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Review Article

Enhancing AV fistula function: An update review on the role of percutaneous angioplasty for stenosis management

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Abstract

Arteriovenous fistulas (AVF) are the preferable vascular access for hemodialysis due to the improved patency and decreased complication rates. However, primary failure remains as a significant obstacle, typically related to juxta-anastomotic stenosis triggered by neointimal hyperplasia. The site of stenosis differs by AVF type, influencing functionality and necessitating specific therapies. Percutaneous transluminal angioplasty (PTA) is the primary intervention, with elevated success rates in reestablishing AVF patency. Optimal technique, lesion site selection, and superior balloon angioplasty markedly improve results. Utilizing an evidence-based methodology enhances AVF performance, diminishes thrombosis risk, and augments long-term dialysis effectiveness.

Keywords: Arteriovenous fistula, angioplasty, stenosis, hemodialysis

INTRODUCTION

Chronic kidney disease (CKD), defined as renal dysfunction persisting for over three months, increases the risk of cardiovascular complications and mortality [1,2]. End-stage renal disease (ESRD) impacts 10% of the worldwide population, with more than 70% undergoing hemodialysis [3]. ESRD is an escalating public health concern globally, including Türkiye, where 81,055 individuals underwent renal replacement therapy (RRT) in 2018, resulting in a prevalence rate of 988 per million [4]. Three in Indonesia, more than 713,000 individuals were diagnosed with ESRD in 2018 [3].

Fistula thrombosis, a common complication in hemodialysis patients, is often managed surgically. Endovascular procedures such as percutaneous angioplasty and thromboaspiration are employed [5]. The KDOQI 2019 guidelines advocate for a patient-centered methodology in vascular access management, suggesting intervention for arteriovenous fistulas (AVF) exhibiting clinically severe stenosis instead of routine preventative measures. Treatment is warranted for AVF demonstrating insufficient flow, venous stenosis, aneurysm development, or ischemia, especially when accompanied by clinical complaints, abnormal physical examinations, or diminished dialysis efficacy [2].

Arteriovenosus Fistula (AVF)

The primary kinds of AVF are radiocephalic fistula, brachiocephalic fistula, and brachial artery-to-transposed basilic vein (BTB). The radiocephalic fistula links the lateral side of the radial artery to the terminal end of the cephalic vein. In contrast, the brachiocephalic fistula connects the lateral aspect of the brachial artery to a laterally positioned and elevated basilic vein [6].

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Pathogenesis AVF Stenosis

AVF are optimal for hemodialysis; however, they may experience primary failure, a prevalent consequence. Primary failure rates vary between 30% and 50%, frequently attributable to juxta-anastomotic stenosis resulting from neointimal hyperplasia. Neointimal hyperplasia is a physiological healing response to vascular damage characterized by the migration of smooth muscle cells from the media to the intima, their proliferation, and the deposition of extracellular matrix, resulting in luminal constriction. This process is initiated by endothelial injury from surgery, angioplasty, or changed blood flow, leading to platelet activation, leukocyte adhesion, and inflammatory signaling, finally resulting in vascular stenosis [7]. Primary failure is linked to comorbidities, surgical stress, endothelial dysfunction, inflammation, and altered flow conditions (Figure 1) [8-10].

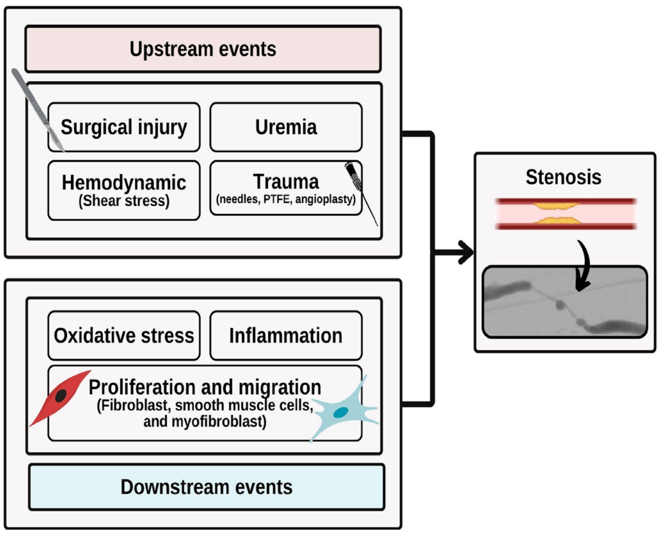

Figure 1. Upstream and downstream events resulting in stenosis of the arteriovenous access [7,8]; Picture reproduced by BioRender.com

The success of an AVF for hemodialysis depends on its structural and mechanical integrity. The mechanobiology of vascular access includes flow dynamics, biological mechanisms, and the reactions of vascular endothelium and smooth muscle cells. A problematic feature leading to AVF maturation failure or abandonment is the onset of neointimal hyperplasia, which causes excessive proliferation of vascular smooth muscle cells (VSMCs) and/or myofibroblasts. This leads to reduced blood flow, increased pressure, stenosis, and thrombosis, finally resulting in maturation failure or the discontinuation of vascular access [11].

Native venous or AVF stenoses may arise from multiple factors, including neointimal hyperplasia at, distal to, or proximal to anastomoses, hyperplasia in regions of both slow and rapid flow, intimal injury resulting from CVC for hemodialysis, pericatheter thrombosis, infection, external compression from a perivenous hematoma, and accelerated venous atherosclerosis. Stenoses may be detected as early as three weeks post-creation of the AVF. Stenosis locations in central veins, such as the thoracic inlet, may become essential in individuals with AVF and increased venous flow. Venous valves can create turbulence, impede blood flow, and result in hypertrophy. Thoracic outlet syndrome may exacerbate stenoses, aggravating symptoms, and functional impairment [12].

Anastomosis Angle

The anastomotic angle in an AVF refers to the geometric configuration at which the artery and vein are surgically connected, significantly affecting hemodynamic conditions, maturation, and long-term patency [13,14]. Studies suggest that smaller angles (≤30°) minimize disturbed flow and improve AVF maturation, whereas larger angles (≥75°) increase turbulence and wall shear stress, potentially accelerating neointimal hyperplasia and stenosis [14]. Computational simulations indicate that an intermediate angle, such as 45°, optimally balances blood flow, venous outflow rate, and shear stress, promoting successful AVF function [13]. Yang et al. (2020) determined that an anastomotic angle of 30° to 46.5° is optimal for minimizing turbulent flow; however, angles outside this range lead to shear stress concentration in the AVF. Carroll et al. (2019) discovered that altering the anastomosis angle from 45° to 135° decreased flow disturbances [11].

Anastomosis Type

Four forms of anastomosis, including end-to-side (ETS) anastomosis, are associated with the angle of anastomosis. ETS ensures consistent shear stress distribution and enhances AVF patency after 12 months. Clinical trials indicate no substantial difference in successful outcomes. The optimal angle is contingent upon the kind and neointimal hyperplasia [11].

Vessel Selection

Krampf et al. (2021) identified an association between input artery diameter, length, and flow volume in AVF. Anastomotic decision-making must be customized to patient requirements, prioritizing vessels with greater diameters. The efficacy of arteriovenous grafts is associated with arterial and venous diameters, the artery-to-vein ratio, and patency [11].

Blood Flow Parameters

Research indicates that multiple flow variables, including flow pattern, wall shear stress (WSS), flow velocity, rate, volume, vorticity, pulsatility, and resistance index, influence the maturation and patency of AVF and arteriovenous grafts (AVG). WSS is the primary determinant, with increased WSS

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on Day 1 forecasting successful AVF development (Figure 2). Nevertheless, elevated wall shear stress around the AVG anastomosis may be detrimental. Inflammation may arise when wall shear stress and oscillation index persistently increase, resulting in diminished blood velocity and reduced patency [11].

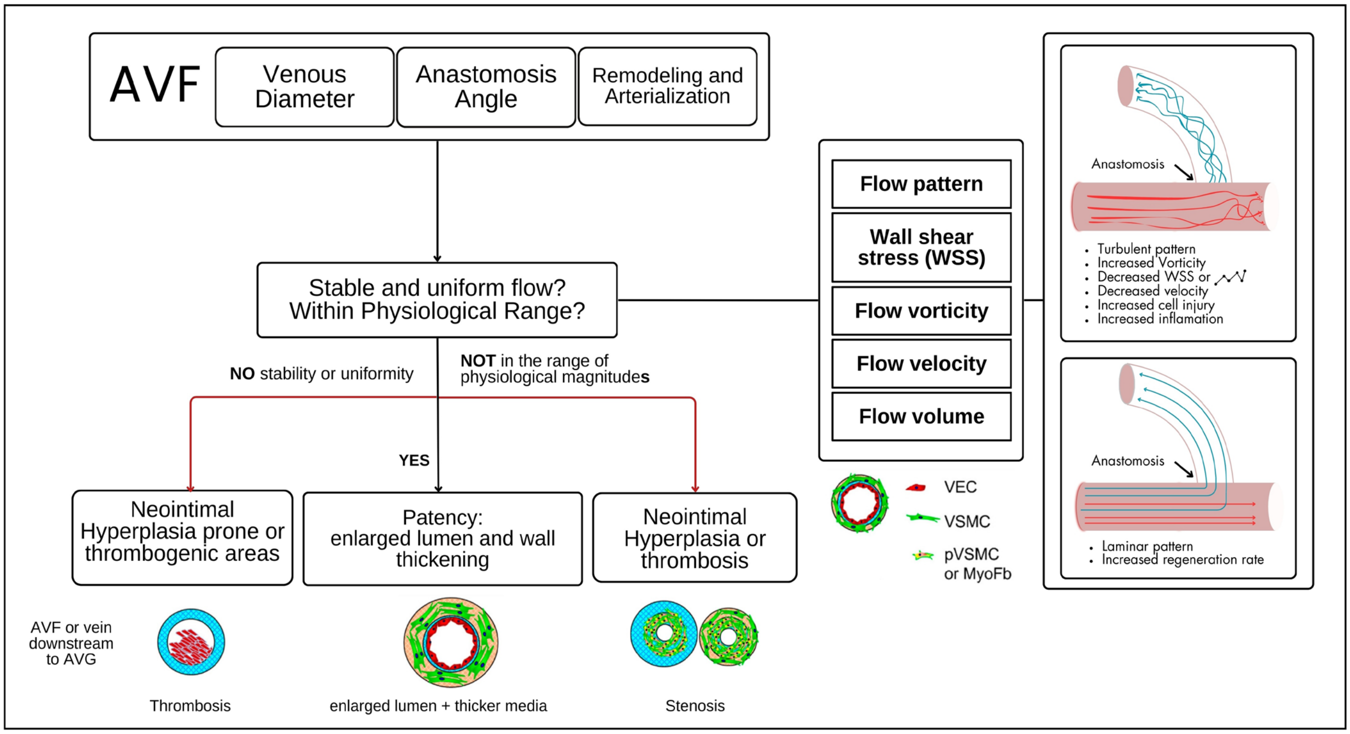

Figure 2. The images of the factors influencing and outcomes resulting from flow in dialysis access; VEC compose the inner layer of the vessels and are essential for sustaining vascular functionality, modulating blood flow, and inhibiting clot formation; VSMCs offer structural stability and contribute in regulating vessel width [10]

Cellular Mechanisms

Increased blood flow from arteries to veins induces inflammation and neointimal hyperplasia, failing AVF. Signaling components such as Akt1-mTORC1 and endothelial nitric oxide synthase (eNOS) facilitate arteriovenous fistula formation and maintain patency. The overexpression of these factors may result in the development of neointimal hyperplasia (Figure 3). Macrophages, as immune cells, determine long-term access results. The transition from M1 to M2 is essential for the healing of anastomosis and the effectiveness of AVF [11].

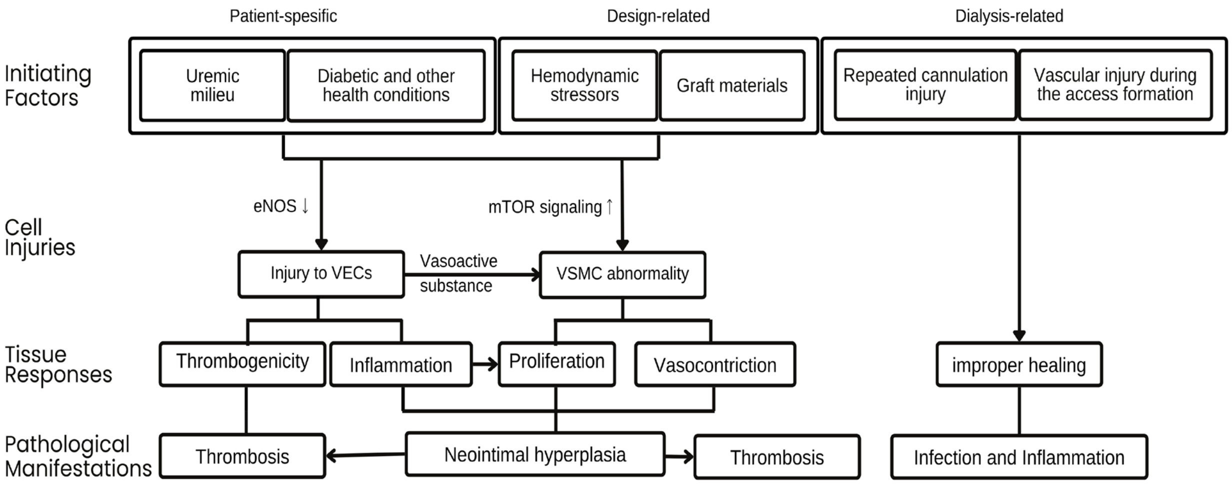

Figure 3. Identification of several initiating factors contributing to pathological manifestation in dialysis access [10]

Cannulation-Related Complications

Repeated needle punctures during hemodialysis result in cannulation difficulties, leading to the destruction of AVF and graft walls, which can induce infiltration, hematoma formation, and blood extravasation. The meticulous selection and upkeep of vascular access is essential [11].

AVF Characteristic Locations of Stenosis

Certain anatomical locations in each type of fistula are susceptible to stenosis (Table 1). For the radiocephalic fistula, the pertinent portion is the juxtaanastomotic segment; for the brachiocephalic fistula, it is the cephalic arch; and for the BTB fistula, it is the proximal swing segment [6].

Table 1. Typical locations of stenosis for the three most prevalent AVFs [6]

AVF	Most prevalent stenosis	Positive aspects	Negative aspects
Radiocephalic fistula	Juxtaanastomotic segment stenosis (JAS)	Effortless to set up, preservation of the upstream vein for future access establishment, little incidence of steal syndrome, infrequent occurrence of ischemic monomelic neuropathy.	Reduced maturation rate, reduced flow rate
Brachiocephalic fistula	Cephalic arch stenosis (CAS)	Effortless to set up, elevated flow rates, accelerated maturation rate	High incidence of steal syndrome, frequent occurrence of ischemic monomelic neuropathy, increased prevalence of symptomatic central venous stenosis
Bracial artery-to-transposed basilic vein fistula (BTB)	Proximal swing segment	elevated flow rates, accelerated maturation rate	Challenging surgery associated with heightened perioperative morbidity; elevated incidence of steal syndrome, increased ischemic monomelic neuropathy, and greater prevalence of symptomatic central venous stenosis

Angioplasty

Hemodialysis AVF-induced thrombosis is an established intervention for stenotic lesions, with recent thromboses demonstrating heightened susceptibility to endovascular therapy. The Gruntzig balloon catheter, initially employed in 1981 for angioplasty of arteriovenous fistula stenosis, has demonstrated favorable outcomes in three of five trials [15]. Research indicates that transluminal angioplasty and surgical revision yield comparable results; nonetheless, angioplasty is regarded as the primary treatment option due to its user-friendliness, minimally invasive characteristics, and enhanced venous preservation [9].

Indications

Endovascular intervention is recommended for AVF stenosis with ≥50% luminal constriction, clinical manifestations, hemodynamic irregularities, or dialysis impairment [2,16]. The KDOQI 2019 guidelines advocate for clinical indicators rather than imaging and oppose routine preemptive angioplasty [16]. Intervention is required for extended post-dialysis hemorrhage, challenges in cannulation, absence of thrill or bruit, elevated venous pressures, and dialysis recirculation. Hemodynamic criteria for AVFs encompass access flow below 600 mL/min, a venous pressure increase exceeding 50%, and declining Kt/V values. Percutaneous transluminal angioplasty (PTA) is the primary treatment, with stenting indicated for recurrent stenosis, elastic recoil, or central venous involvement [2]. The intervention focuses on alleviating symptoms instead of monitoring to restore arteriovenous fistula patency, avert thrombosis, and enhance dialysis efficacy [16].

Clinical signs and imaging criteria are essential for diagnosing stenosis, which necessitates NIH intervention. Judicious angioplasty is advised to avert injury and restenosis. Angioplasty is the principal intervention for NIH resulting in AV access insufficiency, with technical success rates between 90% and 95%. Nonetheless, it may induce barotrauma, vascular injury, and increased restenosis rates [9,15].

Technical Factors

Angioplasty is a minimally invasive procedure using local or general anesthesia to restore central venous access. The procedure entails the insertion of wires and catheters, utilizing balloons that are categorized as standard, high-pressure, or cutting varieties. A stent or stent graft is employed, with the surgeon accounting for potential future stenosis and providing additional space for subsequent operations. Self-expanding stents are favored because of their minimal migration risk [15]. Enhanced angioplasty outcomes have facilitated superior therapies (Figure 4). A generic algorithm takes into account lesion-specific characteristics, hence improving the efficacy of angioplasty interventions [9].

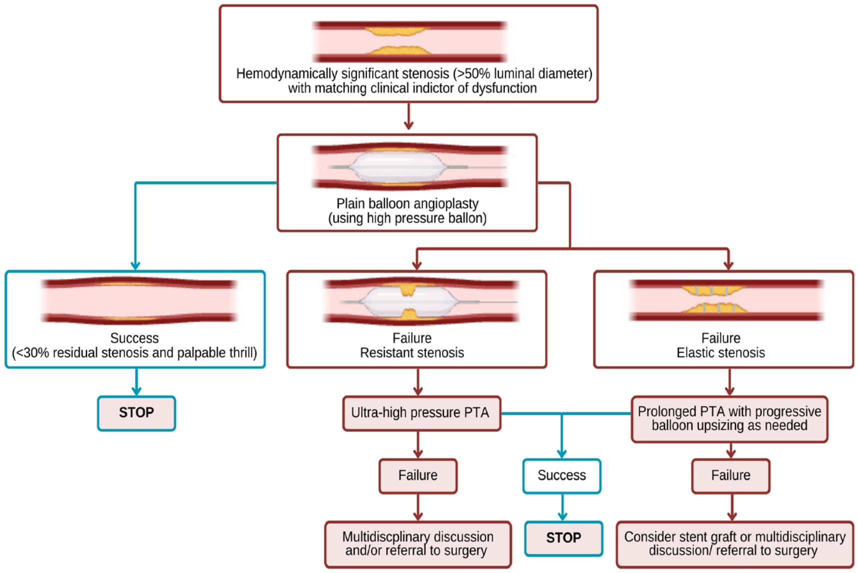

Figure 4. Algorithm for regular arteriovenous access stenosis; this method offers a comprehensive selection tree applicable to the management of most stenotic lesions [8]; Picture reproduced by BioRender.com

Types of Balloons and Dilatation Pressure

Stenoses in arteriovenous access have been a considerable difficulty since the advent of Grüntzig's polyvinyl chloride balloon in 1982. The Olbert balloon attained technical success rates of approximately 90%. Subsequent high-pressure balloons (HPB) possess a burst pressure rating of approximately 20 atm and may attain pressures of up to 27 atm due to uncontrolled overinflation. HPB angioplasty operates at pressures below 20 atm, whereas ultra-high pressure balloon (UHPB) angioplasty functions at pressures over 20 atm. Studies indicate that 8%, 13%, and 34% of stenoses necessitate inflation pressures surpassing 20 atm for successful dilatation. UHPB angioplasty is optimal for treating refractory stenotic lesions. Both approaches allow interventionalists to attain technical success in addressing the majority of lesions. Numerous devices, such as infiltrate and perforate, parallel wire approach, atherectomy devices, and cutting balloons, are constrained by high success rates with UHPB and are inadequate for rectifying flaws in arteriovenous grafts or fistulas [9].

Balloon Sizing

Balloons are utilized in numerous procedures, with lengths and diameters selected by the operator. In arteriovenous grafts, they are often 1 mm larger than the graft, but in arteriovenous fistulas, they are 10-20% larger. Smaller balloons are employed for vascular anastomotic lesions owing to their diminished caliber. Balloons can be progressively expanded for elastic stenoses. The length is contingent upon the severity of the stenotic lesion, to treat the entire lesion while reducing the need for angioplasty [9].

Elastic Stenosis and Balloon Inflation Times

Balloon inflation durations are typically employed to address residual or elastic stenosis, with prolonged durations leading to diminished stenosis. Research indicates a technical success rate of 75% for 1-minute inflation and 89% for 3-minute inflation, with no significant difference in primary patency at 1, 3, and 6 months. Extended 1-minute inflation intervals exhibit an increased incidence of access failure at 3 months, potentially attributable to further arterial damage. Incremental upsizing balloons have been utilized for the management of elastic stenosis, although their effectiveness remains ambiguous [9].

In Practice, Simple Balloon Angioplasty: AVF

Hemodialysis vascular access entails a sophisticated network of cardiac and vascular systems, whereas stenosis may manifest at any location. Treatment entails lesion identification, execution of fistulograms, and modification of methods [9].

Inflow Stenosis

Inflow stenosis includes juxta-anastomotic, arterial, and anastomotic lesions, characterized by peri-anastomotic stenoses occurring within one centimeter of the anastomosis and those situated within the native artery [9].

a. Arterial stenosis

Remote arterial stenoses in the brachiocephalic, subclavian, brachial, or forearm arteries infrequently result in access dysfunction, comprising 1-10% of clinically severe lesions. If suspected, a specialized upper extremity arteriogram with suitable endovascular intervention is advised [9].

b. Arterial anastomotic stenosis

True arterial anastomotic lesions, comprising 10-20% of stenotic lesions in arteriovenous fistulas, are less prevalent than juxta-anastomotic lesions, frequently recurring after angioplasty and possibly requiring surgical intervention [9].

c. Juxta-anastomotic stenosis (JAS)

JAS is the predominant lesion in dysfunctional radiocephalic fistulas, representing 50-60% of patients. Traditional surgical techniques provide enhanced patency and diminished recurrence of stenosis. Angioplasty maintains functional fistulas [9].

Inflow lesions exhibiting overlapping clinical manifestations necessitate intervention; however, a sophisticated strategy utilizing catheter-based hemodynamic evaluations dictates the necessity for therapy, which is implemented in 16% of instances [9].

Cannulation Zone Stenosis

The cannulation zone, a vital region of stenosis in the forearm and upper arm fistulas, is frequently neglected in treatment strategies. The outcomes of PTA for lesions in the cannulation zone may be comparable to those of AVF angioplasty. If unsuccessful, stent-graft placement may be contemplated; nevertheless, associated hazards encompass stent fracture, pseudoaneurysm formation, and infection [9].

Venous Outflow Stenosis

Radiocephalic fistulas display juxta-anastomotic lesions, but upper arm brachiocephalic and transposed fistulas demonstrate venous outflow lesions, complicating treatment and leading to a higher prevalence of upper arm fistulas.

a. Cephalic arch stenosis (CAS)

CAS is a common condition in 40-75% of dysfunctional brachiocephalic fistulas, resulting in a heightened prevalence due to elevated flow rates and venous valves. Treatment is difficult, has diminished success rates, and may result in venous rupture. Patients may contemplate other medicines or surgical interventions [9].

b. Swing point stenosis

Swing point stenoses are distinct BTB lesions originating from the basilic vein in the upper arm. They are the tertiary option for fistulas owing to their technical intricacy. They manifest in 60-75% of dysfunctional BTB patients and may constitute up to 90% of treatments (Figure 5). Stent grafts demonstrate advantages in target lesion and access patency relative to PTA [9].

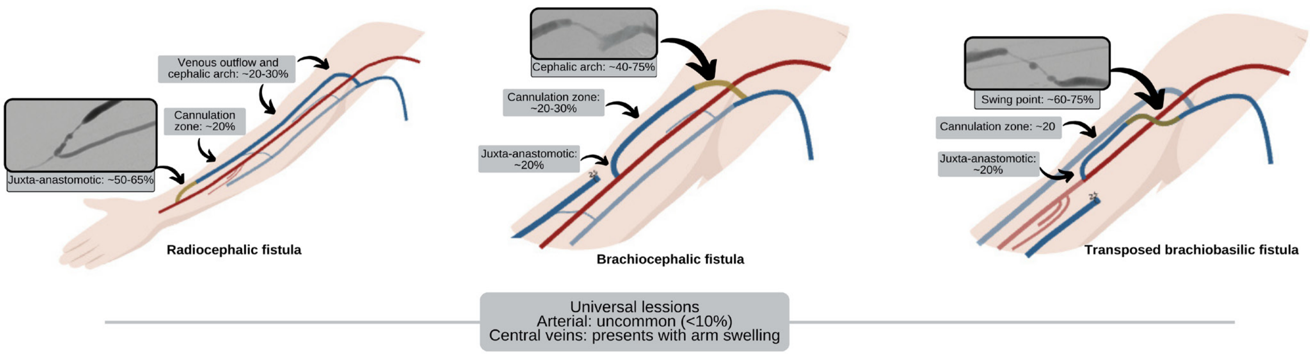

Figure 5. Distribution and estimated prevalence of stenotic lesions across various access configurations [8]; Picture reproduced by BioRender.com

In-Stent Restenosis

A RESCUE trial demonstrated that PTFE stent grafts surpassed PTA in efficacy for in-stent restenosis, with 66% superior target lesion patency rates and improved access circuit patency rates [17].

Primary and Secondary Patency After PTA

Studies indicate that balloon PTA can attain a primary patency rate of 50% or above; nevertheless, recurring angioplasty is necessitated by arterial wall hyperplasia. Subsequent angioplasties may yield a secondary patency rate of 91% after one year. Early angioplasty elevates the risk of restenosis; however, factors such as the location of the stenosis and the diameter of the artery also affect restenosis [15].

Procedure Success-Stenosis

The efficacy of stenosis treatment is assessed via physical, hemodynamic, or clinical tests, signifying a successful intervention [18].

a. Anatomic Success-stenosis: This is examined during the initial procedure and is defined as achieving an immediate post-operative residual stenosis of less than 30%, measured at the narrowest point of the lumen, as demonstrated by direct visualization or quantification post-surgery [18].

b. Hemodynamic Success-stenosis: This is the resolution of a pre-procedural signal indicating hemodynamically significant stenosis. Procedural indicators according to K/DOQI criteria may include any of the following (11) [2,18]:

1. Reduced blood flow leads to an improvement in intra-access blood flow exceeding 20%.
2. Elevated static or derived venous pressures are adjusted to venous pressures.
3. Elevated negative arterial pre-pump pressures that obstruct sufficient blood flow rates revert to baseline pre-pump pressures and return to baseline blood flow rates.
4. Elevated access recirculation through urea concentrations leads to the elimination of access recirculation.
5. Enhanced access recirculation utilizing dilution methods (non-urea-based) yields less than 5% access recirculation.
6. Unexplained decreases in the measured delivery of HD (urea reduction ratio, Kt/V) need the re-evaluation of dialysis adequacy as determined by urea kinetics.
7. Abnormal duplex ultrasound returns to baseline duplex ultrasound (or intra-access) Doppler flows above 400-500 ml/minute for AVF, exceeding 600 ml/minute for AVG, and/or residual stenosis below 30%.
8. Physical evidence of chronic extremities edema indicates a lessening or remission of the swelling.
9. Prolonged bleeding following needle withdrawal should return to normal bleeding time.
10. Modified attributes of the pulse or thrill at the access site result in an intensified pulse and a persistent thrill.
11. The modified characteristics of the access bruit return to a low-frequency systolic and diastolic bruit.

c. Clinical Success-stenosis: The intervention must facilitate the re-establishment of traditional dialysis through two-needle cannulation and designated blood flows for two-thirds of monthly sessions, thereby averting catheter dependence and clinical failure [18].

d. Functional Success-stenosis: This indicates a successful two-needle cannulation following the intervention, enabling the delivery of prescription dialysis and allowing for catheter removal [18].

Complication

Renal problems following angioplasty can be addressed conservatively; nevertheless, stent or covered implantation may be required. Blood transfusions are infrequent, and the use of cutting balloons elevates the danger of rupture [19-21].

CONCLUSION

The increasing number of hemodialysis patients highlights the need for effective interventions to maintain fistula patency. While PTA is the gold standard for managing stenosis in hemodialysis AVF and AVG, standard balloon angioplasty effectively addresses most cases. Drug-eluting balloons represent an innovative approach to alleviating stress on fistula walls. Additional trials are required.

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