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EBPG on Vascular Access

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1. Patient referral

Guideline 1.1. An early plan for venous preservation should be a substantial part of pre-dialysis care and education in any chronic kidney disease (CKD) patient regardless the choice of treatment modality (Evidence level IV).

Guideline 1.2. Every chronic renal failure patient, who have opted for haemodialysis, should start dialysis with a functioning vascular access (Evidence level III).

Guideline 1.3. Potential chronic haemodialysis (HD) patients should be ideally referred to the nephrologist and/or surgeon for preparing vascular access when they reach the stage 4 of their CKD (glomerular filtration rate $<30\,\text{ml/min/1.73}\,\text{m}^2$) or earlier in case of rapidly progressive nephropathy or specific clinical conditions such as diabetes or severe peripheral vascular disease (Evidence level III).

Rationale

Early referral of CKD patients to the nephrologist and/or vascular surgeon is strongly recommended. This is to start a policy to preserve access sites and to allow adequate time for planning, creation and maturation of the vascular access. The planning stage involves examination and pre-operative vascular mapping. An autogenous fistula requires at least 6 weeks for maturation before it can be used. Additional time may be required for interventional or surgical revisions to enhance maturation. For these reasons, it is recommended that the fistula is created at least 2–3 months before the earliest likely date for starting haemodialysis. Prosthetic graft AVFs do not need a maturation period and can be cannulated 2–3 weeks after implantation. However, prosthetic graft AVFs are not recommended as primary vascular access. This approach is recommended to minimize the use of catheters and to reduce catheter-related morbidity and need for hospitalization. Early referral to the nephrologist is also required for psychological preparation for dialysis, discussion of all options for dialysis modality, interventions to delay progression of renal damage and to correct the hypertension, anaemia and metabolic effects of renal failure [1–5].

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Recommendations for future research

Streamlining of early patient referral and organization of predialysis care are major subjects for research. A policy of venous preservation should be educated and implemented.

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2. Pre-operative evaluation

Guideline 2.1. Clinical evaluation and non-invasive ultrasonography of upper extremity arteries and veins should be performed before vascular access creation (Evidence level II).

Guideline 2.2. Central vein imaging is indicated in patients with a history of previous central vein catheters (Evidence level IV).

Rationale

There is a significant failure rate for autogenous arteriovenous fistulae (AVFs), estimated at 0.2 events per patient/year. For graft AVF, this increases to 0.8–1.0 events per patient/year. In a recent meta-analysis, the primary failure rate for autogenous wrist AVF was 15.3%. Primary and secondary 1-year patency rates were 62.5 and 66.0% [1]. Nowadays, the chronic dialysis population is becoming elderly and is increasingly likely to have diabetes, peripheral arterial obstructive disease (PAOD) or coronary artery disease. Many of these patients have poor vessels for construction of autogenous fistulae and this may be the major reason for the high primary failure and moderate long-term patency.

Physical examination

Careful selection of suitable vessels based on objective evaluation, is required for successful creation of a functioning AVF. Physical examination is used for pre-operative assessment and access planning. This includes assessment of the distal arterial pulse and the presence, diameter and course of the superficial fore- and upper arm veins. Physical examination may be difficult in obese patients and depends on the experience of the examiner.

Ultrasonography

Pre-operative vessel assessment with ultrasonography enhances the success of creation and the outcome of autogenous AVF. In a randomized trial, the primary AVF failure rate was 25% when pre-operative assessment depended on physical examination alone, compared with 6% ($P = 0.002$) when ultrasonography was used [2]. In the study performed by Silva *et al.* [3] strategies for vascular access creation were based on pre-operative duplex scanning. Patients with a radial artery diameter of $\geq$2 mm and a cephalic vein diameter of $\geq$2.5 mm received radial-cephalic AVFs (RCAVF). Grafts were used in patients with insufficient radial arteries or cephalic veins and in those with outflow vein in the elbow with a diameter of $\geq$4 mm. The percentage of RCAVF creation increased from 14% to 63%, while the early failure rate decreased from 36% to 8% [3]. In other studies, the fistula rate increased from 17–35% to 58–85% [4–7]. All studies were performed in American dialysis facilities with their historical low autogenous fistula creation rate in past years.

One study showed that the functional maturation rate of AVFs decreased from 73% to 57% as the autogenous fistula creation rate increased from 61% to 73% after the implementation of pre-operative duplex scanning [8]. This outcome suggests that other selection criteria based on findings at pre-operative imaging are needed to further refine and optimize arteriovenous access surgery. Pre-operative ultrasound screening is especially useful in obese patients. AVF rates were similar in 50 patients with body mass index (BMI) $>27\,\mathrm{kg/m^2}$ compared with 130 patients with lower BMI when pre-operative vein mapping was employed [9].

Arterial imaging

Radial artery diameter predicts the outcome (failure or dysmaturation) of RCAVF and influences the strategy for vascular access creation. Wong *et al.* [10] observed either thrombosis or failure to maturation in all RCAVFs created in patients with a radial artery diameter of <1.6 mm. In another study, successful RCAVFs had a pre-operatively measured radial artery diameter of 2.7 mm *vs* 1.9 mm in failed RCAVFs [11]. Malovrh discriminated between RCAVFs created with radial arteries, with a diameter >1.5 mm *vs* $\leq$1.5 mm. Immediate patency rate in the >1.5 mm group was 92 *vs* 45% in the $\leq$1.5 mm group, while the patency rates after 12 weeks were 83% *vs* 36%, respectively [12]. The predictive value of the radial artery peak systolic velocity (PSV) and resistance index (RI), calculated from pre-operative ultrasonographic parameters, is uncertain [10,13,14]. However, Malovrh showed a significant correlation between radial artery RI (0.50 *vs* 0.70), diameter (0.294 *vs* 0.171 cm), and flow (90 *vs* 33 ml/min) during pre-operative hyperaemia testing and the outcome of AVF creation [15].

Venous imaging

Vein diameters of <1.6 mm have been associated with AVF failure [10], while good patency rates were obtained in patients with RCAVFs where the diameter of the cephalic vein at the wrist was >2–2.6 mm or upper arm veins >3 mm) [16]. The cephalic vein diameter increase after application of a proximal tourniquet is an important predictor of success. In a group of successfully created AV fistulae, the vein diameter increased by 48%, while vein diameter only increased by 11.8% in the group of failed AV fistulae [15].

Table 1. Vessel diameters for successful RCAVF creation

Author	Radial artery (mm)	Cephalic vein (mm)
Wong *et al*. [10]	1.6	1.6
Malovrh [12]	1.5	1.6
Silva *et al*. [3]	2.0	2.5
Ascher *et al*. [21]	–	2.5

Arterial and venous vessel selection

From the available literature (Table 1) a minimal diameter of the anastomosed vessels (radial artery and cephalic vein) of 2.0 mm is advisable for the creation of successful RCAVFs. Critical minimal diameters of cubital and/or upper arm vessels for the creation of successful elbow/upper arm fistula creation are not established.

Venous preservation with additional handgrip exercise may enhance the quality and diameters of arteries and veins for fistula creation [17].

Venography and magnetic resonance angiography

Conventional iodine venography may cause permanent deterioration in renal function in patients with severe renal damage. It is, therefore, not suitable for patients who are preparing for dialysis or for dialysis patients with some residual renal function. Gadolinium is a safe alternative to iodine venography with acceptable inter-observer correlation regarding imaging quality ($\kappa = 0.62$) and strategy planning ($\kappa = 0.64$) [18]. CO_2 angio/venography can also be employed, because of its low risk of renal function deterioration.

Magnetic resonance angiography (MRA), with either time-of-flight (TOF) or contrast-enhanced (Gadolinium) technique (CE-MRA) has been rarely used for access planning. CE-MRA results in a good visualization of arm veins. Diameter measurements were closely correlated overall ($r = 0.91$) and on a vein-to-vein basis ($r = 0.84$–0.98) compared with conventional venography [19]. Studies on the diagnostic accuracy of preoperative MRA *vs* duplex scanning, however, are lacking. Central vein imaging can be accurately performed by CE-MRA [20]. Alternatively, MRA has the potential for imaging of both arterial and venous vessels.

Recommendations for future research

Detection of significant pre-operative parameters for successful fistula creation and maturation remains a major issue for further investigation. Newer imaging techniques with high-resolution quality should be further developed.

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3. Strategies for access creation

Guideline 3.1. The access should provide sufficient blood flow to perform adequate haemodialysis (Evidence level II).

Guideline 3.2. Autogenous arteriovenous fistulae should be preferred over AV grafts and AV grafts should be preferred over catheters (Evidence level III).

Guideline 3.3. The upper extremity arteriovenous fistula should be the preferred access and should be placed as distal as possible (Evidence level III).

Guideline 3.4. Fistula maturation should be monitored to allow pre-emptive intervention if needed (Evidence level III).

Rationale

For decades there have been remarkable differences in strategy for access creation between Europe and the USA. In Europe, the majority of new and incident patients receive autogenous arteriovenous fistulae (AVF), in the USA prosthetic graft placement remains the access of choice in most of the dialysis facilities (AVF 80 *vs* 24%; graft 16 *vs* 70%). The reason for this marked difference is not clear, although patient comorbidity seems to be more pronounced in USA and this could influence the strategy for access creation. Data from DOPPS (Dialysis Outcome and Practice Pattern Study) showed that rates of diabetes mellitus (46 *vs* 22%), peripheral arterial obstructive disease (PAOD) (23 *vs* 19%), coronary artery sclerosis (37 *vs* 25%) and obesity are significantly higher in the American dialysis population [1,2]. It is estimated that an AVF needs 0.2 interventions per patient/year compared with 1.0 intervention per patient/year for prosthetic graft fistulae for access salvage. In addition, long-term primary access survival (patency rate) differs significantly, ranging from 90% to 85% for AVF and from 60% to 40% for graft at one and 2 year of follow up [3]. With intensive access monitoring and surveillance, the secondary survival of grafts may rise due to a pre-emptive stenosis repair policy. The patency rate for grafts may be comparable with AVFs, ranging from 90% to 70% at 1 and 2 years of follow-up, respectively.

Ifudu *et al*. [4] stated that grafts do not permit the delivery of better haemodialysis than autogenous arteriovenous fistulae. They analysed 214 patients over a period of 1 month by urea reduction ratio; serum albumin concentration was used as a secondary outcome measure of dialysis adequacy [4].

Primary choice for vascular access

Autogenous AVF creation

Radial-cephalic AVF. The wrist radial-cephalic (RC) AVF is the first option for access creation. When the RCAVF matures adequately, it may function for years with a minimum of complications, revisions and interventions. The high early thrombosis/non-maturation percentage is the major disadvantage of this access and is usually influenced by patient factors like age, diabetes mellitus and the presence of cardio-vascular disease. Early failure rates range from 5% to 30% [5,6] and long-term patency from 65–90 to 60–80% at one and 2 years of follow-up, respectively. The incidence of thrombosis (0.2 events per patient/year) and infection (2%) is low.

Proximal forearm AVF. When a wrist RCVF is impossible due to poor vessels a more proximally located anastomosis from the mid-forearm to the elbow between the radial artery and cephalic vein may be employed.

Brachial-cubital/cephalic/basilic AVF. When peripheral vessels are too tiny and diseased for the creation of an RCAVF, more proximal fistulae are indicated at the elbow and upper-arm region. These AVFs (brachial-cubital = Gracz; brachial-cephalic and brachial-basilic) generate a high blood flow which is favourable for high-efficiency dialysis. The incidence of thrombotic and infectious complications is low and long-term outcome is usually good [7–17]. The major disadvantages of these high-flow AVFs are the risk of distal hypoperfusion, which may lead to symptomatic hand ischaemia, and high-output cardiac failure, particularly in patients with coronary artery disease and/or cardiac failure [18].

Early access failure and interventions

The success rate for AVFs should be enhanced by pre-operative vessel assessment (see Guideline 2), perioperative vasodilatation [19] and post-operative monitoring of maturation. Access blood flow measurement by Doppler ultrasound at day 1 and 7 after operation is indicative of successful maturation. AVFs with initial blood flow rates of <400 ml/min fail to mature in the majority of cases [20,21]. Increased post-operative blood flow through the AVF with high shear stress on the vessel wall initiate the process of vessel adaptation (remodelling) resulting in vessel dilatation and further flow increase. Inability of vessel adaptation is usually due to the presence of significant stenoses or small arterial inflow vessels. Diagnostic angiography or ultrasound evaluation is indicated when there is failure of maturation. Percutaneous intervention (PTA) is indicated for any stenosis, and when not successful surgical revision can be considered [22–24].

The use of non-penetrating vascular clips for arteriovenous anastomosis may cause less endothelial cell damage and reduce the smooth muscle cell proliferation which leads to intimal hyperplasia (IH) [25–27].

Patient variables and outcome of vascular access

Several studies have shown that patient variables may have an important impact on the choice and outcome of vascular access. Age may have an influence on post-operative blood flow in newly created autogenous fistulae, which results in a slightly higher failure rate compared with young patients (18.9 *vs* 13.6%) [28]. However, the combination of age and diabetes does have an impact on fistula outcome with significantly higher failure rates (28.6%). Large European, Australian and American population-based studies have shown an increased percentage of grafts in elderly patients. In Europe, the use of grafts increased from 5% in patients <45 years to 8.8% in patients >75 years of age [29,30]. In Australia and USA, significant odds ratios were calculated indicating age as a predictive factor for graft use in incident and prevalent patients. In addition, grafts were associated with poor outcome in terms of primary failure and with a higher incidence of revisions compared with fistulae [31–34]. On the other hand, grafts may do well in the higher age group over 70 years. Staramos *et al.* [35] showed better patency at 2 and 3 year for prosthetic grafts compared with fistulae. This difference can be explained by the high number of dropouts due to early failure of the fistulae (24 *vs* 11%).

Women usually have smaller arteries and veins and, therefore, may do worse compared with men. And this may be the reason for poorer maturation and survival rates of vascular access. However, the literature remains contradictory. Caplin *et al.* [36] showed that arterial and venous diameters were not significantly different between men and women and functioning fistulae were created in 72% of the female and 77% of the male patients. In a meta-analysis of RCAVFs, women had similar maturation and 1-year patency rates as men. It is possible that pre-operative vessel selection for AV anastomosis influenced the outcome of access creation, irrespective of gender [5].

Other studies showed that female gender was associated with an increased use of grafts and a higher number of access revisions [30,32,34,37–40]. In the HEMO study, Allon *et al.* [41] found female gender, PAOD, black race, body mass index (BMI) and older age, significant predictor variables for the chance on fistula use. In addition, they found remarkable differences in the percentage of fistulae used in the different dialysis facilities (ranging from 4% to 77%).

Influence of comorbidity on vascular access creation and outcome

During the past decade there has been a shift in the aetiology of end-stage renal failure. Diabetes mellitus and arteriosclerosis are now the most important causes for dialysis treatment. The presence of diabetes and concomitant arteriosclerosis may have an additional negative impact on the chance of successful access creation [38]. These patients usually have poor, thickened and calcified arteries with proximal and/or distal vessel obstruction [42]. Access creation is more difficult, and the risk of symptomatic ischaemia of the upper and lower extremity due to access-induced steal syndrome is significant (see Guideline 9). Many studies report a correlation between the use of prosthetic graft AVF and the prevalence of diabetes in their population. The probability of graft thrombosis is significantly higher in diabetic patients, which results in decreased graft survival [43]. On the other hand, autogenous fistula creation can certainly be successful in patients with diabetes. Similar percentages of primary fistula creation with the use of comparable vessel diameters in non-diabetic and diabetic patients have been reported but more vessel calcifications were detected in diabetics [44]. Excellent results of primary fistula creation even in diabetics have been described by Konner *et al.* [17]. Three types of fistulae were created and none of the patients needed grafts. RCAVFs were created in 62 and 23% of patients (non-diabetics *vs* diabetics), while more proximal forearm and elbow AVFs were needed in diabetics (77%). Primary access survival was similar, however, secondary survival was better in non-diabetics at 2 years of follow-up. Ischaemia occurred significantly more frequently in the diabetic group (7 *vs* 0.6 events per 100 patient/years).

Homocysteine levels do not have any influence on vascular access failure [45], while elevated lipoprotein among black dialysis patients may be a risk factor for access complications [46]. Chou *et al.* [47] identified in a retrospective analysis CRP as an independent predictor for AV fistula thrombosis. The association between specific drug use and access failure was investigated in the DOPPS study. Treatment with calcium channel blockers, aspirin and angiotensin-converting enzyme inhibitors resulted in improved graft and fistula patency [48].

Non-patient variables and success of fistula creation

Late referral and starting dialysis treatment with a central venous catheter reduce the chance of successful autogenous fistula creation [49–51]. Experience and dedication of the physician performing vascular access surgery have a considerable influence on outcome. Prischl *et al.* [52] showed that the experience of the operating surgeon was the major determinant for the patency of RC fistulae. Some nephrologists create vascular access themselves and it has been shown that this approach may result in a higher number of functioning fistulae [53,54].

Vascular access morbidity, hospitalization and mortality

The probability of any access-related hospitalization is greater for patients with grafts than for those with fistulae. Reasons include thrombosis, infection and septicaemia [55–58]. In diabetic patients, the mortality rate is higher for those with grafts or central venous catheters, compared with those with autogenous AVF. In particular, there were more infection-related deaths in both diabetic and non-diabetic patients with central venous catheters compared with those with AVF. AV shunting may increase cardiac risk and death, however, this hypothesis could not been proven in a large patient group [59]. On the other hand, left ventricular hypertrophy does occur in patients with vascular access [60] and may be normalized after access closure in patients with functioning renal transplants [61].

Second choice for vascular access

Upper extremity non-autogenous vascular access

When autogenous AVF creation is impossible or the fistula has failed, one may decide to implant grafts as a vascular access conduit. Greater saphenous vein translocation or homologous saphenous vein implants have been used for some time with moderate results [62]. Nowadays bovine mesenteric vein (Procol®) or ureter (Synergraft®) are popular materials as an alternative access conduit, with acceptable patency and low infection rates [63]. Prosthetic grafts are available as polyurethane (Vectra®) [64], poly-ester (Dacron) and poly-tetrafluoroethylene (Goretex®; Impra®) material. Short-term functional patency is usually good, but stenosis formation (mostly at the graft-vein anastomoses) will lead to thrombotic occlusion within 12 to 24 months. The primary patency rate of prosthetic graft AVFs vary from 60% to 80% and from 30% to 40% at 1 and 2 years of follow-up. Secondary patency ranges from 70% to 90% and from 50% to 70% at 1 and 2 years, respectively [65–69]. Intimal hyperplasia (IH) with smooth muscle migration and proliferation and matrix deposition is the major cause for stenosis formation and thrombosis. The aetiology of IH is unknown, however, high shear stress will denudate the endothelial layer, resulting in platelet adhesion and initiation of a cascade of proteins that stimulate the smooth muscle cells to proliferate and migrate [70–74].

Grafts may have similar outcomes compared with fistulae, in elderly patients in particular. Staramos *et al.* [35] showed good results of graft implantation in very old patients. They argued that this patient group has a very limited life expectancy and early cannulation may be considered with the advantage of avoiding central venous catheters. Also the risk on non-maturation is low as compared with autogenous fistulae.

Measures to improve graft patency

Numerous experimental and clinical studies have been employed to outline the influence of type of graft and graft design on graft patency. Modulating the geometry of the arterial inlet and/or venous outlet of the graft could possibly have a beneficial effect on IH. Clinical studies using tapered (at the arterial side of the graft) grafts did not show better patency rates nor did cuff implantation at the venous anastomosis. However, primary patency did improve with the use of a cuff-shaped prosthesis (Venaflo®) [75–79]. Compliant grafts could probably influence IH by the better matching of the stiff prosthesis with the compliant vein at the anastomotic site. However, in clinical studies this feature was not proven [80].

Anticoagulants and graft patency

The use of warfarin or aspirin on graft survival has been studied [81–83]. In a randomized controlled trial, time-to-graft failure was not significantly different in the treatment group receiving warfarin compared with controls. However, major bleeding occurred in 10% of patients in the warfarin group compared with none in the control group [84]. In the DOPPS study, patients that used anticoagulants such as warfarin, showed even worse graft survival [48]. In another study, aspirin and dipyridamole (Persantin®) administration was compared with a placebo group. Only dipyridamole showed a beneficial effect on thrombosis with a relative risk of 0.35 ($P = 0.02$) [85]. Kaufman *et al.* [86] showed no effect of aspirin and clopidogrel (Plavix®) on graft thrombosis and in their randomized study the risk of bleeding complications was substantial.

A Cochrane database study showed good results of ticlopidine on AVF and graft patency in a total number of 312 patients [87]. The administration of pentoxifylline does not improve graft patency [88].

Radiation and graft patency

External beam radiation and intravascular brachytherapy have been administered to prosthetic graft AVFs to inhibit smooth muscle cells to proliferate at the venous anastomosis [89]. In animal studies, beneficial effects could be demonstrated, however, in patient groups no improvement in graft patency was shown and the risk of adverse effects such as infection increased [90]. Randomized studies could not show any advantage of external radiation on graft patency rates [91,92].

Lower extremity autogenous and non-autogenous vascular access

Probably the only indication for lower extremity vascular access is bilateral central venous or caval vein obstruction, which endangers the outflow of upper extremity AVF. Saphenous or superficial femoral vein transposition are primary options for thigh AVF with a relatively high risk on ischaemia (see Guideline 9). Clinical follow-up and primary flow reduction by tapering of the anastomosis are indicated to prevent ischaemia [93,94]. Prosthetic graft implantation in the thigh has a high risk of infection and septicaemia [95–97].

Third choice for vascular access

Central venous catheter

There may be a few indications for permanent tunnelled central venous catheters as an (primary) option for vascular access. Patients with severe access-induced upper extremity ischaemia or cardiac failure may be candidates for catheters. Life expectancy for these patients is likely to be poor and the need for vascular access limited to some months. The same holds true for patients with disseminated cancers.

Recommendations for future research

Despite the rationale of creating autogenous fistulae for vascular access, research into the development of new non-thrombotic grafts and the prevention of IH remains of utmost importance.

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4. Role of nurses and staff in access management

Guideline 4.1. Nurses and medical staff should be involved in vein preservation and monitoring of the vascular access. Every patient with chronic kidney disease should have a declared plan for preserving the vascular access and potential access sites (Evidence level IV).

Guideline 4.2. Any staff involved in handling vascular access or cannulating veins in renal patients should be adequately trained and be in a continuous training scheme for access management (Evidence level IV).

Guideline 4.3. An autogenous fistula should be cannulated when adequate maturation has occurred (Evidence level III).

Guideline 4.4. The rope ladder technique should be used for cannulation of grafts (Evidence level III).

Rationale

A substantial part of the pre-dialysis care is the preservation of veins in both arms, favouring the use of the veins of the dorsum of the hand for blood sampling, infusions and transfusions [1]. After placement of the initial vascular access, preferably an autogenous AVF, the correct needling technique has a favourable influence on maturation and fistula lifespan. Nurses play a pivotal role in the care for vascular access: they see the patient every dialysis, perform cannulation and assess function of the vascular access [2]. The vascular access should be checked before each cannulation by inspection and palpation. Nurses train patients and partners to perform home haemodialysis. This includes teaching about vascular access and (self-) cannulation [3].

Nurses generally have more practical experience and skills for cannulating and managing vascular access than physicians. Written protocols for cannulation, handling central venous catheters and physical examination of the vascular access prior to cannulation should be provided. The nephrologist bears ultimate responsibility to ensure adequate standards and training in the delivery of care for the vascular access. While this care is almost always delivered by others, the nephrologist should be involved in the training and monitoring of standards. Training courses in vascular access have been initiated for residents, vascular surgeons and nephrologists in the Netherlands and for nurses in France and Turkey [4]. Examinations and qualifications should be mandatory in the future. Societies like the EDNA/ERCA and the European Vascular Access Society or other dedicated initiatives should implement new structural approaches in the care for vascular access.

Technique and Timing of cannulation

While few scientific data concerning access handling and the outcome of specific cannulation techniques have been reported, the rope ladder technique is advised for the cannulation of AV grafts [5], to avoid graft disintegration and the formation of pseudo-aneurysms. In autogenous fistulae, particularly those with only a short vein segment available for needling, the buttonhole method is preferred over area puncture. The timing of access cannulation has been reported from the DOPPS study [6]. For grafts, first cannulation occurred within 2–4 weeks at 62% of USA, 61% of European and 42% of Japanese facilities. For fistulae, first cannulation occurred <2 months after placement in 36% of USA, 79% of European and 98% of Japanese facilities. Earlier cannulation of a newly placed fistula may be associated with impaired AVF survival. Cannulation after <2 weeks should be avoided while usually the minimum maturation period should be ideally >4 weeks. Adequate fistula flow (>600 cc/min) and diameter (>5 mm) measured by ultrasonography can improve the documentation of matured fistulas [7–9].

Recommendations for future research

Studies on cannulation complications and techniques are needed.

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5. Surveillance of vascular access

Guideline 5.1. Prior to any cannulation, autogenous arteriovenous fistulae and grafts should be assessed by physical examination (Evidence level IV).

Guideline 5.2. Objective monitoring of access function should be performed at a regular base by measuring access flow (Evidence level II).

Rationale

It is necessary to evaluate the vascular access clinically prior to any cannulation, both in autogenous AV fistulae and AV grafts. Inspection may reveal swelling, infection, haematoma, aneurysm or stenoses. Palpation evaluates the characteristic thrill and the intravascular pressure as it may differ between a pre- and a post-stenotic vessel segment. Post-stenotic collapse of the vein after elevation of the arm above the heart is proof of the haemodynamic relevance of a stenosis in autogenous AV fistulae. Auscultation is indicated if a stenosis is suspected and a high-pitched bruit can be heard in the presence of a stenosis. Clinical evaluation for the monitoring of prosthetic grafts may be difficult because of their rigidity, however, has been reported reliable to indicate flow changes [1]. Usually, no dilatation is observed, except in case of cannulation-related pseudo-aneurysm formation. Any suspicion of complications arising from the clinical examination should be confirmed by objective measurements. There are a wide variety of functional and anatomic imaging techniques such as access flow measurement, ultrasonography and angiography, each with their own applicability and accuracy rates. The goal of these measurements is the early diagnosis of AV fistula or AV graft dysfunction, aiming at a pre-emptive correction by interventional techniques [2] (See Guideline 7). These measurements require technical equipment and can never substitute for physical examination. Modern dialysis machines always provide venous and arterial pressures which can be used to monitor access function. Numerous dialysis facilities exclusively rely on this type of monitoring, although standardization and comparability is lacking as the pressures are influenced by blood flow, needle diameter and cannulation site. Today, we know that these parameters have a poor predictive value compared with access flow measurements [3]. With the introduction of prosthetic graft materials and their well-known high complication rate, more sophisticated methods came into use such as dynamic and static venous pressure measurements [4,5]. Static intra-access pressure ratio (static venous pressure in relation to mean arterial pressure) as introduced by Besarab [6] offers some advantage over dynamic pressure [7]. Smits *et al*. [8] reported that standardized monitoring of either venous pressure, access flow or the combination of both with subsequent corrective intervention can reduce thrombosis rate in grafts. Recently, Spergel *et al*. [3] concluded in a preliminary report that all types of pressure measurements should be abandoned in favour of access flow measurements.

Various techniques to measure access flow have been described:

Duplex ultrasound, Ultrasound flow dilution (Transonic®), Crit-Line III, Crit-Line III TQA, Variable flow Doppler, In graft Velocitymetry, Blood Velocity Meter and Glucose Pump Test. There is no clear preference for any one of these techniques [7].

In summary, access flow measurement is an accurate predictor of fistula/graft dysfunction, which may result in access thrombosis. An access flow <600 ml/min in AV grafts [8–10] respectively, a reduction of flow >20% per month [9] or <300 ml/min in forearm AV fistulae is an indication for pre-emptive intervention [11]. For upper arm fistulas these flow data are lacking. Monthly flow measurements for grafts and three monthly for fistulae are recommended. Monitoring and surveillance with subsequently pre-emptive radiological or surgical intervention reduce the rate of thrombotic events in AV grafts as well as in AV fistulae, thus substantially decreasing patient morbidity, hospital admissions and costs of healthcare delivery [12–14]. Access monitoring programmes should be included as an integral part of routine dialysis care [13].

Recommendations for further research

Improvement of monitoring methods to accurately detect failing vascular access remains an important issue for research.

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6. Diagnosis of stenoses in AV fistulae and AV grafts

Guideline 6.1. If a haemodynamically significant stenosis is suspected by physical examination and/or flow measurement, imaging should be performed as soon as possible (Evidence level III).

Guideline 6.2. Pre-emptive intervention should be performed percutaneously or surgically without further delay and imaging should be performed immediately before the intervention (Evidence level II).

Guideline 6.3. If the complete arterial inflow and venous outflow vessels need to be visualized, magnetic resonance angiography (MRA) should be performed (Evidence level III).

Rationale

Clinical examination should remain the key method for the diagnosis of stenosis in autogenous arterio-venous fistulae and AV grafts [1]. However, the decision on whether clinical examination alone is sufficient or additional imaging examination must be performed before treatment, depends on local customs and practice. In cases of percutaneous treatment of stenoses, pre-, intra- and post-operative angiography must be conducted. When surgical revision is carried out, on-table angiography after completion should also be conducted when available. Angiography entirely for diagnostic purposes, without concommitant treatment should be avoided. Once thrombosis has occurred, surgical or interventional radiological clot removal is necessary to allow haemodialysis through the vascular access without the need for central venous catheter insertion. Correction of the underlying stenosis is an integral part of any declotting procedure.

Diagnosis of stenosis

Duplex ultrasonography

Whenever stenosis is suspected, duplex ultrasonography can be performed to locate and to quantify the degree of diameter reduction due to the stenosis [2–5]. Duplex ultrasonography in the hand of an experienced clinician or vascular technician is an adequate diagnostic tool except for hand arteries and central veins [6] and can be helpful in defining thrombus extent. Angiography is not necessary if duplex indicates a stenosis at the arteriovenous anastomosis in forearm fistulae, which usually are only amenable to surgical revision by proximal re-anastomosis. Duplex examination is especially valuable in detecting stenoses and to perform flow measurements in non-maturing AV fistulae in which iodine injection should be avoided, because of the risk of renal function deterioration. Recently, duplex was suggested as the initial imaging modality of dysfunctional fistulae, but complete access should be depicted at DSA and angioplasty to detect all significant stenoses eligible for intervention. Magnetic resonance angiography (MRA) should be considered only if DSA is inconclusive [7].

Angiography

Diagnostic angiography with iodinated contrast agents without subsequent dilatation or surgical revision is not advised. However, angiography is typically performed before, during and after dilatation or percutaneous thrombolysis and after surgical thrombectomy in order to guide the treatment and depict inflow as well as residual stenoses and/or clots or central venous obstruction [8]. To avoid impairment of residual renal function, gadolinium-enhanced digital subtraction angiography may be an alternative. Le Blanche *et al.* [9] found no impairment of renal function using gadolinium in their patient collective. They concluded, that gadolinium-enhanced digital subtraction angiography is an effective and safe method to assess the cause for malfunctioning AVFs. It can also be used to plan and perform percutaneous transluminal angioplasty. As an alternative, diluted iodine may be used, with a low risk of further renal function detoriation. Arterial inflow stenosis may be missed by diagnostic angiography. By introduction of a catheter through the access up into the arterial tree, also the subclavian and brachial arteries can be imaged [10].

Magnetic resonance angiography

MRA has been reported to be an useful, safe and practical imaging modality in complex fistulae with fewer complications and side-effects compared with fistulography [11]. It allows non-invasive evaluation of the arterial and venous system in one examination [12]. If MRA is performed as an alternative, it should be employed with contrast-enhanced (Gadolinium) technique (CE-MRA), since the latter shows a good visualization of arm veins with diameter measurements closely correlating with conventional venography [9]. In one study, MRA depicted all 13 stenoses and two false-positive findings, resulting in a sensitivity of 100% and a specificity of 94% for the arterial and venous tree [13]. Froger *et al.* found a sensitivity, specificity and positive and negative predictive value of MRA in the detection of stenosed vessel segments of 97, 99, 96 and 99%, respectively [14]. When central venous obstruction is suspected, angiography of the complete venous outflow system up to the right atrium is mandatory. MRA of the central veins is accurate and even superior to contrast venography, which may fail to show all patent thoracic vessels [15,16]. However, it is an elaborate procedure, and therefore not possible in every hospital. Also, an additional intervention is not possible at the same time [17].

Recommendations for further research

New imaging modalities may be applied for a more accurate diagnosis of access stenosis.

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7. Treatment of stenosis and thrombosis in AV fistulae and AV grafts

Guideline 7.1. For venous outflow stenosis percutaneous transluminal angioplasty (PTA) is the first treatment option (Evidence level III).

Guideline 7.2. Thrombosed autogenous and graft fistulae should be treated either by interventional radiology or surgery. Individual centres should review their results and select the modality that produces the best results for that centre (Evidence level III).

Management of autogenous AV fistula stenosis

Relevant stenosis

Stenoses should be treated if the diameter is reduced by >50% and is accompanied with a reduction in access flow or in measured dialysis dose. Other indications for stenosis treatment are difficulties in cannulation, painful arm oedema, prolonged bleeding time after cannulation or after removal of the cannulae (due to high venous pressure) and handischaemia due to arterial inflow or distal stenoses. A stenotic lesion, due to intimal hyperplasia, is the most common cause for low access flow. In RCAV fistulae, 55–75% of these stenoses are located close to the AV anastomosis and 25% in the venous outflow tract [1,2]. In brachial-cephalic and/or basilic AV fistulae, the typical location (55%) is at the junction of the cephalic with the subclavian vein and the basilic with the axillary vein, respectively [1]. An arterial inflow stenosis >2 cm from the anastomosis is uncommon, but may endanger the flow in the AV fistula.

Stenosis of the anastomotic area

Surgical treatment is indicated in stenoses of the anastomotic area located in the lower forearm. Alternatively, PTA is possible although its results are likely to be less long-lasting. Primary interventional treatment is indicated in stenoses of the anastomotic area located in the upper forearm and in the upper arm. Surgery should be considered in cases of early or repeated recurrences of the lesions. Dilatation or surgical revision of anastomotic stenoses in upper arm fistulae can cause steal syndrome and access-induced hand ischaemia. Careful dilatation up to 5 or 6 mm initially is recommended. Dilatation to >6 mm is rarely indicated.

Venous outflow stenosis

PTA is the first treatment option in the outflow veins (cephalic/basilic) [3]. Junctional stenoses, of the superficial veins with the deep venous system, can also be treated by PTA. If a stent is placed in the final arch of the cephalic vein, it must not protrude into the subclavian vein where it could induce stenosis and preclude future use of the distal (basilic, brachial and axillary) veins [4].

Balloon angioplasty

In order to visualize the stenoses, angiography is performed by retrograde puncture of the brachial artery, in case of anastomotic problems, or by direct antegrade puncture of the vein above the anastomosis if an outflow problem is suspected [5]. It is controversial, whether long-segment stenoses should be treated radiologically or surgically. While some authors recommend surgical intervention [6], either by graft interposition [7] or vein transposition, others recommend radiological intervention [8]. Studies proving the superiority of one of the two treatment options for the treatment of long-segment obstruction are not available. However, PTA of short-segment stenoses (<2 cm) has a better outcome compared with long-segment stenoses (>2 cm) [9].

Persistent stenosis

Some stenoses cannot be dilated by conventional balloon angioplasty. These 'hard' stenoses can be treated with cutting balloons or ultrahigh pressure balloons (up to 32 atm) [10,11].

Recurring stenosis

Recurring stenosis can be treated radiologically, with or without stent placement, or surgically [5]. The strategy for treatment should be made considering the individual condition of the patient in relation to the invasiveness of the surgical treatment. In spite of complete opening of the PTA balloon of sufficient diameter, the dilated vessel wall may collapse immediately after removal of the balloon. This elastic recoil can be prevented by stent implantation, especially in central veins [12]. Stent placement in the needling areas of forearm fistulae should be avoided except for PTA-induced ruptures not controllable by protracted balloon inflation.

Management of autogenous AV fistula thrombosis

Fistula thrombosis should be treated as soon as possible or within 48 h. The duration and site of AV fistula thrombosis as well as the type of access are important determinants of treatment outcome. Timely declotting allows immediate use without the need for a central venous catheter. Thrombi become progressively fixed to the vein wall, which makes surgical removal more difficult. Thrombosis may affect the post-anastomotic vein segment as result of anastomotic stenosis or may begin at the needle site. When the clot is localized at the anastomosis in radial-cephalic and brachial-cephalic fistulae, the outflow vein may remain patent due to the natural side branches that continue to carry venous blood flow. In these accesses it is possible to create a new proximal anastomosis [7,13]. Thrombosis in transposed basilic vein fistulae usually leads to clot propagation of the entire vein. Although comparative studies are missing, the available literature [4,5,14–22] suggests that thrombosed autogenous AV fistulae should, preferably, be treated by interventional radiology. The single exception may be forearm AV fistulae, thrombosed due to anastomotic stenosis. It is likely that in such cases, proximal re-anastomosis will provide good results.

Interventional thrombolysis

Thrombolysis can be performed mechanically or pharmacomechanically [23–25]. While the immediate success rate is higher in grafts than in autogenous AV fistulae (99 *vs* 93% in forearm fistulae), the primary patency rate of the forearm AV fistula at 1 year is much higher (49 *vs* 14%). One year secondary patency rates are 80% in forearm and 50% in upper arm AV fistulae, respectively [14]. In AV fistulae, the combination of a thrombolytic agent (urokinase or tissue plasminogen activator = tPA) with balloon angioplasty resulted in an immediate success rate of 94%. Liang *et al.* [21] reported a success rate of 93% and a primary patency rate at one year of 70%. Haage *et al.* [4] performed 81 percutaneous treatments of thrombosed AV fistulae. Flow restoration was achieved in 88.9% of the AV fistulae. The primary 1-year patency rate was 26% and the secondary 1-year patency rate 51%.

Surgical thrombectomy

Surgical thrombectomy is performed with a thrombectomy catheter (Fogarthy). Manual retrograde thrombus expression can be helpful. On-table venous outflow angiography of the recanalized vein as well as the central veins should be performed whenever possible to find/exclude additional stenoses or residual thrombus. Identification and concurrent correction of the underlying cause(s) of thrombosis are essential parts of any surgical or interventional declotting. The best results of surgery probably will be encountered after proximal re-anastomosis for anastomotic stenosis of forearm AV fistulae, which is the most frequent location of stenosis in this type of access. Primary patency of the new proximal anastomosis has been reported to be as high as 80% at 1 year and 67% at 2 years [13]. If access failure recurs frequently in a short time period, a new fistula may need to be created.

Management of AV graft stenosis

A diameter reduction of >50% of the lumen together with a significant flow decline is considered as an indication for treatment [26].

Stenosis at the arterial anastomosis

As in autogenous fistulae, most arterial inflow stenoses in grafts can successfully be treated by PTA [27]. Stenosis of the arterial anastomosis itself can be dilated, if only the afferent artery and the graft at the anastomosis are affected and there is no stenosis in the efferent artery. If there is an additional stenosis of the efferent artery, angioplasty of the anastomosis alone will enhance graft flow with the risk of peripheral ischaemia due to reduced peripheral arterial perfusion. In these patients, either dilatation of the efferent artery by interventional radiology or through surgical revision of the anastomosis may resolve the dilemma.

Intra-graft stenosis

Intra-graft (or mid-graft) stenoses are found in the cannulation segment of grafts. They result from excessive ingrowth of fibrous tissue through puncture holes. These stenoses can be treated by PTA [28], graft curettage [29], or segmental graft replacement. When only a part of the cannulation segment is replaced, the access can be used for haemodialysis without the need of a central venous catheter. When re-stenosis occurs in a non-exchanged part of the graft, this can be replaced after healing of the new segment.

Stenosis at the venous anastomosis

The most common cause for graft dysfunction and thrombosis is venous anastomotic stenosis [28,30,31]. Since grafts should be implanted only in patients with exhausted peripheral veins, vein-saving procedures like PTA or patch angioplasty should be favoured to graft extensions to more central venous segments, even though the latter may have superior patency rates. When PTA repeatedly fails, additional stent implantation should be considered [2,32,33].

When a stent or a patch fail, graft extension is still possible. This staged therapy improves cumulative graft function. In 20–30% of the grafts, PTA does not increase blood flow to >600 ml/min, indicating insufficient dilatation with an undersized balloon, immediate recurrence of stenosis, or the existence of an unidentified and not corrected stenosis either more centrally or at the arterial inflow.

Management of AV graft thrombosis

Graft thrombosis should be treated without unnecessary delay and within 48 h, at least before the next dialysis session. Early declotting allows for immediate use of the access without the need for a central venous catheter [34–53]. There is always a compact ''arterial plug'' present. Old thrombi (>5 days) are often fixed to the vessel wall beyond the venous anastomosis, making surgical extraction more difficult. This is less of a problem for the interventional radiological treatment.

Surgical thrombectomy

Surgical thrombectomy is performed with a thrombectomy catheter. On-table angiography should be performed after completion of the arterial and venous limbs of the graft. This should visualize the central venous outflow as well as the graft. It is required to exclude residual thrombi and define the cause of thrombosis. Identification and simultaneous correction of the underlying stenosis are integral parts of any surgical or interventional declotting procedure [30,31].

Interventional thrombolysis

Prosthetic graft thrombosis can be treated with various percutaneous techniques and tools, including combinations of thromboaspiration, use of thrombolytic agents such as tissue plasminogen activator (tPA), mechanical thrombectomy and mechanical thrombectomy devices. An initial success rate of 73%, with primary patency rates of only 32 and 26% at 1 and 3 months, respectively, are reported [36–54]. Smits *et al.* [55] have compared different mechanical devices for percutaneous thrombolysis and concluded, that the treatment of the underlying stenoses was the only predictive value for graft patency. Each centre should, therefore, choose the technique according to their expertise. Independent of the applied technique it is important to perform thrombolysis as soon as possible to avoid the need for a central venous catheter and as an outpatient procedure to decrease costs, whenever possible. Post-procedural angiography to detect and correct inflow, intra-access or venous outflow stenosis is mandatory.

Recommendations for further research

Development of better catheter and balloon designs and (drug-eluting) stents may improve the outcome of interventional access treatment.

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8. Diagnosis and treatment of central venous obstruction

Guideline 8.1. If symptomatic central venous obstruction is suspected, angiography of the access and complete venous outflow tract should be performed (Evidence level III).

Guideline 8.2. Treatment should be performed by percutaneous intervention (Evidence level III).

Diagnosis of central venous obstruction

Chronic swelling of the access arm is the most important clinical sign of central venous obstruction [1]. The superficial veins may become prominent (collaterals). Pain and paraesthesia may occur. Central venous lesions have to be treated when they are severe and disabling such as those resulting in arm swelling, troublesome pain or inadequate haemodialysis [2]. In obvious central venous obstruction, angiography of the access and complete venous outflow tract must be performed, since the central veins cannot be examined with ultrasonography. Thus, to completely visualize all mediastinal veins, venography using digital subtraction technique is needed [3]. This can be done preferably with direct antegrade puncture of the access [4]. In the majority of patients central vein obstruction is due to previous inserted central vein catheters. In 40% of the patients with subclavian vein catheters central venous obstruction develops, compared with 10% of patients with jugular vein catheters. In patients without a history of central venous catheterization, other causes, such as extrinsic compression of mediastinal veins (e.g. lymphoma, goitre, thoracic aortic aneurysm, mediastinal fibrosis, pacemakers), hypercoagulopathy, thoracic outlet syndrome or pacemaker wires should be considered. In these cases plain X-rays, computed tomography or MR imaging may be helpful for the differential diagnosis. If treatment of the underlying disease is not possible or fails to resolve arm swelling, PTA with stent insertion is indicated [5].

Management of central venous obstruction

Interventional treatment

In the last decade, several studies of patients treated with PTA alone have been published. Primary patency rates of $\leq$10% at 1 year and numerous restenoses were reported [6–8]. Stent implantation has clearly been shown to improve primary 1-year patency rates to 56% and more [1,4,6,9]. Regular follow-up and reinterventions are required to maintain patency and achieve long-term clinical success [10]. These figures do not differ significantly from those of surgical intervention [1,6,9]. Nevertheless, due to the invasiveness of surgery for central venous obstructions and the less invasive interventional therapy, PTA with or without stent implantation is recommended as primary option for treatment [4]. Reports show, that symptomatic central venous obstruction in dialysis patients can be treated with a high success rate through radiological intervention [11,12]. Stent placement should avoid overlapping the ostium of a patent internal jugular vein to achieve a safe and sufficient result, since this latter vein is essential for future placement of central venous catheters. Similarly, a stent placed in the innominate vein should not overlap the ostium of the contralateral vein, otherwise contralateral stenosis may occur and preclude future use of the contralateral limb for access creation [4]. Little data are available on the use of thrombolytic agents in central venous thrombosis. It is, therefore, not recommended as a primary treatment regimen.

Surgical treatment

When interventional treatment of central venous obstruction is impossible or fails, assessment of the patient is necessary to define the most effective surgical method and to guarantee long-term vascular access. Surgical evaluation focuses on the general risk (see ASA Physical Status Classification System [13]) and life expectancy as well as on the vascular pathology. If surgery is an option, all angiograms have to be re-evaluated. If an ipsilateral surgical bypass to the jugular vein is impossible due to innominate vein obstruction, additional venography of the contralateral arm should be performed to assess whether a new access can be constructed in that arm or a subclavian–subclavian or subclavian–jugular cross-over bypass should be performed [14–16]. In case of bilateral obstruction of the mediastinal veins, including the superior caval vein, ultrasonography of ilio-caval veins is indicated in the planning of arterio-venous thigh access. Alternative surgical options for upper extremity vascular accesses with compromised venous outflow, are axillo-saphenous/iliac or right atrial bypasses [17,18].

As ultimate treatment access ligation can be considered, which will relief local symptoms.

Recommendations for further research

Improvement of central venous catheter design, may probably prevent vessel wall damage and the development of central venous stenoses. Stent improvement and newer guidewires may enhance central venous obstruction intervention and outcome.

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9. Diagnosis and treatment of access-induced ischaemia

Guideline 9.1. Access-induced ischaemia should be detected by clinical investigation and the cause should be identified by both non-invasive imaging methods and angiography (Evidence level III).

Guideline 9.2. Enhancement of arterial inflow, access flow reduction and/or distal revascularization procedures are the therapeutic options. When the above methods fail, access ligation should be considered (Evidence level II).

Rationale

Access-induced upper extremity ischaemia is a serious complication that, when not treated in time may lead to major amputation [1] From published series, it can be estimated that the incidence of symptomatic ischaemia varies from 2% to 8% of the haemodialysis population [2,3]. Elderly patients, diabetics and patients with peripheral and/or coronary arterial obstructive disease are more prone for the development of access-induced ischaemia. In addition, previous ipsilateral vascular access increases the risk. Access-induced ischaemia occurs more often in proximally located fistulas [4]. These high-flow AVFs induce a steal phenomenon with lowering of distal perfusion pressures and, when collateral circulation is inadequate, symptoms may occur [5–8]. A grade 1–4 classification for access-induced ischaemia (grade 1: pale/blue and/or cold hand without pain, grade 2: pain during exercise and/or HD, grade 3: ischaemic pain at rest and grade 4: ulceration, necrosis and gangrene) can be used to outline the severity of the disease and this ranges from minor symptoms to finger necrosis. A number of these patients have increasing pain during dialysis treatment. For grade 1 and 2 ischaemia a conservative treatment is indicated, while with grade 3 and 4, interventional treatment is indicated [9].

Diagnosis of access-induced ischaemia

Physical examination, including observation and palpation of peripheral vessels, may be inadequate and misleading for the diagnosis of symptomatic ischaemia. Additional non-invasive testing with measurement of digital pressures and calculation of the digit-to-brachial index (DBI), transcutaneous oxygen determination, ultrasonography of forearm arteries and access blood flow measurement are important steps in the diagnosis and decision-making process [10,11]. Finally, angiography with visualization of the upper extremity arterial tree from the proximal subclavian artery to the distal palmar arches with and without AVF compression to enhance distal flow, is obligatory to outline the strategy for treatment and to determine whether interventional or surgical options are preferred [12].

Management of access-induced ischaemia

The options for treatment depend on the aetiology of the ischaemia: inflow arterial obstruction and/or distal arterial lesions are recanalized with small-calibre balloons and stent implantation [13–15], high-flow AVFs, as mainly observed in patients following successful renal transplantation are eligible to flow-reducing procedures like banding and distal arterial extension [16–18]. Steal in itself may be cured by ligation of the artery distal of the arteriovenous anastomosis [19]. In most patients it is necessary to add a saphenous vein graft bypass to the forearm arteries (DRIL = distal revascularization + interval ligation). The results of these procedures are usually good with relief of symptoms and preservation of the access site (Table 1) [20–27]. A simple alternative of the DRIL procedure is the PAVA (proximal arteriovenous anastomosis) technique, in which the AV anastomosis at the elbow is disconnected and moved to the axilla by means of a graft interposition [28,29]. Intra-operative digital pressure measurement or transcutaneous oxymetry ($TcPO_2$) is mandatory to guarantee an adequate surgical intervention with acceptable outcome. A digital-brachial pressure index >0.60 or $TcPO_2$ of >40 mm Hg is indicative of a sufficient distal hand perfusion [30–32]. The same DBI threshold may be also predictive for the development of ischaemia in predialysis patients receiving new vascular access [33–35]. In some patients, AVF ligation and change in renal replacement modality (to continuous ambulatory peritoneal dialysis = CAPD) or transition to central venous catheter access, may be the only solution.

Prevention of access-induced ischaemia

An adequate preoperative evaluation and surgical technique are the keystones to avoid ischaemia. Physical examination of peripheral pulses, bruits, and measurement of bilateral arm blood pressures are essential for the work-up before AVF creation. Duplex ultrasonography is very useful in the assessment of not only superficial veins but also arteries. Preoperative measurement of digital pressures may be helpful to indicate patients at risk for ischemia. Patients with preoperative digit-to-brachial indices (DBI) <1.0 are more likely to develop steal, but there is no DBI threshold below which steal is inevitable. If there is any doubt concerning the status of the peripheral circulation, angiography or MRA is advised. Steal is more likely in patients undergoing brachial-based arteriovenous fistulae than in those receiving prosthetic grafts.

Table 1. Results of distal revascularization and interval ligation (DRIL) procedure for the treatment of access-induced ischemia

Author	No. of patients	Success in %	AVF patency (%)
Schanzer *et al.* [20]	14	93	82
Haimov *et al.* [21]	23	96	73
Katz *et al.* [22]	6	83	100
Berman *et al.* [23]	21	100	94
Lazarides *et al.* [3]	7	94	–
Stierli *et al.* [24]	6	100	100
Knox *et al.* [25]	52	90	83
Diehl *et al.* [26]	12	100	100
Sessa *et al.* [27]	18	73	94

Therefore, a limited length of the arteriovenous anastomosis of 10 mm in radial-cephalic and 5–7 mm in graft and/or brachial-cephalic/basilic AVFs, may contribute to the prevention of large volumes of blood shunting through the AVF. Either a "non-smooth" anastomosis (90° or 180° angle) adds to a greater anastomotic resistance and thus limitation of flow.

Recommendations for further research

Further search for pre-operative indicators that outline the risk on post-operative ischaemia may help to take adequate measures for prevention.

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10. Central venous access

Guideline 10.1. Central venous catheters should be inserted as a last resort in patients without a permanent access and the need for acute haemodialysis (Evidence level III).

Guideline 10.2. The percutaneous route should be used for both acute and chronic catheter insertion. Insertion should be guided by ultrasound. A plain X-Ray (chest or abdomen) should be performed before use to locate catheter and detect any complication (Evidence level II).

Guideline 10.3. The right internal jugular vein is the preferred location for insertion (Evidence level II).

Guideline 10.4. Non-tunnelled catheters should only be used in emergency situations and should be exchanged as soon as possible for tunnelled catheters (Evidence level III).

Indications for catheter insertion

Central venous catheter insertion is required in incident CKD-stage 5 patients who need to start dialysis in an acute or emergency situation, and are not equipped with a permanent vascular access [1,2]. Catheter insertion is also indicated in prevalent CKD-stage 5 patients on renal replacement therapy presenting with vascular access failure [3], and waiting for interventional or surgical access salvage or the creation of a new access. In some patients, all surgically created arteriovenous vascular access options may have been exhausted. A central venous catheter may then represent the only access option. Some patients have a contraindication for the creation of an arteriovenous fistula (severe cardiac failure, chronic respiratory insufficiency) [4], because of the risk of heart failure.

Patients with severe pain in the hand due steal syndrome, causing peripheral ischaemia, or with major difficulties in needling [5], may also benefit from a permanent central venous catheter. Catheters offer immediate vascular access for haemodialysis and may be used over several months or years. Long-term catheters also have positive properties: they are easy to use and do not need maturation.

Technique of catheter insertion

Catheter insertion is considered a high-risk intervention which deserves careful attention, must be performed under strict aseptic conditions and should ideally be performed by trained and senior physicians. Percutaneous catheter insertion is the preferred method for catheter insertion. The right internal jugular vein is the first option for insertion, followed by the left internal jugular vein. The femoral route is preferred for short-term catheters (<1 week) since there is no risk for central vein stenosis. Ultrasound-guided insertion technique is mandatory to prevent accidental carotid artery puncture and to ensure successful cannulation [6,7]. In addition, fluoroscopy to follow and locate the position of the guide wire is advisable. In a recent study 60 patients were randomized for ultrasound guided *vs* 'blind' catheter insertion. First attempt venous cannulation success rate was 56.7% compared with 86.7% in non-guided *vs* guided insertion technique. The risk of adverse outcome was significantly greater in the blind procedure ($P = 0.020$). The ultrasound-guided procedure for internal jugular vein catheter insertion using an ordinary ultrasound machine was significantly safer and more successful as compared with the blind technique [8]. For patients presenting with acute and/or life-threatening conditions requiring immediate dialysis (pulmonary oedema, hyperkalaemia, respiratory distress) the femoral vein is the most favourable insertion site. Because of the high risk on central venous stenosis (see Guideline 8), the subclavian vein route has been abandoned [9].

Catheter performance and care

Catheter performance (maximum flow rate, blood resistance and recirculation) should comply with delivery of adequate dialysis dose without altering treatment schedule (frequency, dialysis duration) [10,11]. Tunnelled catheter morbidity (dysfunction, thrombosis, infection) is significantly reduced compared with non-tunnelled catheters and tunnelled catheters should be preferred in all patients [12]. Port-catheter devices (Dialock, LifeSite) offer comparable flow performances to long-term catheters while improving patients' aesthetic satisfaction and improving patients comfort [13,14]. Unfortunately, the risk on infection is high with these devices. Catheter care and handling conditions under aseptic manipulation are essential to prevent infection in catheter and venous port devices.

Recommendations for further research

Improvement of catheter design and locking solutions are major subjects for further research.

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11. Management of central venous access complications

Guideline 11.1. Catheter dysfunction should be corrected by local fibrinolysis designed to restore flow patency. Repetitive catheter dysfunction requires local fibrinolysis with additional catheter imaging, microbiological assessment and systemic coagulation evaluation (Evidence level III).

Rationale

Catheter dysfunction is a relatively common event for haemodialysis patients. It reduces the effective blood flow rate and reduces dialysis dose. Catheter dysfunction may be minimized by using the appropriate material, a perfect insertion technique [1] and strict protocols for catheter care [2]. Catheter design and material are essential for achieving high blood flow and adequate performance [3,4]. Tunnelled catheters provide usually higher flows (up to 400 ml/min) at low resistance and reduced recirculation compared with non-tunnelled catheters. Dual catheters with independent lines and side holes at the tip provide higher flows than dual-lumen catheters [5,6]. Catheters inserted in the right internal jugular vein offer the best flow compared with other central venous sites [7]. Catheter dysfunction must be detected and corrected early in order to restore blood flow and dialysis dose. Catheter dysfunction may occur in different ways:

(i) Complete obstruction, making dialysis impossible.
(ii) Incomplete obstruction (endoluminal fibrin deposits restricting catheter lumen or obstructing catheter side holes at the tip, external fibrin sleeves surrounding catheters) resulting in inadequate flow and/or excessive extracorporeal blood pressure alarms during the dialysis session. Depending on the location of the fibrin clot (arterial and/or venous line), there may be high negative arterial pressure (obstruction at the arterial catheter line) or high positive venous pressure (obstruction at the venous catheter line).

Catheter care and handling are very important to prevent catheter dysfunction. Prevention of catheter clot formation in the catheter tip during the interdialytic period is crucial. This may be achieved by installing an antithrombotic lock solution (standard heparin, low molecular weight heparin, sodium citrate) [8,9]. A certain amount of the antithrombotic lock solution may leak into the circulation via side- and central catheter holes. Loss of antithrombotic locking solution facilitates catheter clot formation while it increases the haemorrhagic risk. Regular use of low dose of antithrombotic drugs such as coumarin derivatives or antiplatelet agents in dialysis patients have failed to improve catheter outcomes [10–12].

Catheter performance monitoring is required to detect catheter dysfunction. Such monitoring is an integral part of the quality assurance process to ensure dialysis efficacy and to reduce catheter-related morbidity [13]. It relies on markers evaluating catheter flow performances such as estimations of effective blood flow rate, venous and arterial pressure values at constant flow, recirculation and dialysis dose delivery as measured by Kt/V [14].

Catheter maintenance is important to achieve the prescribed blood flow during dialysis sessions. To prevent and/or to correct catheter dysfunction it is recommended to clean the catheter lumen periodically by applying fibrinolytic agents (urokinase, tPA) either as lock solution or continuous infusion on both arterial and venous lines [15]. Occluded catheters are reopened either by means of a mechanical method (brush) or pharmacological method (urokinase, tPA) [16–18]. Removal of the fibrin sleeve may be achieved either by lasso wire stripping or by infusing a fibrinolytic solution (urokinase, tPA), during 3–6 h [19]. Alternatively, the catheter may be exchanged over a guidewire [20].

Recommendations for further research

Investigation into better thrombolytic agents and mechanical tools to declot thrombosed catheters are of importance.

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12. Management of the infected vascular access

Guideline 12.1. Infection of autogenous AV fistulae without fever or bacteraemia should be treated by appropriate antibiotics for at least 2 weeks (Evidence level III).

Guideline 12.2. Infection of autogenous AV fistulae with fever and/or bacteraemia should be treated by appropriate antibiotics given intravenously for 2 weeks. Excision of the fistula is required in case of infected thrombi and/or septic emboli (Evidence level IV).

Guideline 12.3. Infected graft AVFs should be treated by appropriate antibiotics given intravenously for 2 weeks and continued orally for 4 weeks. Depending on the presence of bacteraemia and/or infected thrombi segmental explantation of the graft with bypass needs to be considered (Evidence level III).

Guideline 12.4. Anastomotic infection is an indication for total graft explantation (Evidence level II).

Guideline 12.5. Catheter removal must be considered when catheter infection is suspected. Immediate removal should be performed in non-tunnelled catheters when infection is diagnosed (Evidence level III).

Guideline 12.6. In tunnelled catheters with a short febrile and/or bacteraemic reaction, a delayed removal may be considered (Evidence level III). In septicaemia, immediate removal should be performed in tunnelled catheters as well.

AVF and prosthetic graft infection

Infection of autogenous AVF usually responds well to appropriate antibiotics given either orally or intravenously according to the presence of fever and/or bacteraemia. Surgical revision or excision of the fistula is required when infected thrombi, aneurysms and/or septic emboli are detected. Infection of graft AVFs is two to three times more frequent than autogenous AVFs [1]. Infection of the graft bears a worse prognosis and requires usually a surgical revision and/or explantation in addition to the antibiotic therapy. Salvaging prosthetic grafts may be attempted in certain circumstances. Several surgical techniques have been described in combination with antibiotic therapy. For localized abscesses, incision and drainage with graft preservation is needed. For more severe infection, such as infected thrombi, false aneurysms, cellulitis, explantation of the infected graft segment and segmental bypass with a new graft is indicated. However, these salvaging techniques may be complicated because of local or generalized infection and sepsis. Therefore, in severe cases a complete explantation of all graft material with drainage is usually necessary.

Central venous catheter infection

Catheter-related infection is the major cause of morbidity in HD patients with central venous catheters [2–4]. Catheter infection is a potentially severe event that requires early diagnosis and appropriate management to prevent further complication. Diagnosis of catheter infection is relatively easy in symptomatic patients presenting with fever, pain, skin exit and/or track infection and bacteraemic episodes. It is much more difficult in silent catheter endoluminal contamination or low grade infection. In these cases, only specific blood and catheter clot culture will help to make the diagnosis [5]. Recently, it was shown that catheter clot culture after endoluminal brushing was more sensitive than blood culture to identify asymptomatic catheter infection (catheter contamination) [6,7]. Symptoms of infection includes chronic fever, bacteraemic episodes, catheter pain, inflammation of the exit site or tunnel. Infection of the catheter exit site or tunnel tract is usually observed by the dialysis nurse while clinical examination is performed at the time of dialysis connection. Silent contamination is suspected when recurrent febrile reactions during haemodialysis occur and bacterial pathogens (*Staphylococcus aureus, S. epidermidis* or other bacteria such as Gram-negatives) are identified in blood cultures. Catheter-related septicaemia is usually associated with symptoms of endocarditis, arthritis, spondylarthritis or osteomyelitis.

Specific blood markers (leucocyte count and differentiation), C-reactive protein (CRP) and procalcitonin (PCT), help to diagnose early bacterial catheter infection. Catheter-related infection should be considered as a severe and potentially lethal complication. Prevention of infection should be a permanent preoccupation for care providers, that relies on hygienic measures [8] and strict protocols for handling catheters based on aseptic manipulation [9] and using specific dressings [10]. The regular and pre-emptive use of locking solutions (Citrate) with both antithrombotic and/or antiseptic properties has been confirmed to be effective in preventing catheter infection [11–14]. The topical application of antibiotic ointment on the skin exit site has proved to be efficient in reducing the incidence of bacteraemia at the expense of selecting antibiotic-resistant strains of bacteria [15–17]. The use of antibiotic-coated catheters or silver-treated catheters has been proposed to reduce the risk of infection, but conflicting results has been reported [18–20]. Identification of patients at risk of infection is particularly important in diabetic patients and nasal carriers of methicillin-resistant *S. aureus* (MRSA). In the latter patients, eradication of bacteria by means of topical antibiotic ointment has been associated with a significant reduction of bacteriaemias [21,22].

Catheter removal should be considered as the first line of treatment. Catheter withdrawal must be immediate when infection occurs in non-tunnelled catheters. Removal may be postponed for several days in tunnelled catheters. When this last option is applied the risk of septic complications of delayed catheter removal should be balanced with the benefits of keeping it *in situ*. This conservative option implies that the patient is regularly and carefully observed. In addition, the catheters should be disinfected by means of antimicrobial lock solutions and dissemination of the infection must be prevented by adequate systemic antibiotic therapy. When the catheter is left in place and in the absence of precise microbial information, antimicrobial therapy should include systemic antibiotic therapy effective against Staphylococcus species plus an adjunctive antimicrobial catheter lock. Antibiotic therapy is given for 2 weeks in order to sterilize all potential bacterial foci. Topical antibiotic therapy (catheter exit site) is initiated when there is associated local infection. Imaging techniques may help to diagnose catheter-related infection. Ultrasound doppler methods can detect tunnel infection and/or subcutaneous abscesses along the catheter track. Phlebography and catheterography are indicated to diagnose infected thrombi located in the vein or fibrin sleeves surrounding the catheter tip. Isotopic imaging techniques using positron emission tomography (PET) may help to identify infected venous catheters and port devices [23].

Recommendations for further research

Improvement of needle design and education on strict aseptic cannulation techniques may possibly lower the incidence of infection in fistulae and grafts. Antibiotic-bonded grafts may possibly lower the incidence of graft infection. Newer catheter designs and locking solutions are important issues for further investigation of the prevention of central venous catheter-related infections.

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