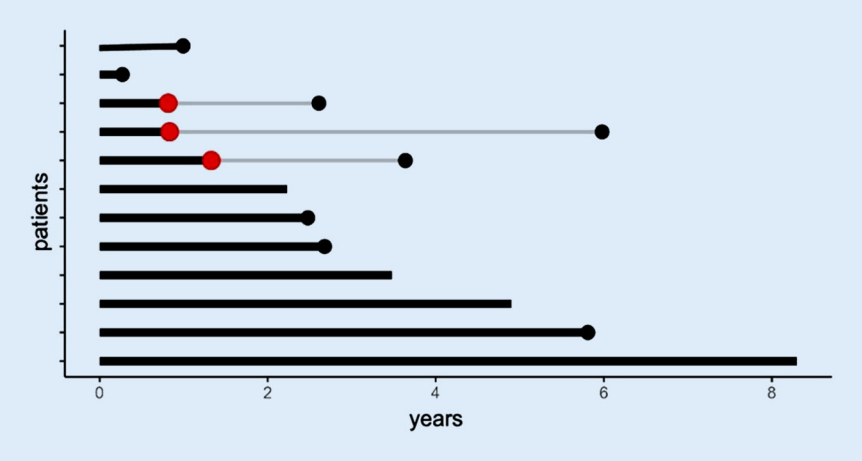

Fig. 4 ▲ Life history plots of the 12 patients who underwent IG with Omniflow® II. *Black dots* death, *red dots* reinfection, *black full line* follow-up, *grey line* follow-up after a second episode of infection

which also has the same typical profile of risk factors [12]. These findings underline the fact that a careful and aseptic cannulation technique is the key in ESRD patients who are per se susceptible to septic complications.

The first clinical results of Omniflow® II used as graft material in primary AVG placement in patients without veins were reported in the 1990s showing a primary patency of 43–64% after 3 years with a low risk of infection and a minimal risk of aneurysmatic dilatation [10, 24]. Shakarchi et al. published three cases of patients with a high risk for infection using an Omniflow® II. All three patients did not show any signs of AVG infection during follow-up [1]. In their review of four case series published between 2009–2011, with a total of 236 procedures using Omniflow® II for AVG creation, the pooled primary patency rate was 60.1% (95% confidence interval, CI 53.6–66.5%) and the secondary patency rate was 82.1% (95% CI 76.7–86.9%). The largest study in the review with 158 procedures, reported an infection rate of 5.7% using Omniflow® II as AVG [3]. The low risk for infection of Omniflow® II prostheses was a trigger to use these ovine collagen grafts in other fields of vascular surgery, especially in the lower limbs. Van de Laar et al. reported a primary and secondary patency at 1 year for Omniflow® II as arterial bypass material in an above-knee position (in comparison to PTFE) of 60% vs. 46.9% and 80.8% vs. 82.5%, respectively, with significantly more wounds and ischemia as well as a higher foot infection (WiFi) score in the Omniflow® II group [22]. Currently, Omniflow® II is not only used as an alternative to expanded PTFE (ePTFE) but also to replace infected aortic and peripheral prosthetic grafts in situ [4, 6, 9, 19]. In all these publications no graft ruptures were reported.

The technique of rerouting to avoid in situ reconstruction is a convincing concept even if three patients in the Omniflow® II group suffered from a reinfection after approximately 10–17 months. Interestingly, rerouting procedures were successfully attempted again due to a localized reinfections. It was even possible to intervene in the same manner again in two patients 4 and 15 months after the second rerouting. Successful preservation of vascular access appears to be worthwhile even when the cost for a biological prosthesis is higher than for a regular synthetic AVG.

All reinfections seemed to be related to cannulation, with its inherent risk of bacterial contamination, in a population with a general risk for infections due to renal insufficiency [21]. This case series shows that more than half of the patients could profit in the long term and use the Omniflow® II graft as a vascular access conduit for more than 3 years, with a maximum of 8 years. The patient long-term mortality rate was similar to other reported data [8].

This study also revealed vast differences in the use of adjuvant antibiotic therapy among the cases, especially considering the length of treatment. Although individualized treatment is certainly warranted for infected dialysis access sites, standardized treatment schemes, also with respect to the choice of vascular graft materials, should be developed and implemented on an institutional level or within vascular societies, helping surgeons to choose adequate therapeutic measures and reduce confounding factors for further studies investigating the outcome of treatment for VAI.

In terms of limitations, this retrospective study included procedures with considerable heterogeneity as demonstrated in **Fig. 3**. The data were also gathered over a long period with potentially changing treatment standards over time. As the cause of death in patients who died was unknown in the majority of cases, more infections, even severe ones, could have been missed. Nevertheless, the use of Omniflow® II for this indication is durable in the long term and even further reinfections can be repetitively treated.

Conclusion

In patients with a VAI and partially well-integrated AVG, the technique of rerouting using a biosynthetic graft, such as Omniflow® II as an interposition graft shows favorable results, even over time but with the necessity of secondary and even tertiary rerouting procedures in a minority of patients. The possibility to do so can help maintain a vascular access site for several years. Meticulous and standardized data collection in registries of patients with VAI is mandatory to further improve the concept of the best treatment for patients with VAI.

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Declarations

Conflict of interest. D. Müller, C. Kohler, S. Weiss and M.K. Widmer declare that they have no competing interests.

This retrospective study was performed after consultation with the institutional ethics committee and in accordance with national legal requirements.

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Zusammenfassung

Rerouting bei Infektionen des vaskulären Zugangs unter Verwendung eines biosynthetischen Gefäßtransplantats (Omniflow® II)

Hintergrund: Die chirurgische Behandlung infizierter arteriovenöser Transplantate (AVT) bei gleichzeitigem Erhalt des Hämodialysezugangs stellt nach wie vor eine Herausforderung dar. Die partielle Transplantatexzision, direkt gefolgt von einer Interpositionsplastik ist eine etablierte Methode, die jedoch mit einer hohen Rate lokaler Reinfektionen assoziiert ist. In dieser retrospektiven Studie wurde die Technik des Reroutings mit einem biosynthetischen Gefäßtransplantat (Omniflow® II) untersucht.
Methoden: Es handelt sich um eine retrospektive Analyse aller Patienten an einem tertiären Referenzzentrum, die sich zwischen Januar 2009 und Dezember 2018 einer chirurgischen Behandlung von AVT-Infektionen mit partieller Transplantatexzision und Interpositionsplastik mit der Rerouting-Technik unter Verwendung von Omniflow® II unterzogen. Die Nachbeobachtungsdaten wurden bis Mai 2021 erhoben.
Ergebnisse: Von den Patienten wurden 15 (53% männlich, mittleres Alter: 62 Jahre, Spanne: 49–81 Jahre) für die weitere Analyse identifiziert. Von diesen 15 Patienten erhielten 12 ein Omniflow®-II-Gefäßtransplantat; 11 Patienten hatten positive lokale mikrobielle Kulturen, wobei *Staphylococcus aureus* der am häufigsten identifizierte Erreger war (9 Fälle). Die Sterblichkeitsrate und die Reoperationsrate innerhalb von 30 Tagen lagen bei 0%. Die mediane Nachbeobachtungszeit betrug 32 Monate (Spanne: 2–101 Monate) mit einem medianen Follow-up-Index von 0,92 (Spanne: 0,18–1). Während der Nachbeobachtung war bei 3 Patienten mit Omniflow® II ein chirurgischer Eingriff aufgrund einer Reinfektion erforderlich, wobei der Median 304 Tage betrug (Spanne: 298–485 Tage).
Schlussfolgerung: Die partielle Transplantatexzision und die direkte Interposition mit einem biosynthetischen Omniflow®-II-Gefäßtransplantat ist eine valide Behandlungsoption bei ausgewählten Patienten mit AVT-Infektionen, wenn eine vollständige Transplantatexzision vermieden werden kann. Durch eine sorgfältige Rerouting-Technik unter Beibehaltung klinisch nicht infizierter Transplantatabschnitte kann das Risiko einer frühen Reinfektion minimiert und der Dialysezugang aufrechterhalten werden.

Schlüsselwörter
Dialyse · Arteriovenöses Transplantat · *Staphylococcus aureus* · Reoperation · Behandlungsergebnis

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