REVIEW PAPERS

Percutaneous balloon angioplasty in dialysis fistula stenosis

Przezskórna angioplastyka balonowa w leczeniu zwężeń przetok dializacyjnych

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KEYWORDS:

- dialysis fistula
- dialysis fistula stenosis
- angioplasty

ABSTRACT

The formation of stenosis in dialysis fistula disturbing blood flow is the most frequent complication and factor limiting its long-term function. Depending on the time and location stenosis lead to various clinical symptoms, triggering dialysis impairment. Due to its minimally invasive nature and high efficacy, percutaneous transluminal angioplasty is the treatment of choice for dialysis fistula stenosis in most locations. An important limitation of angioplasty is the significant risk of recurrent stenosis. Most procedures are performed by puncturing the fistula, performed either in line with the blood flow or opposite to the blood flow, depending on the location of the stenosis. Due to technical differences in dialysis fistula angioplasty – higher pressures of the insufflation used, shorter distance between the stenosis and the vascular access site – dedicated medical devices have been developed: balloon catheters on a shorter shaft, allowing higher insufflation pressures (up to 40 atmospheres). To reduce the risk of recurrent stenosis, drug coated/eluting balloons are also used during such surgeries.

SŁOWA KLUCZOWE:

- przetoka dializacyjna
- zwężenie przetoki dializacyjnej
- angioplastyka

STRESZCZENIE

Powstawanie zwężeń w przetoce dializacyjnej zaburzających przepływ krwi jest najczęstszym powikłaniem i czynnikiem ograniczającym jej długotrwałą funkcję. W zależności od czasu i lokalizacji zwężenie prowadzi do różnych objawów klinicznych, wywołujących zaburzenia dializy. Przezskórna angioplastyka wewnątrznaczyniowa z uwagi na mało inwazyjność i dużą skuteczność, jest metodą z wyboru leczenia zwężeń przetok dializacyjnych w większości lokalizacji. Istotnym ograniczeniem angioplastyki jest istotne ryzyko powstawania nawrotowych zwężeń. Większość zabiegów wykonuje się poprzez nakłucie przetoki, wykonywane zgodnie z prądem krwi lub wstecznie, w zależności od umiejscowienia zwężenia. Z uwagi na odmienności techniczne angioplastyki przetok dializacyjnych – wyższe ciśnienia stosowanych insuflacji, krótszą odległość między zwężeniem a miejscem dostępu naczyniowego opracowano dedykowane wyroby medyczne: cewniki balonowe na krótszym trzpieniu, umożliwiające uzyskanie wyższych ciśnień insuflacji (nawet do 40 atmosfer). Dla zmniejszenia ryzyka powstania nawrotowych zwężeń stosuje się podczas tych operacji również balony lekowe.

Introduction

Stenosis, which impairs blood flow, is the main factor limiting the long-term performance of dialysis fistulas. Despite this problem, fistulas are widely recognized as the best vascular access for hemodialysis – the most common modality of renal replacement therapy in a significant proportion of developed countries, including Poland.

The formation of stenosis in dialysis fistulas is a consequence of a number of processes related to vascular adaptation to changes in blood flow: a significant increase in flow volume and blood pressure, flow direction disturbances

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and turbulent flow. The changes in haemodynamics after establishing the arteriovenous anastomosis lead to stimulation and alteration of the properties of many cell types, primarily endothelial cells, smooth muscle cells and cells responsible for the inflammatory response, and changes in the composition and structure of the extracellular matrix. In a desirable situation, these processes lead to outward remodelling of the vessel wall consisting of lumen widening and wall thickening, thanks to which the fistula can be regularly punctured and effectively used for dialysis therapy. Under unfavorable conditions, vessel wall cell activation leads to inward remodelling and lumen narrowing. Additional factors that may induce stenosis are co-morbidities, especially diabetes mellitus, post-inflammatory changes in the veins, genetic polymorphisms, regular puncturing of the fistula and associated hematomas and repair processes, unfavorable hemodynamic conditions (areas of stagnant and turbulent flows associated with very large changes in shear stress values).

Narrowing of dialysis fistulas occurs at specific locations. In the case of a fistula created by direct arteriovenous anastomosis, the stenosis is most often located at the anastomosis or the initial few centimeters of the venous segment of the fistula (swing segment). On the other hand, for fistulas created using a prosthesis made of artificial material (usually polytetrafluoroethylene, PTFE), stenosis occurs in the area of the anastomosis between the prosthesis and the vein and additionally along the course of the prosthesis.

Depending on where and when the stenosis develops within the fistula, different clinical consequences occur. In the early period after the creation of the fistula, the stenosis prevents the normal process of maturation of the fistula – increasing blood flow, enlarging a vessel diameter, and thickening the vein wall – making it impossible to use the access for dialysis purposes. Puncturing the insufficiently thickened wall of an immature fistula is associated with a high risk of complications, primarily significant damage to the fistula, abnormal healing or haematoma formation. Undilated fistula vessels are difficult to puncture, and insufficient flow prevents sufficient blood exchange with the dialysis machine. Stenosis developing in mature fistulas used as vascular access for dialysis can lead to reduced flow in the fistula, ultimately to thrombosis, development of collateral vessels, alternative outflow routes, pathological fistula dilatation and venous hypertension. The presence of dialysis fistula stenosis and the majority of its consequences lead to impaired dialysis and ineffective renal replacement therapy.

According to the recommendations of the European Society for Vascular Surgery (1) and the US National Kidney Foundation (2), dialysis fistula stenosis exceeding 50% of the vessel lumen – coexisting with the aforementioned clinical symptoms – is an indication for repair procedures. Depending on the degree of dialysis fistula stenosis, it can be divided into: mild (50-75%), moderate (75-90%) and severe (>90%). Open procedures, such as vascular patch plasty, bypasses, anastomotic replacement or excision of the pathological segment with primary anastomosis of the normal fistula segments, are currently used in cases of stenosis located around the arteriovenous anastomosis or coexisting with large pathological dilations. In the vast majority of cases, dialysis fistula stenosis is now treated with percutaneous transluminal angioplasty (PTA). It has become the treatment of choice for the vast majority of cases of dialysis fistula stenosis due to the procedure's low invasiveness, excellent technical efficiency and low risk of complications.

Percutaneous transluminal angioplasty in the treatment of dialysis fistula stenosis

Percutaneous angioplasty of the dialysis fistula is routinely performed using radiological imaging. Due to the superficial location of the fistula vessels, the procedure can also be performed under ultrasound guidance without the use of X-rays. In this case, there is no need to use nephrotoxic contrast agents, which can damage residual renal function in pre-dialysis patients and accelerate the need to start renal replacement therapy. Ultrasound is also very useful for obtaining optimal vascular access and selecting the diameter and length of the balloon to be used. Angioplasty of the dialysis fistula is routinely performed via puncturing the fistula. Only in exceptional cases is access obtained through puncturing the artery proximally to the arteriovenous anastomosis, via the femoral artery or via a surgically dissected portion of the fistula. In the latter case, as a hybrid procedure stage. Depending on the location of the stenosis and the vascular access site used, the fistula puncture is *antegrade* (in the direction of the blood flow) or *retrograde* (opposite to the blood flow). Usually, qualification for angioplasty is performed on the basis of the ultrasound result, much less frequently on the basis of computed tomography or magnetic resonance angiography. The use of the latter two imaging methods is much more common in diagnosing fistula outflow pathology at the level of the central veins, within the body cavities, where direct ultrasound imaging is not possible.

Ultrasound imaging of the fistula is indicated immediately prior to the angioplasty procedure, preferably on the operating table. This is because the morphology of the fistula changes dynamically. Imaging results from the qualifying period, a few weeks before, may be outdated. Secondly, ultrasound examination enables a physician to accurately assess the stenosis, its length and diameter, and adjacent fistula sections. This allows for the correct selection of endovascular instruments and hemodynamic assessment of procedure effectiveness. Thirdly, it allows for accurate planning of the vascular access, which is a very important part of the procedure. If the fistula is punctured too close to stenosis, angioplasty may be very difficult and, in some situations, impossible. In most cases, the fistula is punctured as far as possible from the site of stenosis, in a convenient location. Distance usually does not exceed 30 cm, and the pushability of endovascular instruments is very good. Once the puncture site for the fistula has been determined, the selected area is locally anesthetized. Vascular access to the vessels of a mature fistula is usually not difficult to obtain, as they are located very superficially, a few millimeters below the skin surface and are more than 5-6 mm in diameter. It is much more difficult to obtain proper vascular access in case of a fistula that is not maturing properly. In this case, the punctured vessels are much narrower and have a thinner wall, which further increases the risk of complications at the puncture site. When puncturing a narrow, thin-walled, and therefore highly vulnerable wall of an immature fistula, gaining access may be facilitated by a temporary blockage of the outflow, which increases the diameter of the vessel and increases blood pressure. In addition, local anesthesia can already be administered after fistula puncture, which, in turn, prevents the vessel lumen from being constricted by increased interstitial pressure.

An important facilitation of fistula puncture is the use of ultrasound examination of the puncture site and the use of micropuncture kits. After dialysis fistula puncturing, arterial blood outflow, sometimes pulsative, is observed. The magnitude of the outflow depends on blood flow, pressure in the fistula, and the thickness of the needle used. Fistula transpuncture should be avoided, as this causes blood extravasation that is difficult to stop. A guidewire is inserted through the needle into the fistula lumen. Like with other transluminal procedures, the guidewire should be inserted very gently. Any resistance indicates an abnormality and should not be overcome with force. In this situation, the guidewire should be withdrawn slightly and rotated. If repeated attempts are unsuccessful and the guidewire cannot be introduced into the fistula lumen without resistance, radiographic or ultrasound imaging may be used to assess the position of the tip of the guidewire. This allows a possible change in the direction of guidewire insertion. However, in such situations, the guidewire should be removed from the needle, and once blood flow is confirmed, angiography should be performed to accurately depict the course of the fistula and the possible cause obstructing guidewire insertion. Once the guidewire has been inserted into the fistula lumen, the needle is removed (while applying pressure to the puncture site to prevent haematoma formation), and the vascular sheath is inserted. The sheath should be inserted along the guidewire with slight rotation. During angioplasty of dialysis fistulas, vascular sheaths with a diameter of 5-6 F are most commonly used. Due to the usually shorter distance between the vascular access and the pathology being treated than in other percutaneous procedures, shorter, dedicated vascular sheaths are used, or standard length sheaths are inserted more shallowly. Therefore the vascular sheath must be well protected from slipping out of the vessel by suturing or sticking it to the skin. Angiography is then performed, visualizing the stenosis of the fistula. In the case of pathology located in the blood outflow from the fistula, it can be perfectly visualized through the use of a small volume of contrast agent. More often, it is more problematic to visualize the stenosis located on the side of the arteriovenous anastomosis.

The next stage of the procedure is to guide the guidewire through the stenosis. For this stage of the procedure, the roadmap* technique is used, which allows the current movement of the guidewire, or possibly the catheter, to be superimposed on the recorded angiographic image. For stenosis located at the initial segment of the dialysis fistula and retrograde access, the guidewire is introduced into the artery, if possible, towards the heart. Then the catheter can be inserted into the artery, and an examination can be performed from the side of the artery used to create the fistula. It often happens that only such angiography visualizes the stenosis of the dialysis fistula. In case of stenosis located in the outflow from the fistula, the guidewire is guided distally through an antegrade introducer sheath.

Once the guidewire has passed through the stenosis, the transluminal procedure can be performed. The guidewire must remain outside the stenosis throughout the procedure until the final angiography, which allows minimally invasive rescue procedures in case of a fistula vessel rupture. Selection of the balloon catheter used for angioplasty must take into account the length and diameter of the stenosis and the diameter of the adjacent fistula segments. Due to the short distance between the vascular access and the stenosis, as described earlier, catheters with short shafts, even 50 cm, can be used to facilitate angioplasty and speed up the procedure. After insertion of the balloon into the stenosis under the guidance of radiographic or ultrasound imaging and measurement of insufflation pressure, the balloon is gradually expanded. A characteristic feature of transluminal angioplasty of dialysis fistula stenosis is the use of very high pressures, up to 40 atmospheres, far in excess of those used in other arterial pathologies. Frequently, dialysis fistula stenosis does not yield to pressures of 20 atmospheres. It shows that the devices used for dialysis fistula angioplasty differ from the ones used as standard for transluminal procedures. This concerns the length of the balloon catheter shaft and, above all, the maximum insufflation pressure. After angioplasty of the dialysis fistula stenosis, the balloon catheter is withdrawn, leaving the guidewire, and follow-up angiography is performed. This examination assesses the effectiveness of the procedure – the degree of dilatation of the stenosis, presence of the residual stenosis and the possible presence of collateral circulation vessels. Angiography also allows for diagnosing procedure complications, primarily extravasation of the contrast agent outside the fistula vessel, but also arterial spasm and persistence of the stenosis. Detection of a complication requires corrective management. In case of residual stenosis, repeat angioplasty using a shorter balloon and higher insufflation pressures is most often necessary. Visualization of a contrast agent outside the vessel means blood extravasation and requires immediate action, consisting in the first stage of a few minutes of low-pressure balloon distension at the site of damage to the fistula wall, which can be combined with local external compression. This procedure is most often effective and allows for reliable repair of the damage while maintaining fistula patency. Only if the low-pressure

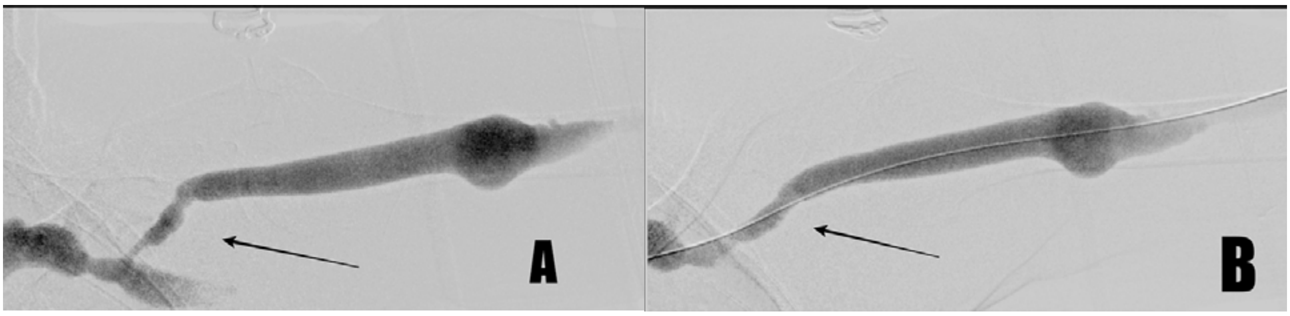

Figure 1. Percutaneous transluminal angioplasty of the cephalic vein arch stenosis of the brachiocephalic fistula. Angiography before angioplasty (A), status post angioplasty (B), the stenosis is marked with an arrow.

Source: own collection.

* roadmap – radiological technique that enables visualization of anatomic structures using image subtraction at peak opacification: Weigt J, Obst W, Kandulski A, et al., Road Map fluoroscopy successfully guides endoscopic interventions in the esophagus, Endosc Int Open, 2017.

inflated balloon procedure is unsuccessful other repair procedures – stent graft implantation or classic surgery – are used. During angioplasty, its outcome can also be assessed by evaluating changes in blood flow conditions in the brachial artery on the side of the fistula. After a successful procedure, a significant decrease in resistance and an increase in blood flow are visible.

Once a normal view of the fistula is obtained, which indicates a successful procedure and no complications, the transluminal surgery instruments are removed. Closure of the fistula puncture site is most easily achieved by placing a 5-0 vascular suture or special closures dedicated to dialysis fistulas (The Slip-Not® suture, Merit Medical) over the skin and subcutaneous tissue. The closers used in other vascular accesses are not certified for dialysis fistulas, and compression of the puncture with elastic bandages may lead to fistula thrombosis.

Results of percutaneous transluminal angioplasty of dialysis fistula strictures

Angioplasty of dialysis fistula stenosis is associated with a very high technical success rate, a low risk of complications and worse primary patency in the medium to long term than with conventional surgery. It is the late complications in the form of recurrent stenosis that are the main limitation of the method and necessitate subsequent repair procedures. The effectiveness of dialysis fistula stenosis angioplasty varies depending on the nature of the lesions and the indications for the procedure.

I. Angioplasty of immature fistula stenosis

Study results indicate that the technical success rate of immature dialysis fistula stenosis angioplasty, performed to promote maturation processes, is 95.7-97% (3-4). One-year primary fistula patency after such procedures ranges from 57.6% to 71.9%, and secondary patency from 82.8 to 94.8% (3, 4). The complication rate is low and amounts to 3-5%. The most serious complications are hematomas and fistula wall rupture.

Technical success rate	95.7-97%
Primary patency	57.6-71.9%
Secondary patency (after one year)	82.8-94.8%
Complications	3-5 % (e.g., hematomas, ruptures)

II. Angioplasty of mature fistula stenosis

Extensive literature evaluating the results of many procedures shows that the technical success rate of angioplasty performed to dilate mature fistula stenosis is 97-98% (5, 6). A one-year primary patency rate is 62-84.5% (6, 7), while a secondary patency rate is 85-90.5% (6, 7). The complication rate is approximately 2-3% (5, 6). Complications are divided into minor ones, such as vasospasm and hematomas, and major ones, which include laceration and fistula thrombosis.

Technical success rate	97-98%
Primary patency	62-84.5%
Secondary patency (after one year)	85-90.5%
Complications	2-3%

Factors affecting dialysis fistula patency after angioplasty

Studies evaluating primary patency after angioplasty (7) of Cimino-Brescia fistula stenosis found that this parameter is significantly impacted by a number of necessary balloon insufflation during angioplasty required to dilate the stenosis, presence of residual stenosis >30%, as well as the location of the stenosis in either the supply artery or the anastomosis.

Another study (8) showed that early (up to 6 months after the surgery) recurrent stenosis is influenced by old age, coexisting diabetes and stenosis located a few centimeters behind the anastomosis. At the same time, the length and degree of the stenosis have not been shown to affect primary patency.

The patency of the fistula after angioplasty may be influenced by the degree of calcification of the aortic arch and also by the location of the fistula stenosis. Patients with a high degree of aortic arch calcification and arm fistula stenosis had shorter primary patency rates at 6, 12, 24 and 36 months of 76.3%, 58.3%, 43.2%, and 38.2%, respectively (9).

Studies on percutaneous transluminal angioplasty of dialysis fistula stenosis

DCB (Drug-coated balloon), DEB (Drug-eluting balloon)

Frequent formation of recurrent stenosis reduces the proportion of good long-term results after dialysis fistula angioplasty. To reduce the risk of this complication, drugs are now administered locally during angioplasty. For this purpose, balloons are coated with an active substance (currently paclitaxel 2-3.5 μg/mm^2, sirolimus 1.25 μg/mm^2), which penetrates the vessel wall during balloon expansion. Both paclitaxel and sirolimus reduce the activation, proliferation and migration of smooth muscle cells, and myofibroblasts, inhibiting neointimal hyperplasia and stenosis formation.

Angioplasty using drug balloons maintains patency of 70-80% of dialysis fistulas after 6 months. Primary patency of 40-50% after 12 months results in an almost 1.5-fold reduction in stenosis and thrombosis compared to traditional balloons. This allows for time prolongation before secondary intervention and a reduction in the number of secondary interventions needed to maintain the patency of the dialysis access (10, 11).

In contrast to other indications, there are currently no clear recommendations for antiplatelet or anticoagulant treatment after dialysis fistula angioplasty. During studies investigating the efficacy of DCB in the treatment of dialysis fistula stenosis, dual antiplatelet treatment for at least several months was routinely used. Further studies evaluating optimal pharmacotherapy after dialysis fistula angioplasty are needed, and such recommendations should be developed.

Another element that may influence the results of dialysis fistula angioplasty is balloon expansion characteristics other than the pressure used. Analyses of the results of angioplasties performed for other indications, e.g., superficial femoral artery atherosclerosis, have shown that the use of a longer angioplasty time (5 min.) gives better results compared to a shorter balloon expansion time (12). Similarly, balloon expansion conditions during coronary artery angioplasty produced better results (13).

Summary

The formation of stenosis in dialysis fistula disturbing blood flow is the most frequent complication and factor limiting its long-term function. Depending on the time and location stenosis lead to various clinical symptoms, triggering dialysis impairment. Due to its minimally invasive nature and high efficacy, percutaneous transluminal angioplasty is the treatment of choice for dialysis fistula stenosis in most locations. An important limitation of angioplasty is the significant risk of recurrent stenosis. Most procedures are performed by puncturing the fistula, performed either in line with the blood flow or opposite to the blood flow, depending on the location of the stenosis. Due to technical differences in dialysis fistula angioplasty – higher pressures of the insufflation used, shorter distance between the stenosis and the vascular access site – dedicated medical devices have been developed: balloon catheters on a shorter shaft, allowing higher insufflation pressures (up to 40 atmospheres). To reduce the risk of recurrent stenosis, drug coated/eluting balloons are also used during such surgeries.

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