An overview of permanent vascular access in hemodialyzed patients

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Abstract
In the last decade, because of significant number of end-stage renal disease individuals in need of renal therapy replacement and permanent quest of nephrologist to optimize kidney disease patients’ quality of life, there is an increased interest in achieving a suitable permanent vascular access, essential for an efficient dialysis. Furthermore, it is of high importance to preserve arteriovenous fistula in optimal condition and therefore, it is vital to correctly understand the histopathology and pathophysiological mechanisms implicated in maturation and well function of dialysis vascular access.

Keywords: arteriovenous fistula, complications, treatment, prognosis.

Introduction
The creation of a suitable dialysis vascular access, “the Achilles’ heel of hemodialysis” [1], without related future complications, still represents an important challenge for physicians, even after significant steps have been made in solving or improving the major problems of dialyzed population (e.g., anemia, renal osteodystrophy) by the implementations of new drug lines (e.g., erythropoietin stimulating agents (ESA), vitamin D receptor activators (VDRA) or calcimimetics).

Reviewing the literature medical data, the best and safest modality of dialysis initiation is the creation of a vascular access by performing an anastomosis between an artery and a vein of the arm and allowing the development of a native arteriovenous fistula (AVF). Unfortunately, this is not an ideal procedure. Over 60% of the patients in need for renal replacement therapy suffer a failure or a dysfunction in creating the arteriovenous fistula – and this is a situation highlighted by a recent initiative Fistula First National Vascular Access Improvement Initiative, a program financed since 2003 to support the native vascular access, essential for an efficient dialysis. Differences in failure and complication rates between countries and even centers are notable [9, 10]. Every center’s experience is valuable and can provide new ideas to be added at the procedures used today. Therefore, before attempting in performing a permanent vascular access, it is highly important to understand the histopathology of AVF and pathophysiological mechanisms responsible for early and late associated failures.

Histopathology of arteriovenous fistula
In the last decades, there have been important improvements of hemodialyzed (HD) patients’ prognosis due to the possibility of vascular access development and performing dialysis using arteriovenous fistula (AVF). The burden problem of medical team is represented by early (within three months since the initiation moment [11, 12]) and late complications caused by AVF per se [11, 13–18]. According to DOQI (Disease Outcome Quality Initiative) recommendations, a suitable AVF presents the following features [11, 19]: flow >600 mL/min. and diameter >0.6 cm.

Although Fistula First National Vascular Access Improvement Initiative [2–4, 11] recommendations are to create as soon as possible a vascular access in end-stage
renal disease (ESRD) patients, there are studies suggesting that the rate of AVF failure is linked to early complications setting, especially in individuals presenting cardiovascular risk factors and an unsuitable vessel bed [11, 13].

It was observed that in 23–46% cases, AVF early failure develops [11, 14–17, 20] and the pattern lesion, noticed also in late complications, is vascular stenosis [11, 12, 21]. Additionally, there are still important questions regarding the pathophysiological mechanisms incriminated in AVF early failure setting [11]:

- neointimal hyperplasia – caused by increased levels of transforming growth factor β (TGF-β), insulin-like growth factor or other markers of oxidative stress [22, 23];
- significant vascular remodeling – induced by the presence of SMA+ve, vimentin+ve, desmin-ve myofibroblast [24] or abnormal changes of smooth muscle and endothelial cells [22, 24].

Furthermore, as different clinical and experimental trials concluded [11, 25–32], there is a clear association among blood stream, shear stress (frictional force exerted by blood on the vessel wall [11, 33]), transmural pressure [11, 34–36] and intimal thickening with direct impact on AVF failure development.

Summarizing, during AVF maturation period several mechanisms are involved [11]: elevated blood flow inducing increased shear stress on vessel wall, exacerbation of oxidative stress with direct impact on arterial and venous dilatation and high pressure of venous segment.

Therefore, for an adequate AVF, besides understanding pathophysiological mechanisms, it is also important to emphasize the possible risk factors incriminated in early or late vascular access failure [11]: older age, Caucasian race, female gender [37, 38]; diabetes mellitus and/or cardiovascular diseases [37, 38]; poor vessel quality – unsuitable preoperative venous distensibility or small-sized vessels (<1.6 mm for arterial diameter, <2.5 mm for veins) [39, 40]; genetic predisposition – the presence of increased methylene tetrahydrofolate reductase [41], TGF-β [42] and heme oxygenase-1 gene products [43]; abnormal hemodynamic profiles – imbalance between vascular dilatation and constriction (impaired shear stress and increased vessel constriction) [44–46], direct injuries caused by surgery per se [47–49] and also dialysis needles [50, 51], elevated proinflammatory markers (TGF-β, insulin-like growth factor, ICAM-1 – intercellular adhesion molecule-1 and MMP-9 – matrix metalloproteinase-9) [22, 52], and vascular remodeling and repair (endothelial dysfunction of HD patients) [53–63].

**Types of native arteriovenous fistula, complications and treatment**

After more than 50 years of practice, a pattern has been made to summarize the order of preference regarding the place and the technique for creating the native arteriovenous fistula [64–66]:

1. Radial-cephalic anastomosis at level 0, I or II – as previously presented, although radiocephalic AVF (snuff-box, Cimino–Brescia fistula or upper forearm AVF) represents the initial choice when creating a permanent vascular access [67–69], the incidence of early complications is still significant [70–73], mostly due to a preexisting atherosclerosis condition of radial artery translated as important intimal hyperplasia [71, 74, 75].

2. Brachial-cephalic transposition – usually, this type of AVF is performed in special conditions: elderly individuals presenting atherosclerotic lesions, diabetes mellitus, severe malnutrition, after the radio-cephalic fistula is compromised. According to international literature, steal syndrome and heart failure are responsible for AVF failure in this group of patients [76].

3. Brachial-basilic transposition – this type of vascular access must remain as an exception, reserved for difficult cases in which all the attempts to create a native fistula failed or they suffered occlusions/stenosis, or for patients in which the distal vascular capital is compromised from the beginning.

Summarizing, there is a milieu of AVF associated complications with direct impact on long-term prognosis of HD patients [77]: stenosis at the proximal venous limb (48%); thrombosis (9%); aneurysms (7%) [65]; infections; steal syndrome – caused by diabetes mellitus ± hypertension, hyperlipidemia or smoking history [78–84]; use of brachial artery [85, 86]; elderly population (age >60 years) [85]; female gender (67% incidence) [82, 86]; lupus [82]; hematoma; skin rash; red hand syndrome.

There have been several attempts to establish a correct therapy management in case of AVF complications setting:

- the use of systemic agents, but with controversial results and mechanisms not entirely understood (e.g., dipyridamole, fish oil, renin–angiotensin–aldosterone system blockers, Plavix, sirolimus, rosiglitazone) [87–97];
- experimental treatments – endothelial cell infusion [98,99], antiproliferative drugs [100];
- surgical interventions [101]: open surgery, surgical ligation (with poor results due to edema, thickening of the skin and high risk of bleeding), percutaneous endovascular intervention [102].

Although there is a wide range of treatment options for AVF failure resolution, prophylaxis is essential not only for preventing, but also for choosing the suitable anatomical segment for performing a vascular access. As previous trials have indicated B-mode high-resolution ultrasonography (using a 12.5 MHz transducer) may provide useful information and detect abnormal features of patients’ vessels [103–108].

**Conclusions and future perspectives**

Particular in Romania, as in all the countries without a high-developed renal transplant system, the importance of a stable and reliable chronic vascular access must be the key point of the management of the ESRD patient. Achieving an early-particularized vascular access for each patient in need of renal replacement therapy is the adequate solution for a better control of this pathology and prevention of AVF early and late complications. For this reason, an adequate AVF can be considered “the Achilles’ heel of hemodialysis” and a multidisciplinary approach is essential for creating and maintaining vascular access in optimal parameters.

**Conflict of interests**

The authors declare that they have no conflict of interests.
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**References**


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