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Immature hemodialysis arteriovenous fistulas: What should we aim for?

Rui F. Silva[1,2], Hugo Diniz[1,2], Miguel Relvas[1,2], José Silvano[1,2], Ana Malheiro[1,2], Luís Coentrão[1,2,3]

[1] Nephrology Department, Centro Hospitalar e Universitário de São João, Porto, Portugal
[2] Nephrology & Infectious Diseases R&D, i3S – Instituto de Investigação e Inovação em Saúde da Universidade do Porto, Porto, Portugal
[3] Faculty of Medicine, University of Porto, Porto, Portugal

ABSTRACT

Arteriovenous fistulas (AVFs) are the first-choice vascular access for most HD patients. Up to 60% of AVFs do not mature adequately, mostly due to stenosis. Surgical and endovascular techniques can rescue up to 80% of these AVFs from primary failure, allowing them to be safely and effectively used in HD, preserving venous capital, and avoiding placement of CVCs and associated complications. This article reviews and summarizes the existing literature, offering a practical approach on early identification, treatment, and monitoring of immature AVFs.

Key words: arteriovenous fistula, hemodialysis, angioplasty.

INTRODUCTION

Vascular access in hemodialysis (HD) is a sine qua non to treat patients, representing a lifeline. There are three main types of vascular access in hemodialysis – arteriovenous fistulas (AVFs), arteriovenous grafts (AVGs), and central venous catheters (CVCs). Compared to AVGs and CVCs, AVFs have lower complication and reintervention rates and longer cumulative patency. In addition, patients with AVFs have lower access-related hospitalization and mortality rates[1-3]. For these reasons, AVFs are deemed as the first-choice access for most patients who have suitable vessels and a long life-expectancy[4]. However, decisions regarding vascular access creation should always take into consideration the patient's overall End Stage Kidney Disease (ESKD) Life-Plan, which is a personalized strategy for living with ESKD, encompassing vascular access planning, ideally made together and periodically reviewed by the patient and a coordinated chronic kidney disease (CKD) management team. Attainment of the "right access, in the right patient, at the right time, for the right reasons" contrasts with "fistula first" policies as a more patient-centered approach to care[4,5].

AVFs result from an anastomosis between an artery and a vein, which can be created by open surgery or, more recently, percutaneous endovascular techniques. Once created, the arterialized vein goes through a maturation process where it acquires the necessary diameter and flow to be cannulated repeatedly, safely, providing an adequate HD treatment. Provided that all goes well, this process usually lasts 4 to 6 weeks[6]. However, 20 to 60% of newly created AVFs do not mature adequately to be used in HD – primary failure rate or non-maturation rate[7-10]. This largely relates to stenoses adjacent to the anastomosis or in the outflow tract and can be corrected by open surgical or percutaneous endovascular rescue techniques if identified in time[11]. Furthermore, excluding AVFs with primary failure, only 70% of AVFs are patent after one year without being submitted to an intervention to assist patency – primary patency or unassisted primary patency rate[7].

This article reviews and summarizes the existing literature, including recent guidelines, on early identification, treatment, and follow-up of immature AVFs, offering a practical approach to reducing primary failure rates, thrombosis, and to improving their overall longevity.

AVF MATURATION

Once an AVF is created, there is a reduction in vascular resistance which generates increased blood flow. The increased flow in turn results in augmented wall shear and circumferential stress, the hemodynamic forces driving both artery and vein remodeling. The endpoint of this process is referred to as AVF maturation, which can be characterized physiologically using criteria related to blood flow and vessel diameter[12] (Table I). Almost fifty percent of the AVF total flow increase was found to take place on the first day after the procedure[13] and full maturation in uneventful new AVFs is usually accomplished between the second and fourth week[14] – as such, cannulation is preferable after the fourth week[15]. However, if it will avoid placement of a central venous catheter, cannulation might be performed after the second week[15,16] without increasing the risk of AVF failure, according to an analysis from the DOPPS[17]. From the same study, only AVFs cannulated within 14 days were at increased risk of subsequent failure (2.1-fold)[17].

Physical examination by experienced staff may predict maturation in up to 80% of AVFs[14,18]. Equally, physical examination has great accuracy detecting underlying culprit lesions for non-maturation, such

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Table I

AVF maturation criteria[14,16,19,20]

Blood flow	≥ 500 to 600 mL/min
Diameter	≥ 4 to 6 mm
Depth	≤ 6 mm
Cannulation length	≥ 6 cm
Physical examination	Systolic and diastolic thrill, soft and compressible pulse, low rumbling pitch with a prominent diastolic component bruit, accessible to cannulation

as inflow or outflow stenosis[19]. Nonetheless, there is significant variability between dialysis staff and centers justifying the usual added use of objective and reproducible physical parameters (blood flow, vein diameter and depth) obtained by Doppler ultrasound, which is an accurate, noninvasive, inexpensive and diagnostic test (Table I). A 2002 University of Alabama study proposed a combination of blood flow ≥ 500mL/min and vein diameter ≥ 4mm for AVF maturation criteria, generally present after a month, which has a positive predictive value of 95% for adequate AVF utilization and, hence, maturation[14] (Table I). Subsequently, in 2006, the Kidney Diseases Outcomes Quality Initiative (KDOQI) clinical practice guideline proposed, based on expert opinions, a combination of blood flow ≥ 600 ml/min, vein diameter ≥ 6 mm and depth from the skin ≤ 6 mm – "rule of 6"[20] (Table I). More recently, in a study of CKD patients undergoing AVF creation, blood flow, vein diameter, and depth obtained by Doppler ultrasound, moderately predicted the likelihood of AVF maturation at six weeks[21].

Primary failure rates due to non-maturation has increased over the years, which is probably a result of demographic changes in hemodialysis patients from young to elderly, comorbid patients with cardiovascular disease, and diabetes mellitus as a major cause for renal failure[7]. This shift translates into calcified, noncompliant arteries, and sclerotic veins, resulting in inappropriate vascular remodeling, intimal hyperplasia, and failure to mature[22]. However, nearly all immature AVFs have a treatable underlying lesion, mostly stenosis, that can generally be identified and salvaged by surgical or endovascular techniques[23-25]. According to one study, 80% of these AVFs could be rescued, thereby producing an increase in the likelihood of maturation by approximately 50% comparing to immature AVFs not submitted to these treatments[25].

For these reasons, new AVFs maturation criteria should be assessed by physical and Doppler ultrasound examination 4 to 6 weeks after their creation, to identify immature AVFs' underlying problems and consequently program elective treatment[15,16,26]. According to our review of the literature, we propose a synthesized approach algorithm for newly created AVFs (see Figure 1). There are two degrees of AVF immaturity – physiological and/or clinical. An AVF is considered physiologically immature if it has low blood flow and/or a small vessel diameter, as measured by Doppler ultrasound. This is generally related to stenotic phenomena, which can be perceived by physical examination and/or Doppler ultrasound (Table II). Additionally, and despite physiological maturity, an AVF can only be considered fully mature if it is clinically accessible for safe, repeated cannulation, according to depth, location on patient's arm, and/or length. Deep (e.g. arm brachiobasilic AVF or obese patients) or posterior AVFs (e.g. forearm ulnar-basilic AVF) should be considered for surgical superficialization or transposition, whilst AVF stenosis compromising physiological maturity is an indication for surgical or endovascular treatment, depending on its location and available local resources[4,15,16].

IMMATURE AVFS RESCUE TECHNIQUES

There are no randomized clinical trials comparing surgical to endovascular techniques on the rescue of immature AVFs. Stenoses located on the afferent artery or on a vein segment other than the juxta-anastomotic region are usually treated endovascularly by percutaneous transluminal angioplasty (PTA), given its minimally invasive nature and safety[11,16]. Outcomes with PTA on afferent artery stenosis look particularly favorable, comparing to other locations (Table III)[27]. As for juxta-anastomotic venous stenosis (≤ 5cm from anastomosis), a narrative review of 28 non-randomized studies suggests a better primary patency rate with surgical revision, particularly with proximal neoanastomosis (PNA)[11] (Table III). A retrospective study comparing PNA to PTA in immature radial-cephalic AVFs juxta-anastomotic stenosis showed a better primary patency rate with the former (71% vs 41%), despite similar complication and secondary patency rates[28]. This data could point to surgical revision as the first line option for immature AVFs with juxta-anastomotic stenosis[16] – however, due to the lack of randomized clinical trials, this is still not consensual. According to

Table II

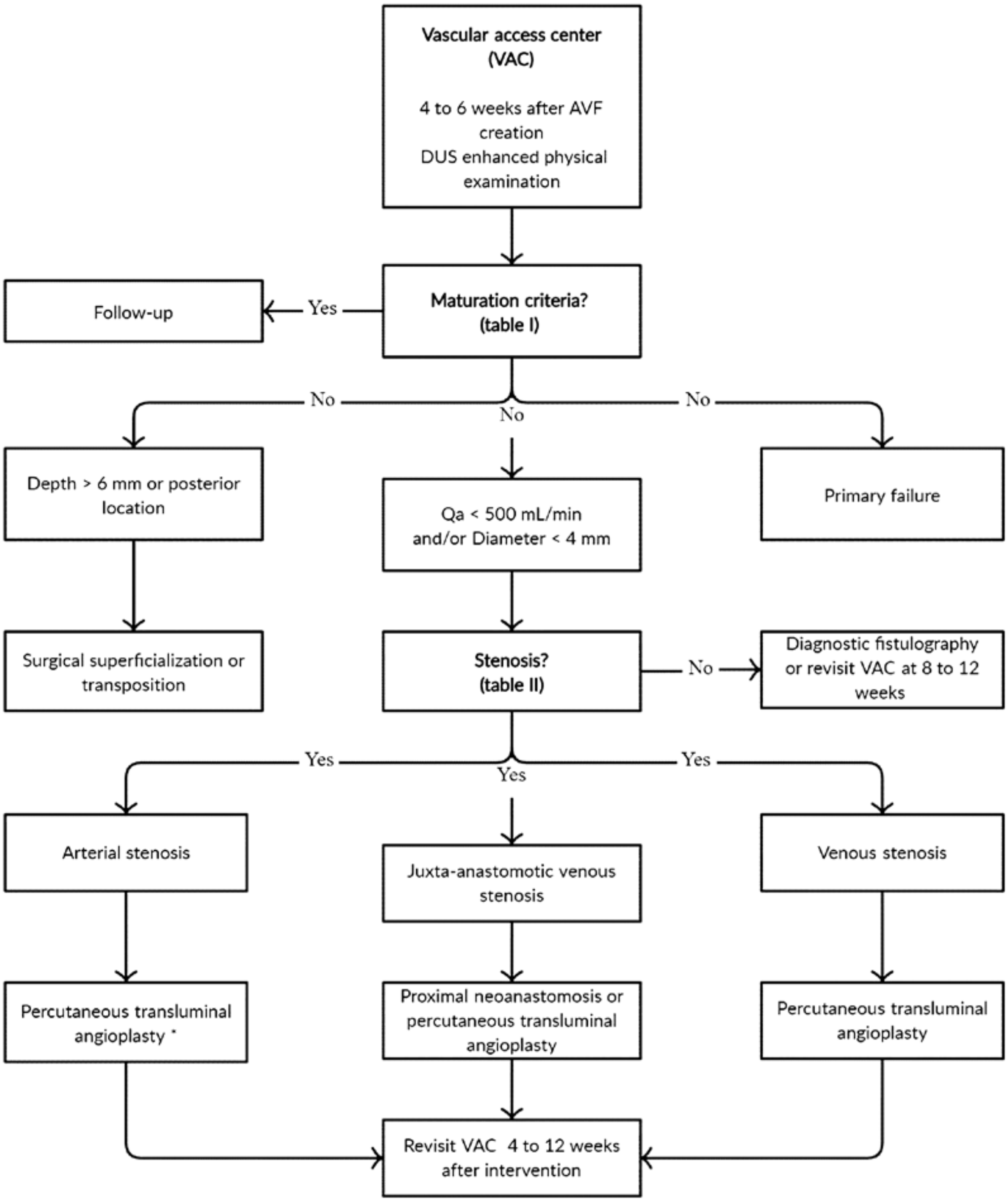
AVF stenosis criteria (considering immature AVFs)[16,19]

Stenosis location	Physical examination	Doppler ultrasound
Inflow (arterial or venous juxta-anastomotic)	• Flat on inspection after stenosis • Absent or weak thrill/pulse after stenosis (increased juxta-anastomotic pulse between artery and juxta-anastomotic stenosis) • Negative pulse augmentation test • Excessive collapse on arm elevation test	• Failure to attain a Qa ≥ 500 mL/min ***and*** • Reduction > 50% of the vessel lumen (morphological criteria) ***and*** *(at least one functional criteria)* • Ratio > 2 of the PSV between the stenosis area and the pre-stenotic area ***or*** • PSV > 400 cm/s in a non-anastomosis zone
Outflow (venous)	• Engorged on inspection between artery and venous stenosis • Systolic thrill (loss of diastolic component) • Strong water-hammer pulse between artery and venous stenosis • Absent drainage on arm elevation test	

PSV – peak systolic velocity; Qa – blood flow

Figure 1

Approach algorithm to recently created AVFs.



AVF – arteriovenous fistula; DUS – doppler ultrasound; Qa – blood flow. Primary failure – deemed surgically or endovascularly unsalvageable by the vascular access center team).
* Assuming no risk of provoking steal syndrome (hand hypoperfusion).

the 2019 guidelines from the European Renal Best Practice and KDOQI, there's insufficient evidence to support one over the other[4,15] (Table IV).

Meanwhile, the role of surgical or endovascular exclusion of accessory veins when rescuing immature AVFs remains to be elucidated, since these almost always coexist with stenosis, which should be treated first[11,29]. However, if this is not the case and manual compression of the accessory vein translates into enhanced blood flow through the AVF, it could be worthwhile to ligate surgically or endovascularly[30]. On the same note, there is currently insufficient data to recommend intraoperative maturation enhancement techniques (type of anesthesia, surgical technique, suture technique, anastomotic devices, intra-operatory angioplasty followed by balloon-assisted maturation), early (< 6 weeks) protocol-driven sequential balloon-assisted maturation or pharmacological interventions to improve AVF maturation rates[4].

Table III

Endovascular (PTA) and surgical (PNA) reported outcomes[15]

Technique	N studies	N patients	Success rate	1-year primary patency rate	1-year secondary patency rate
PTA – venous juxta-anastomotic stenosis/venous stenosis	14	657	43-97%	28-72%	68-97%
PTA – afferent artery	2	99	91-98%	65-83%	86-96%
PNA – venous juxta-anastomotic	2	71	90%	71-78%	87-95%

PTA – percutaneous transluminal angioplasty; PNA – proximal neoanastomosis

Table IV

Clinical guidelines and recommendations on AVF maturation procedures[4,15,26,16]

KDOQI 2019 | "KDOQI Clinical Practice Guideline For Vascular Access: 2019 update"

- There is inadequate evidence for KDOQI to make a recommendation on the preferred use of surgical or endovascular techniques for postoperative maturation. It is reasonable to consider a careful individualized approach to using either surgical techniques or endovascular techniques when needing to intervene on an AV access to enhance maturation postoperatively.

European Renal Best Practice 2019 | "Clinical practice guideline on peri- and postoperative care of arteriovenous fistulas and grafts for haemodialysis in adults"

- We suggest there is insufficient evidence to support open surgical over endovascular interventions as the preferred treatment for non-maturing arteriovenous fistulas in adults with end-stage kidney disease. (2D)

Advice for clinical practice:

- Decisions on how to treat non-maturing arteriovenous fistulas are likely best based on local resources, experience and success rates.
- Institutions likely benefit from building a dedicated multidisciplinary vascular access team, with clinical experience in various techniques available for non-maturing arteriovenous fistulas.

European Society for Vascular Surgery 2018 | "Vascular Access: 2018 Clinical Practice Guidelines of the European Society for Vascular Surgery"

- If an arteriovenous fistula fails to mature by 6 weeks, additional investigations (like duplex ultrasound) should be considered in order to achieve prompt diagnosis and treatment (2C).

Grupo Español Multidisciplinar del Acceso Vascular 2017 | "Spanish Clinical Guidelines on Vascular Access for Haemodialysis"

- We recommend a clinical check-up be performed at 4-6 weeks to definitively detect delay or absence of arteriovenous fistula maturation from its creation to this moment and elective treatment be proposed. We recommend confirming the suspected lack of maturation by Doppler Ultrasound.
- We suggest early treatment of the non-matured native arteriovenous fistula to favour maturation and to prevent thrombosis and definitive loss
- We recommend percutaneous or surgical techniques not be used systematically to promote maturation of native arteriovenous fistulae
- We suggest surgery as the first treatment option (proximal reanastomosis) in native arteriovenous fistulae with maturation failure associated with juxta-anastomotic stenosis. In cases where this is not possible, endovascular treatment (percutaneous angioplasty) should be proposed
- We suggest significant accessory veins associated with maturation failure be disconnected by percutaneous ligation, surgical ligation or endovascular embolisation with coils. We suggest endovascular treatment be used in the presence of stenosis and surgical treatment when there is no stenosis as the first option, given the lower complexity and healthcare costs
- We recommend angioplasty in cases of non-matured native arteriovenous fistulae with proximal venous stenosis
- We suggest angioplasty of the arterial stenosis when this is the cause of non-maturation of arteriovenous fistula, in cases in which the vascularization of the limb is not compromised

MONITORING AFTER MATURATION

AVFs submitted to more than one rescue intervention before maturation have a higher risk of thrombosis and permanent loss than AVFs that mature with one or no interventions. Furthermore, in these cases, more interventions are required to maintain long-term patency[31,32]. Follow-up surveillance programs of mature AVFs operate under the assumption that early identification and preemptive treatment of stenosis may prevent thrombosis and permanent access loss. Clinical monitoring through physical examination of the AVF by experienced staff has high sensitivity and specificity for the detection of AVF stenosis[19]. However, given AVF Qa-based surveillance's possible added benefit on the early identification of stenosis, reduction of thrombosis, and permanent access loss[33-36], periodic assessment by Doppler ultrasound in addition to clinical monitoring could be considered (especially, but not exclusively) on AVFs submitted to rescue interventions before maturation, due to their higher risk of thrombosis and permanent access loss. However, formal evidence-based recommendations for the latter strategy over clinical monitoring alone are lacking due to insufficient data[4,15].

Multidisciplinary care

To start and sustain HD with an adequately mature AVF depends on the work of multiple professionals – nephrologists, vascular surgeons, interventionalists, and nurses. In addition to an adequate referral timing for AVF construction, vascular mapping, and surgical experience, a good outcome is best attained by implementing protocolized programs for AVF follow-up, involving multidisciplinary participation[16]. These programs are probably most effective if there is: 1) consensus regarding procedures to identify AVF non-maturation, underlying problem, treatment, and follow-up; 2) close ongoing communication among all parties involved; 3) a dedicated vascular access coordinator who acts as a liaison between all services; 4) prospective tracking of outcomes with continuous quality assessment and improvement[37]. In Spain, the replacement of an isolated vascular surgery medical appointment by a joint nephrology and vascular surgery appointment with Doppler ultrasound and objective criteria for radial-cephalic AVF creation and AVF elective treatment resulted in an improvement of the primary failure rates[38].

CONCLUSION

AVFs are first-choice vascular access for most HD patients. Some AVFs do not mature adequately, mostly due to stenosis. Surgical and endovascular techniques can rescue an important percentage of these AVFs from primary failure, allowing them to be safely and effectively used in HD, preserving venous capital and avoiding the placement of CVCs and associated complications. Hospitals and HD clinics should aim to systematically evaluate AVFs four to six weeks after surgery to facilitate timely diagnosis of AVF non-maturation and subsequent orientation for elective treatment according to the underlying cause. These AVFs should then be periodically assessed for dysfunction to preemptively correct any reoccurring stenoses, ideally through multidisciplinary protocolized follow-up programs.

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ORCID

Rui F. Silva 0000-0003-4244-2459
Hugo Diniz 0000-0002-8476-1338
Miguel Relvas 0000-0002-2947-1610
José Silvano 0000-0002-5266-2300
Ana Malheiro 0000-0002-0860-4648
Luís Coentrão 0000-0003-1124-5073

Correspondence to:

Rui F. Silva, MD
Serviço de Nefrologia do Centro Hospitalar de São João
Alameda Prof. Hernâni Monteiro, 4200-319 Porto
E-mail: rui.fernando.o.silva@gmail.com