Review paper

Early and long-term complications in haemodialysis vascular access

Powikłania wczesne i odległe dostępów naczyniowych do dializ

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Abstract

The paper presents vascular accesses used for the purpose of haemodialysis in patients with end-stage renal disease. The recommendations of the NKF K/DOQI concern performing a first-time permanent access in the form of an autogenous fistula. Attention has been paid to accurate diagnostic imaging of blood vessels. Early and long-term complications of functioning fistulas are presented, together with the manner of their treatment. Dialysis catheters are also described as the only possibility of dialysis in patients with contraindications to the creation of fistulas. Bloodstream infections are the most common complication of dialysis with catheters. An important element of prevention is monitoring the function of catheters, which reduces the need for medical intervention. New solutions improving the functioning of vascular access have also been presented. Careful use of vascular access, as well as fistula and catheter site function monitoring, contributes to extending the lifespan of an access and reduces complications.

Streszczenie

W pracy przedstawiono dostępy naczyniowe używane w celu prowadzenia hemodializ u chorych ze schyłkową niewydolnością nerek. Uwzględniono zalecenia NKF K/DOQI dotyczące wytworzenia pierwszorazowego dostępu, jakim jest autogenna przetoka. Zwrócono uwagę na dokładną diagnostykę obrazową naczyń. Przedstawiono powikłania wczesne oraz odległe funkcjonujących przetok z uwzględnieniem sposobu ich leczenia. Opisano również cewniki dializacyjne jako jedyny możliwy dostęp do dializy u chorych z przeciwwskazaniami do wytworzenia przetok. Powikłania infekcyjne u osób dializowanych przez cewnik występują bardzo często, dlatego ważnym elementem profilaktyki infekcji jest monitorowanie i utrzymanie drożności cewników dializacyjnych. W artykule przedstawiono nowe rozwiązania, które poprawiają działanie dostępów naczyniowych. Ostrożność przy korzystaniu z dostępów naczyniowych, monitorowanie ich funkcji i miejsc wkłucia sprzyja wydłużeniu żywotności dostępów i ogranicza powikłania.

Introduction

End-stage renal failure is a major medical and social problem. Close to 75% of patients require haemodialysis, which results in continuous efforts to maintain properly functioning vascular access. This is increasingly difficult due to the increasing patient survival rate and a growing number of complications limiting the patency of functioning vascular accesses. In patients with end-stage renal disease, three methods of renal replacement therapy are available: a kidney transplant, haemodialysis, or peritoneal dialysis. If there are contraindications to the pre-emptive transplantation, performing a dialysis access is necessary in order to keep the patient alive.

Arteriovenous fistulas and dialysis catheters are the basic elements in carrying out haemodialysis and keeping patients with end-stage renal disease alive in order to prepare them for the planned kidney transplant. The preferred vascular access, which remains the gold standard, is an autogenous arteriovenous fistula [1, 2].

Arteriovenous dialysis fistula

The guidelines of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (K/DOQI) recommend fistulas made from the patient's own vessels as the first choice. Based on long-term observation results, these fistulas demonstrate longer primary and secondary patency compared to the fistulas made of artificial material. The preferred site of performing the first fistula, if the necessary vessel adequacy criteria are met, is a radiocephalic arteriovenous fistula (Cimino-Brescia). Fistulas made from native vessels are characterised by the highest patency rate and the lowest risk of complications compared with graft fistulas and dialysis catheters. According to the recommendations of the K/DOQI, 50% of patients starting dialysis and 40% of all dialysis patients should use autogenous fistulas [3].

Creation of a fistula should be preceded by a thorough diagnosis of the vascular system, including a Doppler ultrasound of arteries and veins of the upper limb including subclavian veins, and, in the case of any doubts, by venography. To classify the patient to produce optimal vascular access it is essential to gather accurate information concerning past and concomitant diseases and their medical history, as well as previous endovascular and surgical interventions in the area of central veins [4, 5]. In order to assess the blood flow to the hand and find the dominant artery of the forearm, an Allen's test should be performed. The condition for creating a primary fistula on the forearm is normal arterial blood flow to the hand, intact superficial veins, adequate vessel diameter (the artery diameter of more than 2 mm and vein diameter of more than 2–3 mm), and unobstructed venous return [4, 6].

Following its creation, an autogenous fistula requires time before it can be used. The so called "maturation" time lasts between 4 and 6 weeks. On average, after this period, the vein increases its diameter from 2 mm to 4–6 mm, and its wall thickens and begins to pulsate. It is then ready to be punctured. The blood flow parameters in the correctly created fistula are 600–1200 ml/min, PI = 0.8; RI = 0.5. The decrease in the flow capacity below 300 ml/min in an autogenous fistula and below 500 ml/min in a graft fistula is a sign of dysfunction. In practice, the suggested optimal capacity flow through the fistula amounts to 300–500 ml/min, because higher values can lead to cardiovascular overload and heart failure. Sometimes effective dialysis can be performed at the flow of 150–200 ml/min [6].

With well-developed circulation and well-filled veins of the forearm, creating a classic fistula by Brescia in the wrist in one of its four variations is the best solution [4, 5]. In the case when there are no adequately healthy vessels in the forearm, vascular access is made higher, through the vessels located in the cubital fossa, in the arm, or through the subclavian or carotid artery. As a last resort, in the absence of the possibility to create an access in the upper limbs, access to the blood vessels in the lower limbs is considered. However, it is associated with a very high risk of cardiac and infectious complications and is performed when other possibilities have been used [4, 5].

In the absence of native veins to create a fistula, grafts are used, made of artificial materials. Their advantage is the possibility of early puncture, performed even immediately after their creation, while their disadvantage is the higher propensity to develop stenosis because intimal hyperplasia often occurs in the region of such venous anastomosis. This leads to a greater risk of thrombosis, deteriorating the primary and long-term fistula patency. Fistulas with the use of grafts are, therefore, considered a secondary/second-choice vascular access solution, following the exhaustion of the possibilities of creating native vascular access. Two types of grafts are used: straight and loop ones. They can be located in the forearm and arm [4].

Another option, considered the third-choice vascular access, following the exhaustion of all the possibilities in the region of upper limbs, may be axillary-axillary or carotid-brachial loop graft [4].

A fistula between the superficial femoral artery and the saphenous vein is an access created very rarely, in the lower limb, because it does not develop to provide a good conduit for dialysis. Theoretically it would have more advantages, but in practice it does not work [4, 5].

TVA Medical's everLinQ everAVF system, presented at LINC in January 2017 in Leipzig, is a new, very promising alternative to surgical fistula creation. It consists of the intravascular creation of a connection between the artery and the vein at the level of the forearm with the use of two catheters and the energy of low-frequency radio waves. The system has received the European CE mark of approval for use in patients with end-stage renal failure requiring dialysis, and it is currently awaiting recommendation from the FDA in the United States. It is characterised by a fast fistula maturation rate of about 91% within 30 days, high patency rate, low incidence of thrombosis, and minimal need for intervention when compared with a fistula created with the use of the classical method [7].

Temporary (non-tunnelled) and permanent (tunnelled) catheter

In patients with absence of native vessels that meet the relevant criteria for fistula creation or in patients with contraindications for arteriovenous fistula, such as cardiological reasons, chronic respiratory insufficiency and cases where the creation of a fistula would lead to the exacerbation of circulatory insufficiency, a dialysis catheter inserted into one of the central veins has to serve as the vascular access [1, 5, 8]. The catheter is also placed in patients with end-stage renal disease, who require immediate dialysis while the access they have is insufficient.

Temporary catheters mainly used in cases of emergency, to provide swift vascular access and perform acute dialysis in detoxification, plasmapheresis, fistula dysfunction, temporary suspension of peritoneal dialysis, or the need to perform the surgery in extracorporeal circulation. They should be placed only in situations where the planned dialysis will be limited to about one week. Whatever the reason for using this type of access, the catheter should remain in the patient's body for as short a time as possible. The catheter should not be used for more than three weeks and should not be used as "bridging" in patients who have lost their vascular access or whose fistula is still immature. The high rate of complications associated with this type of temporary catheter disqualifies this type of access with respect to long-term use [1, 8].

A permanent (tunnelled) catheter is reserved for patients in whom the expected time of dialysis exceeds one week, or who suffer from additional diseases, such as congestive heart failure, peripheral vascular disease, or abnormal vessel anatomy, and whose life expectancy is short. The catheter can also be used as a temporary means in patients with chronic renal failure, when the fistula created has not reached the maturation parameters necessary for dialysis and is not suitable for puncture [8].

The right internal jugular vein is the preferred location of dialysis catheter implantation, because of its straight course and ease of puncture. Another place is the left internal jugular vein, while the external jugular, subclavian, and femoral veins are subsequent options. The last chance is translumbar or transhepatic access to the vena cava inferior.

A new method of combining both possibilities of vascular access is the HeRO-graft (Haemodialysis Reliable Outflow) system, a technique that allows avoidance of the placement of a femoral vein catheter increasing the risk of infectious complications. The access is a catheter constructed of two parts: the arterial one made of PTFE and the venal one made of nickel titanium. It joins an artery in the forearm with the right atrium of the heart and runs entirely subcutaneously [9].

Compared with the standard permanent catheter, the HeRO graft:
- is 69% less susceptible to infections,
- provides 16–32% better quality dialysis, reaching the rate of Kt/V = 1.7 (according to KDOQI target clearances Kt/V = 1.4),
- is highly effective and requires less than half the usual number of interventions,
- has the cumulative patency rate of 87% in the period of 2 years,
- reduces the average cost of usage by 23% in comparison with a standard catheter.

Despite the many possibilities presented here, every dialysis access created is burdened with a risk of complications, such as a blood clot, embolism, infection, or haemorrhage. Such situations require immediate surgical intervention in order to improve the functioning of the access and save the patient's life.

Complications following AV (arterio-venous) fistula creation

Early fistula dysfunction may be indicated by a decrease in the capacity of the flow through the dialyser below 150 ml/min, a lower Kt/V value informing about the effectiveness of the dialysis, as well as by an increase in the degree of recirculation.

Depending on the time of their occurrence, complications are classified as early – arising up to 30 days from the creation of an AV fistula, and late – occurring after this period.

With respect to location, they are divided into ones connected with the place of creation, as well as distant ones.

Early complications include: occlusion, thrombus, bleeding and haematoma, oedema, ischaemia, infection, lymphorrhoea, nerve damage, skin necrosis.

Early occlusion of the fistula caused by a clot is most frequently caused by a surgical error. It may also be associated with incorrect qualification for the surgical procedure and poor assessment of the condition of the vessels in the whole limb. Thrombosis immediately following the creation of a fistula may also occur as a result of a fall in blood pressure, application of too tight dressing, or compression of the fistula by the patient during sleep. Technical errors include creation of an overly narrow AV anastomosis or anastomosis performed under too great a tension [4]. The treatment involves the removal of the blood clot. Endovascular treatment is recommended here – among others, mechanical thrombectomy. Three weeks after the procedure of fistula creation, pharmacological thrombolysis consisting of urokinase locally injected into the thrombus by means of a catheter may be used to treat thrombotic complications. Surgical restoration of patency combined with the reconstruction of the fistula and the improvement of its function is another option. Attempts should be made at restoring the patency of all thrombotic AV fistulas.

Another early complication is active bleeding, resulting, most frequently, from leaking sutures, leading to the formation of haematoma or a pseudoaneurysm. It is usually removed surgically.

Early limb oedema is usually associated with persistent hypertension resulting from the venous system overload following end-to-side or side-to-side AV anastomosis, or venous outflow stenosis in the form of occlusion or narrowing of central veins.

Ischaemia in the limb in which a fistula was created is caused by steal syndrome. Steal syndrome may occur following the connection of the end or side of the cephalic vein with the side of the radial artery. Steal syndrome occurs more frequently in proximally located fistulas. As a rule, it is accompanied by the concurrent presence of lesions in arteries located at the periphery of the limbs, which is frequent in patients with renal insufficiency and diabetes [3, 4].

Early infection occurs mostly after the creation of fistulas with the use of an artificial material. Its main symptom may be the presence of pus in the area of the anastomotic site, frequently in the place of punctures.

Lymphorrhoea is caused by a cut to a lymph node and requires protection of the wound against infection or the use of additional compression.

Nerve damage is a rare, although possible, early complication caused by iatrogenic damage to the superficial radial nerve branches, mostly in the case of a wrist fistula, during superficialisation of the basilic vein, or during creation of a fistula on the arm [4].

Late complications occurring after 30 days from the creation of the fistula are as follows: thromboses, stenoses, false aneurysms, haematomas, local and distant infections, venous insufficiency, limb ischaemia, cardiac failure, polyneuropathies.

Thrombosis and stenosis are the most common late complications, representing 80% of the reported problems in patients with dialysis fistulas. It was determined that in half of the patients with stenosis of the fistula of more than 50%, thrombosis and total occlusion develop within 6 months [4]. The reason is probably high blood flow, turbulence, and shear stress on the wall of the blood vessel in the small connection created, which leads to endothelial damage and intimal hyperplasia. Additionally, in the case of using artificial materials in the connection with the vein, there is a large degree of variation in elastic properties, contributing to the formation of stenosis.

The solution to this problem may be the external device Improving Vascular Access VasQ, supporting the fistula, which is deployed on the autogenous AVF to improve the flow and reduce the excessive intima overgrowth. Thus, it eliminates the most common causes of fistula failure [10]. Hypercoagulability of blood present in patients with uraemia, administration of the erythropoietin to them, as well as overly strong compression of the sites where dialysis needles have been inserted, also contribute to the occurrence of thrombosis.

Another late complication are haematomas and pseudoaneurysms caused by incorrect manner of fistula puncture. Stenoses of the fistula are also most often caused by repeated puncture in the same location in the course of its use.

The next important late complication is chronic venous insufficiency leading to the development of post-thrombotic syndrome in the limb with active fistula. High venous pressure can lead to damage to the valves and perforator veins, to vessel dilation, and the backflow of large volumes of blood to the peripheral vessels. Such a situation is also connected with the obstruction of the outflow, caused by the presence of stenosis in the subclavian or brachiocephalic vein. The stenoses are frequently caused by earlier punctures or the use of dialysis catheters. An increase in the volume of blood supplied via the fistula into the venous system leading to the limb leads to the impact of the blood flow on the vessel wall and to wearing out the elastic tissue of the vessel wall, resulting in fibrosis and narrowing of veins at different levels. It most often occurs in end-to-side anastomosis.

Venous hypertension may also be caused by narrowing of the vein draining the side-to-side anastomosis [3, 4].

Each case of hypertension requires diagnostic ultrasound or venography. The treatment consists of the widening of the existing stenosis by angioplasty, and when this is not possible, in superficial peripheral vein ligation or exchanging the side-to-side arteriovenous anastomosis for end-to-side [3, 4].

Ischaemia of a hand or entire limb in patients with active fistula is a rare but serious problem. The main factor leading to its occurrence is the reversal of blood flow in the arteries below the fistula. Increased arterial resistance in the limb periphery present in concomitant atherosclerosis and diabetes contributes to such lesions.

Steal syndrome occurs in 73% of patients with native fistulas and in 91% of patients with grafts. However, the symptoms are manifest only in 2–6% of the patients. They can be exacerbated by the presence of additional narrowing of the arterial section of the fistula. Stealing can lead to paraesthesia, pain, and peripheral ulceration. Sometimes, it necessitates limb amputation [3, 4]. Doppler ultrasound and invasive arteriography should always be performed to establish its cause.

It is possible to improve the blood supply to the hand by reducing the flow of blood to the fistula through application of a band of artificial material (PTFE) on the supplying artery, or making additional sutures that narrow the flow to the fistula. Another option is the ligation of the fistula and the creation of a new one on the other limb. The basic aim of the treatment, however, is to alleviate the symptoms of limb ischaemia and to preserve the present vascular access for dialysis.

Reconstructive procedures of RUDI and DRIL (distal revascularisation interval ligation) type are used to achieve that goal. The RUDI procedure indication is for the hyper-debit A-V fistulas with or without steal [3].

Ischaemic multifocal mononeuropathy is a very rare late complication. It occurs after the creation of a fistula on the arm and results from damage to the nerve fibres due to ischaemia, but without the typical symptoms of steal syndrome. It is probably associated with microangiopathy, especially in concomitant diabetes and atherosclerosis. Another neurological complication, occurring in 10% of dialysed patients, is carpal tunnel syndrome. It is caused by the compression of the median nerve due to oedema caused by venous hypertension. The treatment of choice is to cut the flexor retinaculum.

Pseudoaneurysm is a long-term complication occurring in 2–10% of created fistulas. It is mostly connected with access made of PTFE. It can occur in the sites of multiple punctures. The treatment consists in the surgical removal of the modified section of the vessel [4].

Fistula infections usually take the form of local infections, i.e. a purulent abscess or fistula. General symptoms are rare in such cases, contrary to dialysis catheters. Immune disorders in patients suffering from uraemia, connected with a reduction in the chemotactic and phagocytic function of neutrophils and the impaired immune response mediated by T and B lymphocytes, promote the development of infection. In 70% of the dialysed patients, the presence of *Staphylococcus aureus* is determined in swabs from the nose and throat. Multiple punctures of fistulas breach the natural barriers protecting the body against infection. It is estimated that, during the year, 8.4–16.8% out of 100% dialysed patients become infected [4].

In addition to local infections, distant infections occur, in the form of abscesses of the lungs and the spine, as well as infectious endocarditis and systemic infection – sepsis [2, 10–15].

Treatment consists of the administration of antibiotics based on obtained cultures. In some cases, irrigation drainage with an antibiotic and abscess removal are conducted. Literature in the field indicates that in the majority of patients with fistula infection, especially in the case of those made of artificial materials, it is necessary to remove the fistula and generate a new one. An indication to remove the fistula as fast as possible is the determination, based on the bacteriological examination of cultures from the fistula, of the presence of *Staphylococcus aureus* MRSA or *Pseudomonas aeruginosa* [1, 11, 12].

An asymptomatic bacteraemia with the presence of the bacteria *Staphylococcus aureus* and *Pseudomonas aeruginosa* in dialysed patients with fistulas made of artificial materials is also an indication for fistula removal [1, 4]. Blood infections associated with vascular access are a serious therapeutic and diagnostic problem, which is particularly evident in intensive care units where it constitutes about 20–40% of all hospital-acquired infections. Infections are a common cause of death, and the mortality rate amounts to 25% [1].

Although arteriovenous fistula remains the gold standard in dialysed patients, in the case of contraindications for its creation, a permanent catheter becomes the option of vascular access. In about 10% of dialysed patients, it is an alternative access to the venous system [6]. The catheter may be an alternative bridging solution when the fistula created has not reached "maturity". In elderly patients burdened with multiple concomitant diseases of the circulatory and respiratory system, when creating a fistula poses a problem, catheters are placed to conduct haemodialysis [8, 16].

Complications related to dialysis catheters

The recommended catheter implantation in the right internal jugular vein, followed by the left internal jugular vein. Then catheters are placed in the external jugular, subclavian, and the femoral veins.

Placing catheters in the subclavian veins should be avoided because it involves a high risk of narrowing the outflow tract and future problems with fistula creation [8]. Dialysis catheters introduced into the subclavian vein lead to stenosis or occlusion in almost 30% of cases, which prevents creation of a permanent access on the limb. Implantation of a catheter in the subclavian and femoral vein results in a much higher risk of infection, thrombosis, and stenosis. Therefore, these places are used as a last resort [8]. Tunnelled catheters are burdened with a significant complication rate and need to be frequently replaced. Before the placement of another catheter, another possibility of renal replacement therapy should be considered, such as peritoneal dialysis or kidney transplantation. The most common complications of dialysis catheters are as follows:

Early complications: bleeding, haematoma at the implantation site, pneumothorax, pleural haematoma, air embolus.

Late complications: infections, thromboses, vasoconstriction, malnutrition-inflammation-atherosclerosis (MIA) is a rare, but possible complication, cardiac arrhythmia, impaired flow during dialysis.

Selection of an inadequate length of the catheter – mostly too short – leads to increased recirculation and impaired dialysis. Too long a catheter can lead to dangerous heart rhythm disturbances due to the irritation of the walls of the right atrium of the heart [16].

A permanent catheter can be a source of bacteraemia and even septicaemia. The portals of infection are both the interior and surroundings of the catheter (skin, clothes, hands of the staff). At the same time, infections are promoted by immunity disorders associated with T and B lymphocyte-mediated immune response impairment in dialysed patients.

According to the International Society of Nephrology, the risk of infection is twice as high in patients with vascular access than in those with a native or artificial fistula [8, 17–20].

Catheter-related thrombosis is, similarly to fistula thrombosis, connected with the presence of narrowing and hypercoagulability occurring in patients with end-stage renal disease.

In order to protect catheters from infection and clotting, their channels are filled with heparin between dialyses. However, it does not demonstrate any antibacterial activity, protecting only against thrombosis.

Detected infection of the catheter area requires antibiotic therapy, hospitalisation, and, frequently, the removal of the catheter.

Catheter infection is most commonly indicated by high temperature and shivering during the dialysis or effusion in the place of its outlet. Permanent catheters often do not cause general symptoms indicating the ongoing infection. Therefore, in patients dialysed with the use of a catheter, blood cultures from the outlet of the catheter should be grown every 2–3 weeks [13–15].

In the case of inflammatory symptoms of the skin around the catheter, cultures should also be collected. Having diagnosed an infection of the catheter, attempts should always be made at curing it. Prior to obtaining an antibiogram, the following antibiotics are empirically used: amoxicillin with clavulanic acid or vancomycin [6, 16].

Thrombotic events are dealt with by means of local thrombolysis with the use of urokinase administered to the catheter. If ineffective, the thrombus must be removed using an endovascular method or the catheter should be replaced. Sodium citrate (TSC) is an antithrombotic with activity alternative to heparin when used in catheters. It is an effective means of maintaining the patency of catheter channels, which also has antibacterial properties [16, 21]. Owing to its high osmolarity, TSC in high concentrations of 10–46.7% counteracts the formation of biofilm on the surface of the catheter and bacteraemia, thus preventing infections [8, 16–18, 20].

The use of modern anticoagulants in the form of sodium citrate (TSC), to fill the channels of the catheter in the period between dialysis sessions, is therefore recommended [3, 17, 19].

Big hopes are connected with TauroLock permanent catheter systems.

The taurolidine-based catheter lock solution containing heparin and urokinase and 4% citrate acid significantly reduced complications related to tunnelled haemodialysis catheters when compared to four per cent citrate solution and was overall more cost-efficient [22].

Conclusions

Recent reports clearly demonstrate that the mortality rate of dialysed patients depends largely on the type of vascular access. It has been also demonstrated that the use of grafts and dialysis catheters causes a significant increase in mortality. Furthermore, the use of artificial material in vascular access for dialysis is connected with an increase in morbidity and hospitalisation in dialysed patients, which entails high costs of treatment. Compared to the ones made of artificial materials, native fistulas are characterised by a long survival rate and a small number of complications. Therefore, the recommended first vascular access is an arteriovenous fistula created in the forearm. Dialysis catheters are the last resort dialysis access, burdened with a high risk of complications, such as infective endocarditis and sepsis, posing a serious danger to the life of the dialysed patient. Correct use and care of vascular access in compliance with the recommendations of the K/DOQI, preference of autogenous fistulas, monitoring the parameters during the dialysis, observing patients for the signs of generalised infection, catheter implantation only in cases of necessity, and using taurolidine-lock or sodium citrate to fill them, are important elements in renal replacement therapy, which extend the lifespan of accesses and reduce complications.

Conflict of interest

The authors declare no conflict of interest.

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