

Role of Doppler ultrasonography in the evaluation of hemodialysis arteriovenous access maturation and influencing factors

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Abstract

The goal of vascular access creation is to achieve a functioning arteriovenous fistula (AVF) or arteriovenous graft (AVG). An autologous fistula has been shown to be superior to AVG or to central venous catheters (CVCs) with lowest rate of re-intervention, but vessel obstruction or immaturity accounts for 20 % to 54% of cases with primary failure of AVF. This review is focused on the factors influencing maturation; indication and timing of preoperative mapping/creation of vascular access; ultrasound parameters for creation AVF/AVG; early postoperative complications following creation of a vascular access; ultrasound determinants of fistula maturation and endovascular intervention in vascular access with maturation failure. However, vascular accesses that fail to develop, have a high incidence of correctable abnormalities, and these need to be promptly recognized by ultrasonography and managed effectively if a high success rate is to be expected. We review approaches to promoting fistula maturation and duplex ultrasonography (DUS) of evaluating vascular access maturation.

Keywords

Hemodialysis, vascular access, arteriovenous fistula, maturation, ultrasound

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Introduction

The incidence of end-stage renal disease (ESRD) has substantially increased in the elderly population. Diabetes is the most common cause of ESRD, and accounts for up to 50 % of all cases. Regarding this population, various risk factors and concomitant disease are associated with maturation failure, dysfunction or loss of patency of vascular access. One of the primary determinants of successful vascular access is the preoperative planning process. Early failures of the access site can be minimized by careful preoperative choice of the inflow and outflow vessels. The most suitable vascular access option must be based on thorough assessment of the patient and on knowledgeable selection of the appropriate access technique as well as postoperative care.

Factors associated with maturation disorder

The creation of an AVF/AVG access is an important step and “lifeline” for patients with ESRD. Therefore, access

maturation and continued function are critical for these patients’ well-being. Predictive markers of a successful arteriovenous access maturation have been studied. Research studies of target factors affecting the maturation have failed

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to reach a consensus, because they focused on different aspects and used different definitions of maturation, study design, clinical factors, and patient samples.

There are natural factors (age and gender) that we are not able to influence. It is expected that elderly patients are at greater risk for diabetes and peripheral vascular disease. A meta-analysis of 13 cohort studies provided evidence and showed that elderly individuals with radiocephalic arteriovenous fistula (RC AVF) had a higher primary failure rate and decreased patency.¹ However, the definition of elderly in the included studies ranged from >50 to >70 years. Comparative studies have been conducted on the effect of the intima-media thickness of radial artery on early failure (due to loss of vascular elasticity, vessel luminal narrowing).² Higher intima-media thickness of the feeding artery was related to higher age and higher AVF maturation failure in this study.² Thus, the link between the degree of AVF success and age is unclear, and no definite conclusions can be made. There is a little specific evidence for AVF patency differences between genders: a meta-analysis indicated that 1-year patency level and maturation for RC AVF are similar for men and women.³

Previous research indicated that a higher rate of AVF maturation is influenced by lower body mass index (BMI), the absence of peripheral vascular disease, no smoking history, and lack of diabetes.¹ Multiple blood markers were involved in the functional maturation of AVF. The patients with thrombophilia are at elevated risk for primary patency failure. The patients with hypercoagulable states or combined thrombophilia should be preoperatively identified to tailor antithrombotic therapy and intensify surveillance.

In AVF, thrombosis is also influenced by inflammation, AVG obstruction is more frequently determined by hypoalbuminemia.⁴ It was revealed that, apart from being a sign of dietary deficiency in uremic patients, hypoalbuminemia is also a symptom of inflammation. The role of serum lipid profiles on AVF maturation is still debated. Kirkpantur et al.⁵ conducted a retrospective 3 years study to analyse the association between serum lipid and fistula thrombosis.⁶ The results showed that serum levels of cholesterol and triglycerides in patients with fistula thrombosis and those with functional fistulae were similar. A long-term study by Righetti et al.⁷ was carried out to analyse the effect of drugs on AVF patency. The study results showed improved fistula patency (71.5% vs 39.1%) at 2 years in patients taking folic acids and statins compared to those on no statin therapy. A systematic review was conducted to identify the influence of adjuvant antithrombotic and antiplatelet drug therapy on AVF and AVG patency rates in patients with ESRD.⁸ Results showed that antiplatelet drugs, including ticlopidine, aspirin and clopidogrel, had positive effects on access lifespan. However, most of the included trials had a short follow-up period, so the long-term safety concerns remain unanswered.

Doppler ultrasonography (DUS) enables early evaluation after access creation. Prognosis regarding the success of vascular access maturation is improved with help of DUS as we demonstrate below. Adequate planning and utilization of pre- and intraoperative ultrasound imaging help to plan the creation of successful vascular access.

Indications for arteriovenous fistula/graft creation and timing of preoperative mapping/creation arterio-venous fistula

The indication for the creation of both AVF and AVG is a certain need for beginning hemodialysis in the recent time period. Accordingly, starting hemodialysis on time, through matured and functional VA represents a successful outcome of chronic kidney disease (CKD) patients' treatment. However, in the real life this is not often a common scenario. Based on data from the DOPPS 5 study, high percentage of patients continue starting with hemodialysis (HD) via a central venous catheter (CVC).⁹ Between 71 and 81% of CKD patients in United Kingdom, Japan, Germany, Italy and Sweden, who have been seen by a nephrologist ≥ 4 months before HD start had pre-emptive AVF compared with 55% in US.⁹ These data confirm earlier allegations that the late referral is the most frequent factor that affects the percentage of CKD patients who will begin dialysis via matured AVF.^{10,11}

Timely referral and regular visits to a nephrologist over the time of CKD progression gives us enough time to assess the overall condition of the patient, and to anticipate the need for beginning the renal replacement therapy (RRT) taking into account the rate of decline of glomerular filtration rate (GFR), time required for preoperative preparation and access to vascular surgery as well as additional time for successful AVF maturation need to be taken into account.

The Initiating Dialysis Early and Late (IDEAL) randomized controlled trial showed no difference in survival or clinical outcomes between early (GFR > 10 ml/min per 1.73 m²) and late HD start (GFR < 10 ml/min per 1.73 m²).¹² Some authors also did not find any benefit from the early versus the late onset of dialysis in terms of morbidity, mortality and quality of life,^{13,14} especially in the elderly.¹⁵ It is clear that the IDEAL trial was supported by the current European and US guidelines^{16,17} stating that RRT should not be started until patients become symptomatic. In most patients, this will not happen before they reach the CKD stage 5. Once reaching CKD stage 5, further progression can be accelerated or steady, but in both cases it is the time to organize creation of the permanent vascular access. Among many proposed equations for prediction of CKD to ESRD Tangri's kidney failure risk equation proved to predict and separate those who would require RRT from those who did not,¹⁸ especially when it comes to the elderly,¹⁹

being additionally helpful in the process of patients prepare for RRT. Patients and health providers givers should be instructed to protect the cephalic and cubital veins from punctures and cannulations, especially on the non-dominant arm.

Preoperative mapping

DUS is a non-invasive, easily reproducible, safe, and cost-effective method that provide us valuable information on morphological and functional characteristics of the blood vessels.^{20,21} Obtained information enables us:

1. To assess anatomical possibility for vascular access creation (AVF as the first and AVG as the second choice according to the Guidelines);^{17,22–24}
2. To determine the optimal location of the future access (forearm or upper arm) and thus to try to reduce the risk of failure to mature.

According to the recently published European Society of Vascular Surgery Guideline on vascular access, preoperative DUS mapping is recommend to all patient planned for AVF/AVG based on the results of the randomized controlled studies and meta analyses giving the DUS strength of the recommendations class I and the highest level of evidence—A.^{22,25–27}

Arterial and venous cut-off values for the decision of the appropriate access

Ultrasound evaluation of arteriovenous fistula maturation should be performed with a baseline awareness of the vessel status prior to access operation. For the successful creation of autogenous radiocephalic fistula, a minimal internal radial artery diameter of 2 mm is suggested by the guidelines^{22,23} as supported by a systematic review²⁸ when standard vascular surgical technique are used. However successful fistula creations are feasible with even narrower lumen diameters down to 1.5 to 1.6 mm^{29,30} if the arterial vessel wall is predominantly healthy with a low burden of calcification and showing a satisfactory reduction of resistant index in response to reactive hyperemia.³¹ The latter is performed by a short-time (4–5 min) inflation of a sphygmomanometer cuff around the forearm. Excellent results have been obtained for AVF creation using smaller vessels in both adults and children using microsurgery and a tourniquet²² Similarly, internal diameter is recognized as a key parameter for assessment of venous suitability. Here an augmented (using a proximal tourniquet) minimal internal venous diameter of 2.0 mm is considered to be adequate.²² Additional parameters for venous suitability assessment are a proper position of the vein (including its depth), its distensibility above 0.35 to 0.4 mm with proximal tourniquet augmentation^{21,32} and a Doppler flow pattern with respiratory

variation and responsiveness to distal limb pressure. All measurements should be performed in a zoomed image and with adequate amount of the ultrasound gel to prevent compression by the ultrasound probe. For more proximal brachiocephalic and brachiobasilic fistulas previous EBPG document provided no definite guidance, while more recent ESVS guidelines suggest a minimal arterial and venous diameter of 3 mm.^{22,23} Again, adequate fistula creations are possible with venous diameters in the cubital region lower than this suggested minimal threshold, especially when there is absence of focal fibrotic stenosis of veins that usually arise from vein punctures in the elbow region. Moreover, up to 20% of subjects have high bifurcation of the brachial artery. For arteriovenous grafts a minimal target for outflow vein diameter at 4 mm is set however the level of evidence was not specified.²² For proximal fistulas and grafts we also lack data on the putative minimal diameters of brachial artery associated with a possible risk reduction of access related distal ischemia; however here the health of downstream forearm arteries may be equally important.

Early postoperative complications following the creation of a hemodialysis vascular access

Early postoperative complications comprise adverse events within 1 month after vascular access creation.³³ DUS plays an important role in this period. Early detection of an AVF/AVG with a low probability of maturation indicates the need for earlier intervention to enhance maturation or even replacement with new vascular access. Such approach decreases the duration of central venous catheter exposure and associated morbidity.³⁴

Thrombosis and failure to mature

Primary AVF failure is defined as an AVF that is never usable or fails within the first 3 months of its use. AVF/AVG with primary failure have a high incidence of correctable problems, once these problems are addressed, a high success rate can be expected. Non-maturation that may lead to early thrombosis affects almost always native AVFs.³⁵

The incidence of this complication varies between studies.^{36,37} Ravani and co-workers, for instance, reported that 11.9% of AVFs failed early.³⁶ Preoperative DUS examination should be obligatory to avoid unsuccessful attempts. Aside from vessel diameters and patency, preoperative DUS can provide a crucial information for maturation, such as vein distensibility.^{32,21} Insufficient flow in the feeding artery, impaired draining vein outflow, hypercoagulable state, hypotension, a technical error during surgery, small diameter of vessels used and external compression are some of the reasons of early vascular access thrombosis. Smaller vessel diameters and hypotension are the most

important factors affecting early thrombosis. Preoperative plasma expanders could be helpful in these circumstances.³⁸ At the end of the operation, palpable thrill is a good predictor of successful maturation. Intraoperative access blood flow (Qa) measurement provided by DUS also gives valid information of success prediction. Berman et al. have found a significant difference in maximal intraoperative Qa rates between functional (573.6 ± 103 mL/min) and non-functional (216.8 ± 35.8 mL/min) AVFs.³⁹ In the early postoperative course, Qa measurement 1 day after surgery could also predict successful maturation.⁴⁰ In the study of Ladenheim and colleagues, first week postoperative Qa was highly predictive of primary patency of radiocephalic AVFs.⁴¹ Robin et al. concluded that Qa measurement at 2 weeks after access creation were more predictive of 6-week diameter and Qa than the values 1 day after access creation.⁴² Concerning early thrombosis, the surgeon should decide whether to revise an existing vascular access (open surgical or endovascular) or to create a new one. Before revision and thrombectomy, the underlying cause(s) should be recognized and resolved. In the case of a small artery and/or vein diameter without possibility of adequate distension, it is advisable to create new vascular access on another (usually more proximal) site. During AVF maturation time routine DUS surveillance should be mandatory.⁴³

Incisional bleeding, hematoma and pseudoaneurysm

Chronic kidney disease patients are at the same time prothrombotic and prone to bleeding due to impaired coagulation.⁴⁴ To avoid or to minimize bleeding and hematoma formation, patients who have already started hemodialysis (HD) should not be operated on in the first 24 h after hemodialysis. This delay is recommended to allow platelet function recovery and elimination of heparin used to prevent blood clotting in the HD circuit. The use of antiplatelet drugs in the preoperative and postoperative period, as well as anticoagulation during surgery, remain controversial.⁴⁵ Serious incisional bleeding, large hematoma and pseudoaneurysm are rare and could be caused by a technical error during surgery. Disruption of anastomosis may occur in case of excessive blood pressure increase. For this reason, close intraoperative and postoperative monitoring of blood pressure is recommended. There are many reasons for hematoma formation after surgery: overuse of antiplatelet agents and/or anticoagulants, inadequate hemostasis at the end of the operation, uncontrolled arterial hypertension, hemorrhagic diathesis, and misdiagnosed outflow stenosis. Hematoma in the early postoperative period should be distinguished from a pseudoaneurysm (=non-clotted hematoma communicating with the vessel) which is caused by leakage at an anastomotic site. A pseudoaneurysm typically appears as an echolucent sac that is pulsatile in B-mode, with a swirling flow pattern using color Doppler (CD) study, and a characteristic “to-and-from” flow pattern on spectral waveform analysis in

the pseudoaneurysm neck.⁴⁶ In the event of serious bleeding, expanding hematoma or large pseudoaneurysm, surgical revision and hemostasis are obligatory. Small hematoma without vein compression confirmed by DUS could be managed conservatively. Pseudoaneurysms should be treated surgically because compression and thrombin instillation may cause access loss.

Infection, seroma and lymphatic collection

These complications have a low incidence (0.8%). The early postoperative period infections accounts for only 6% of all VA site infections.⁴⁷ Patients who have already started HD, patients with large incisional wounds and especially those with an arteriovenous graft insertion have a higher risk of infection.⁴⁸ In this group the usage of prophylactic antibiotic therapy at the time of vascular access creation seems reasonable. Wound dressings for surgical site infection prevention applied in the operating room act as a barrier to possible external bacterial contamination. In the case of dry wounds, the dressings could stay in place until the time of stitches removal. For each individual infection it is necessary to achieve the appropriate balance between medical and surgical treatment. The decision must be made based on the type of access involved and the severity of infection and primarily by an experienced vascular surgeon. Although VA infection is primarily diagnosed clinically DUS can provide an objective information on the extent of infected perivascular tissue and associated thrombosis. Seroma and lymphatic collection are rare, but may develop in larger incisional wounds and after graft insertion. Needle aspiration can be a diagnostic and curative measure. Surgical revision and graft removal is necessary in the case of infected fluid collections nonresponding to antibiotic therapy and aspirations.

Steal syndrome and ischemic monomelic neuropathy

Steal syndrome, commonly known as hemodialysis access-induced distal ischemia (HAIDI) or distal hypoperfusion ischemic syndrome (DHIS) or hand ischemia, refers to a process by which the arterial inflow to a vascular bed is diverted to AVF/AVG thus reducing inflow to the hand and resulting in ischemic symptoms. This disabling complication is rare in a distal vascular access (1–2%) and is more often (2–7%) in proximal localization and after graft insertion.⁴⁹ Ultrasonography is the first option in diagnosis of underlying causes and in some cases may replace angiography.⁵⁰ There are many procedures to preserve the access and to treat the ischemia. Access occlusion is a reasonable option in case of severe ischemia, as well as in case of severe acute cardiac decompensation following creation of a vascular access. Steal syndrome usually arises after dilatation of the artery and vein. In patients with arteries affected by atherosclerosis or medial calcinosis and insufficient circulation of

the hand (occlusion of one artery or severe stenosis), ischemic symptoms may appear in the first hours after surgery. Preoperative DUS may reveal individuals in danger of steal syndrome. Allen's test performed with duplex scanning is more objective in assessing blood flow in palmar arches than only physical examination.⁵¹ Ischemic monomelic neuropathy is the most devastating complication in angioaccess surgery. It usually arises immediately after proximal VA creation and is caused by inadequate vascularization of *vasa nervorum* after arterial clamping and/or stealing of arterial blood due to an arteriovenous anastomosis. Nerve conduction studies in patients with ischemic monomelic neuropathy show axonal loss and reduced motor and sensory nerve conduction velocities in the radial, ulnar, and median nerves. These findings develop acutely as a result of sudden ischemia of the nerve trunks. The ischemic event is often too brief to cause detectable skin or muscle ischemia. The weakness or paralysis of muscles in the hand and forearm caused by severe sensorimotor dysfunction of the nerve trunks is without critical hand ischemia. The ischemic monomelic neuropathy occurs in the absence of significant ischemia or necrosis to non-neurologic tissue in the extremity. The hand is usually warm and often a palpable radial pulse or audible Doppler signal is present. It is a clear indication to immediate occlusion of the access, although sometimes the damage is irreversible and only a partial recovery of nerve function ensues.⁵² Fortunately, this dramatic situation is rare. It is more often only present in diabetic patients, especially if they are women.

Maturation

Time from the AVF/AVG creation to the first cannulation is called maturation period and there are significant differences among countries regarding how long this period should be. According to the data from the DOPPS 5 study median time until first successful AVF cannulation was 10 days in Japan, 46 days in Europe/ANZ, and 82 days in United States; until first successful AVG use: 6, 24, and 29 days, respectively.⁵³ Recently published retrospective study by Wilmink and co-workers shows that early AVF puncture is not associated with its reduced survival, but the failure to achieve six consecutive successful cannulations from the onset of dialysis, and higher blood flow during the first week of dialysis.⁵⁴ These data further support the experience and recommendations of the Japanese guideline to vascular access,^{54,55} bearing in mind that this country has the highest percentage of AVF in both incidental and prevalent hemodialysis patients.⁵³

Definition of mature access— ultrasonographer's point of view

There are controversies regarding the ultrasound criteria defining a fistula as mature. Outflow vein wider than 4 mm

and allowing extracorporeal circuit/blood pump flow greater than 250 to 500 mL/min can be considered mature according to some authors.⁵⁶ Depending on the type of HD prescribed (i.e. three times a week or intermittent daily), blood pump flow rates vary between 100 and 500 mL/min. A well-functioning fistula should be capable to deliver flow necessary for adequate dialysis without significant recirculation. Thus, intra-access blood flow becomes one of the most important determinant of AVF/AVG maturation. The other attribute is good quality of cannulation segment (i.e. sufficient length and diameter, acceptable depth for ease of cannulation).

To deliver a flow 350 to 500 mL/min required for dialysis, the fistula blood flow should be at least 250 to 350 mL more than dialysis flow rate to prevent recirculation. Thus, minimum autologous fistula flow is 500 mL/min to prevent collapsing of cannulation segment during dialysis, minimum AVG flow is 600 mL/min. Most well-functioning fistulas have flow ranging between 800 and 1500 mL/min.

Cannulation segment is required straight, at least 10 cm long. If the outflow segment is tortuous, there should be two straight segments at least 4 cm in length. These conditions allow placement of two needles with their tips far enough apart to prevent recirculation.

Most AVGs have conventionally diameter 6 mm. The cannulation becomes difficult as the depth of vein exceeds 6 mm from the skin surface. Although none of these parameters are absolute, they can provide an objective guideline. The 2005 NKF-K/DOQI Guidelines for vascular access refer to these attributes as "The Rule of 6s", that is, 600 mL/min blood flow, 6 mm diameter, and 6 mm depth.⁵⁷

An implementation of DUS in preoperative vascular mapping has partaken in an improvement in AVF creation (i.e. increased the incidence of successful native fistula, a reduction of premature failure). The number of patients, who do not need to undergo preoperative ultrasound mapping is very small. The detection of anatomical abnormalities provides a useful information for planning proximal, as well as distal fistula. A high bifurcation of brachial artery (20–25% of patients) could lower distal artery output and therefore inflict longer maturation period. Knowing anatomical variations and vascular lesions, we can expect problems with fistula maturation. Vascular disorders, a modest stenosis of the radial artery (20–30%) without hemodynamical significance, may cause hemodynamic effect after creation of the anastomosis with the cephalic vein, resulting in failure of a vascular access or impairment of maturation.^{57,58}

Arteriovenous fistula maturation evaluation

The patient should be examined approximately 10 to 14 days after fistula creation. A careful clinical examination can identify infection and vascular or neurological

complications that can occasionally develop after the access surgery and endanger the fistula (see above). The second postoperative examination should be performed at 4 weeks; this evaluation includes a thorough clinical examination and DUS. During this examination the clinician can make a decision, whether the fistula is mature and ready for use or will need a procedure (surgical procedure or balloon angioplasty) to enhance its maturation. Depending on maturation at week 4, fistulas can be categorized into the following groups:⁵⁹

- *Mature AVFs*, fulfilling all objective maturation criteria: Qa > 600 mL/min, cannulation segment straight, at least 10 cm long or two straight segments at least 4 cm in length, > 6 mm in diameter, < 6 mm deep from skin surface.
- *AVFs are maturing well, but not meeting all maturation criteria* (i.e. borderline Qa 400 to 600 mL/min, inner diameter of outflow segment 4 to 6 mm, larger depth from skin surface 6–8 mm). In the absence of a specific correctable problem, these AVFs should be followed for another period of 4 weeks and then a reassessment should be made.
- *Blood flow is adequate, but AVF cannot be used*. AVFs may have a blood flow sufficient for dialysis, but the outflow veins do not meet maturation criteria and the fistula cannot be used. The outflow veins can be situated deeper from the skin surface, not ready to use despite they have adequate diameter. These patients profit from a secondary surgical procedure—vein superficialization or from ultrasound-guided punctures for hemodialysis. Some patients have branched outflow veins or outflow veins collateralizing due to a stenosis in the main outflow vein. These fistulas need mostly further evaluation (angiography) and secondary intervention to make them suitable for use.
- *Problems identified during clinical examination and/or DUS with an indication for surgical or radiological intervention in AVFs having blood flow greater than 400 mL/min*. The abnormalities such as outflow vein occlusion with inadequate collateralization or juxta-anastomotic stenosis or when a feeding artery has previously unrecognized proximal stenotic lesion could be present. Most of these complications can be treated by percutaneous transluminal angioplasty (PTA). In patients with remnant kidney function, after kidney transplantation or with allergy to iodine contrast agents, ultrasound-guided PTA is a safer option.

Some authors use the Robbin's ultrasound criteria for maturation, as the markers of adequate AVF.⁶⁰ The outflow vein size greater than 4 mm has 89% chance of successful use versus 44% if it is smaller in size. The fistula blood flow more than 500 mL/min has 84% chance of successful

use versus 43% if it is less. Combining these two criteria we meet 95% versus 33% success if the criteria are not fulfilled. Experienced hemodialysis nurses have an 80% accuracy in predicting the ultimate utility of a fistula for dialysis.⁶⁰ Comparison of postoperative ultrasound criteria at 6 and 12 weeks after creation to predict unassisted use of arteriovenous fistulas for hemodialysis was retrospectively analyzed in 205 patients in one study.⁶¹ Two ultrasound criteria were assessed: National Kidney Foundation Kidney Disease Outcome Quality Initiative criteria (NKF-KDOQI): AVF outflow vein lumen diameter ≥ 6 mm and blood flow ≥ 600 mL/min; and University of Alabama at Birmingham (UAB) criteria: vein lumen diameter ≥ 4 mm and blood flow ≥ 500 mL/min. Compared to the NKF-KDOQI criteria, the UAB criteria had unsurprisingly a higher sensitivity (89% vs 68%), but lower specificity (42% vs 70%) for unassisted AVF use. For radiocephalic AVFs, the UAB criteria had higher sensitivity (86% vs 46%) and lower specificity (58% vs 83%). For brachiocephalic AVFs, both UAB and NKF-KDOQI had high sensitivity (90% vs 80%) but low specificity (21% vs 53%), respectively. In the presence of good access flow, early problematic lesions can be easily missed solely by clinical examination. With the use of ultrasound postoperative evaluation, one can easily identify the problem.

Ultrasound evaluation of matured AVF /AVG

In many cases, clinical examination is considered to be sufficient for the assessment of vascular access function with reasonable degree of certainty. If an AVF is functioning well, a continuous thrill should be present near anastomosis, and it should be detectable for several centimeters over the outflow vein. Clinical examination, however, has several limitations. It is not reliable in situations in which the outflow veins are deeply situated and depends on the experience of the examiner. It is a useful tool to identify obstructive problems, but poor to evaluate the anatomic reason as well as compensatory mechanism. DUS has been repeatedly proven as an accurate, reproducible method for diagnosing access complications in comparison to access angiography.^{62–64} It is a simple, cheap and accurate method to visualize not only intraluminal, but also extraluminal processes and perivascular masses. There are no absolute contraindications to perform ultrasound examination, but there are some physical limitations that confine a complete DUS: open wound and recent surgery, indwelling catheters, severe edema, contractures and immobility etc. Regardless of whether an examination is requested for failure to mature or dysfunction in a previously usable hemodialysis access, the components of the ultrasonographic protocol of both AVFs and AVGs are analogous. DUS examination of vascular access should be accompanied by a request specifying clinical question and the diagnostic suspicion.

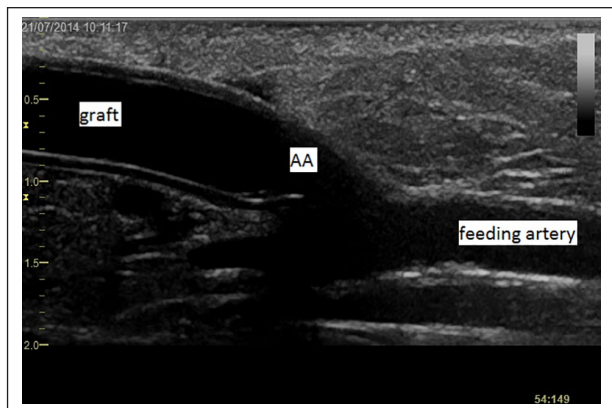


Figure 1. Residual diameter of the outflow vein stenosis. Longitudinal scan in B-mode of AVG with outflow vein stenosis due to excessive intimal hyperplasia. VA: venous anastomosis; L=0.15 cm = residual diameter of stenosis (arrow).

Ultrasound evaluation of native arteriovenous fistulas

DUS examination of an AVF should assess the longest possible part of the outflow vein and it usually follows the direction of the blood flow. Thus, it includes: study of proximal arterial inflow side of the fistula (including calculation of AVF blood flow), distal feeding artery, study of arterial anastomosis, study of venous outflow side of the fistula.

- **Feeding artery examination** begins in a proximal part of an arm, no matter if a brachial artery is a feeding artery or not. It is better to start with transversal scan in B-mode to identify brachial artery, its course and then its bifurcation into the radial and ulnar arteries. High bifurcation of the brachial artery or any other anatomical abnormalities or variety of caliber should not be missed. Proximal brachial bifurcation should be observed, for correct blood flow measurement. The artery supplying the anastomosis is commonly described as the “feeding artery” or “arterial inflow”. The feeding artery is usually dilated, displaying a thin two-layered wall. Color Doppler should depict homogeneously the arterial lumen (therefore the scale should be usually set wider). In the feeding artery of the vascular access, the spectral Doppler curve is physiologically low-resistant, with continuous antegrade flow. We continue by longitudinal scan and with the information of time average mean velocity (TAVM) and diameter of brachial artery we provide the calculation of flow rate (mL/min), corresponding to blood flow in the vascular access. The diameter of brachial artery can be measured in longitudinal scan, or by using M-mode to identify the average diameter in relation to the pulsatility. In

radiocephalic arteriovenous fistula (RC AVF) the (radial) feeding artery is examined from the bifurcation to the anastomosis. Forearm accesses almost uniformly receive flow from both radial and ulnar arteries. The reverse of the blood flow distal to the anastomosis could be easily visualized by the color Doppler mapping of the area of anastomosis by the inverse color. Special attention must be taken to identify possible stenosis of radial artery. The inflow stenosis is rare in a newly created AVF and present in only 5% of patients.⁶⁵ However, severe medial calcinosis limits the dilatation of the radial artery and also the diagnostic power of DUS. The palmar arches and the digital arteries are technically difficult to examine by DUS.

- **Anastomosis** is characterized by two terms: width of anastomosis (mm) and maximum peak systolic velocity (PSV, cm/s). The anastomosis is evaluated for hemodynamically significant stenosis using the diagnostic criteria defined: a peak systolic velocity ratio (PSR) of anastomosis greater than 3:1 compared with the feeding artery 2 cm upstream should suggest anastomotic stenosis. Some labs use a PSR greater than 3 when the absolute PSV is greater than 400 cm/sec at the anastomosis as the indication of stenosis.⁶⁶ Due to angle of insonation and turbulent flow, the quality of the measurement can be unreliable. Too narrow anastomosis is suspected especially if the brachial artery flow volume is low, there is a high-resistant spectral Doppler curve pattern and there is no outflow vein stenosis.
- **Outflow vein** must be examined with copious ultrasound gel and careful attention to avoid the pressure applied by transducer to exclude artificial pseudostenosis. Measurements include vein depth, minimal diameter and length of cannulation segment. We identify collateral vessels that can dissipate the blood flow, description should be based on the size and distance from the anastomosis. Extraluminal changes (hematoma, seroma, edema in the soft tissue) should be also recorded. In the peripheral native AVFs, juxta-anastomotic outflow vein stenosis is the most frequent cause of fistula failure.⁶⁷ This type of stenosis typically occurs in the outflow vein within 1 to 5 cm of the anastomosis. Cannulation segment stenoses are often short, they sometimes develop at the site of venous valves. Upper arm AVFs have other location of the most frequent stenoses. Lesions affecting the central veins are less frequent: in 6 to 8% (Table 1) and develop usually in patients with the history of ipsilateral subclavian vein catheter.

Some vascular access centers detect haemodynamically significant stenoses only by the combination of >50% lumen reduction and PSR >2. The presence of a

Table 1. Localization of stenoses in different types of arteriovenous fistulas.⁶⁸

Localization of stenosis	Feeding artery	Arterial anastomosis	Juxta-anastomotic stenosis	“between needles”	Proximal outflow vein	central vein system
Forearm AVF	8%	–	49%	19%	18%	8%
Upper arm AVF	–	–	17%	22%	55%	6%

AVF: arteriovenous fistula.

significant stenosis is associated with increased risk of thrombosis rate and PTA is the stenosis therapy for the first choice. Allon therefore mentioned in a review that aggressive referral for pre-emptive PTA would necessarily result in many superfluous interventions.⁶⁸ Stenoses after PTA develop faster than de novo access stenoses.⁶⁹ Unnecessary PTA could stimulate progression of stable stenotic lesions.^{70,71} The precise criteria of stenosis significance are therefore necessary for the benefit of ultrasound surveillance. The Spanish guidelines introduced a concept of significant stenosis in AVF with high risk of thrombosis²⁴ The main criteria are reduction of vascular lumen >50% + PSR >2 with at least one additional criterion (1. residual diameter <2 mm; 2. blood flow <500 mL/min in AVFs or <600 in AVGs; 3. reduction in blood flow >25% if blood flow <1000 mL/min). It is notable that the blood flow may fluctuate during a long-term follow period. AVF flow variation within 20% to 25% could be still physiological.⁷²

The failure to document velocity increase in the presence of lumen diameter reduction by B-mode imaging could occur in very low-flow AVFs—usually because of an inflow stenosis, but also due to dehydration. It is necessary to evaluate the stenosis complexly and indicate PTA procedure correctly, in appropriate timing. In case of clinical suspicion of central venous stenosis (dilated shoulder and thoracic subcutaneous venous collaterals, arm swelling, absence of any other etiology for access dysfunction, history of subclavian vein catheterization) central veins of the chest should be examined, although DUS has limitation in this area and some central stenoses may be missed.⁷³ The collapsibility of the subclavian vein during deeper inspiration practically excludes central vein stenosis.

Other complications of vascular access detectable by DUS include aneurysm or pseudoaneurysm formation. It is a rare case during maturation period, since a pseudoaneurysm usually occurs at the site of repeated punctures, at the anastomoses or after PTA due to prolonged bleeding. The definition of aneurysmal development in this setting is difficult, since the abnormal dilated vasculature is the aim of VA creation. Usually, aneurysms are considered in case of a dilatation featuring 1.5 to 2-fold wider than that of the non-dilated vessel.⁷⁴ The recent classification by Balaz et al.⁷⁵ presents four types according to the presence of stenosis and/or thrombosis.

Ultrasound examination of arteriovenous grafts

DUS examination of an AVG includes, on top on inflow artery and outflow vein evaluation, similar to AVFs, a description of the arterial anastomosis (AA) of the graft itself and of the venous anastomosis. The arterial anastomosis of AVG between artery and graft could have a typical narrowing constructed by the surgeon to prevent hand ischemia. The arterial anastomosis of the graft could have more Figure 1 variability in flow velocity relative to the upstream feeding artery than AVF.⁷⁶

- The study of a **graft** includes the average diameter of cannulation segment, its depth from the skin, its course, according to “The Rule of 6s”.⁵⁷ The degree of early AVG affection is indirectly related to lifespan, even defined risk factors (initial AVG blood flow <600 ml/min, mediocalcinosis of the feeding artery and early intimal hyperplasia) play a role.⁷⁷ In order to provide the best follow-up for the access maturation we describe any alteration in two different planes of scans as mentioned above (seroma, hematoma, lymphocele accumulation). Graft stenoses develop usually in the sites of frequent cannulations (area method instead of the preferred rope ladder method). For the quantification of a stenosis, we use the same criteria as mentioned in AVF examination. **Venous anastomosis** (VA) should be described routinely: diameter (mm), PSV (cm/s) and the height of intimal hyperplasia (mm) Figure 2. The venous anastomosis is the most common location of AVG stenosis (in 47% of cases) and the immediate proximal segment of outflow vein within 1 cm accounts for another 11%.⁶⁸ Figure 3 The grading stenosis severity relies again on internal diameter reduction, PSR and blood flow measurement. In case of an asymmetric stenosis, it is necessary to analyse the residual diameter or percentage of lumen reduction by transverse scan. A concept of significant stenosis with high risk of thrombosis includes a combination of morphological and haemodynamic criteria to prevent under-estimation or overestimation. This concept defines significant stenosis if there is a combination of >50% lumen

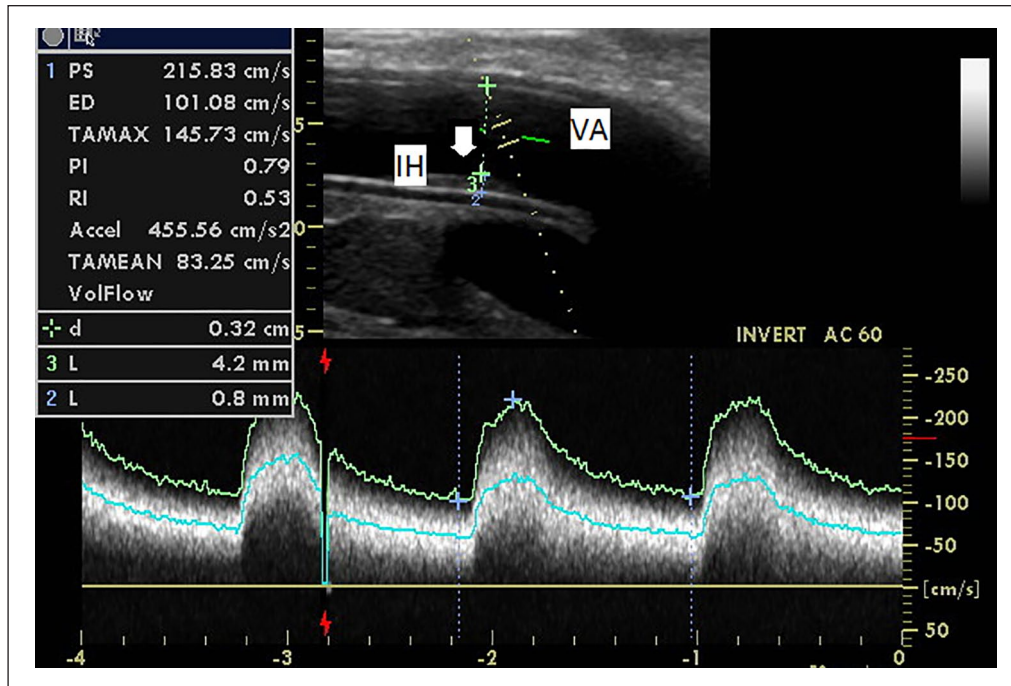


Figure 2. Venous anastomosis of AVG.

Longitudinal scan in B-mode of venous anastomosis of AVG with minimal intimal hyperplasia, which doesn't cause stenosis.

IH: intimal hyperplasia; VA: venous anastomosis; PS: peak systolic velocity; 2L = 0.8 mm = intimal hyperplasia; 3L = 4.2 mm = diameter of venous anastomosis.

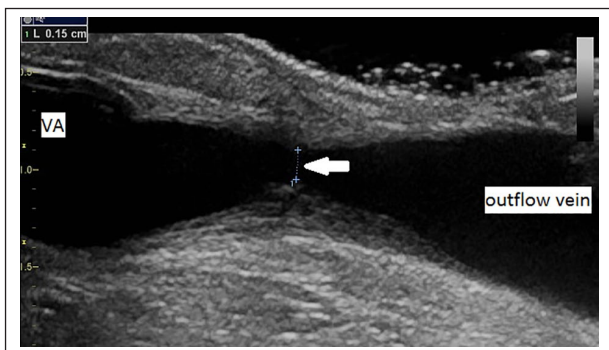


Figure 3. Residual diameter of the outflow vein stenosis.

Longitudinal scan in B-mode of AVG with outflow vein stenosis due to excessive intimal hyperplasia.

VA: venous anastomosis; L = 0.15 cm = residual diameter of stenosis (arrow)

reduction a PSR > 2, together with at least one of the following additional criteria: residual diameter <2mm and/or low blood flow <600mL/min or the blood flow reduction by >25%. Only these significant stenoses are referred to PTA. Stenosis is considered borderline in the absence of additional criteria and the patient is referred to DUS re-examination after 6 to 8 weeks. Within this period, the watch-and-wait strategy is maintained—that is direct referral to PTA in any (clinical or

ultrasound) suspicion of stenosis progression. Delaying PTA of borderline asymptomatic stenosis is safe using watch-and-wait strategy,⁶⁴ even in patients with the increased relative risk (female gender, previous PTA, blood flow <800 mL/min).

Ultrasound calculation of blood flow

The measurement of AVF/AVG flow volume (Qa) is one of the obligatory items of duplex Doppler ultrasonography.⁷⁸ This hemodynamical parameter is an important criterion of a significant stenosis.^{63,64} In each center, the DUS measurement of vascular access flow should be validated against a dilution method.

The calculation of the volume flow rate is based on the following equation:

$$QVA = \pi \times r^2 \times TAVM$$

where r is the vessel radius and TAVM is the time-averaged velocity integral of the mean velocity. The first part of equation ($\pi \times r^2$) is the calculation of the lumen area supposing it is circle shaped. The second part of the equation (TAVM) represents the mean velocity of blood flow through the blood vessel averaged over time (integral value). We do not use mean maximal velocity to calculate the volume flow because this would overestimate the access flow since it describes only the time course of the fastest (usually central) velocity layer.⁷⁹ The mean of

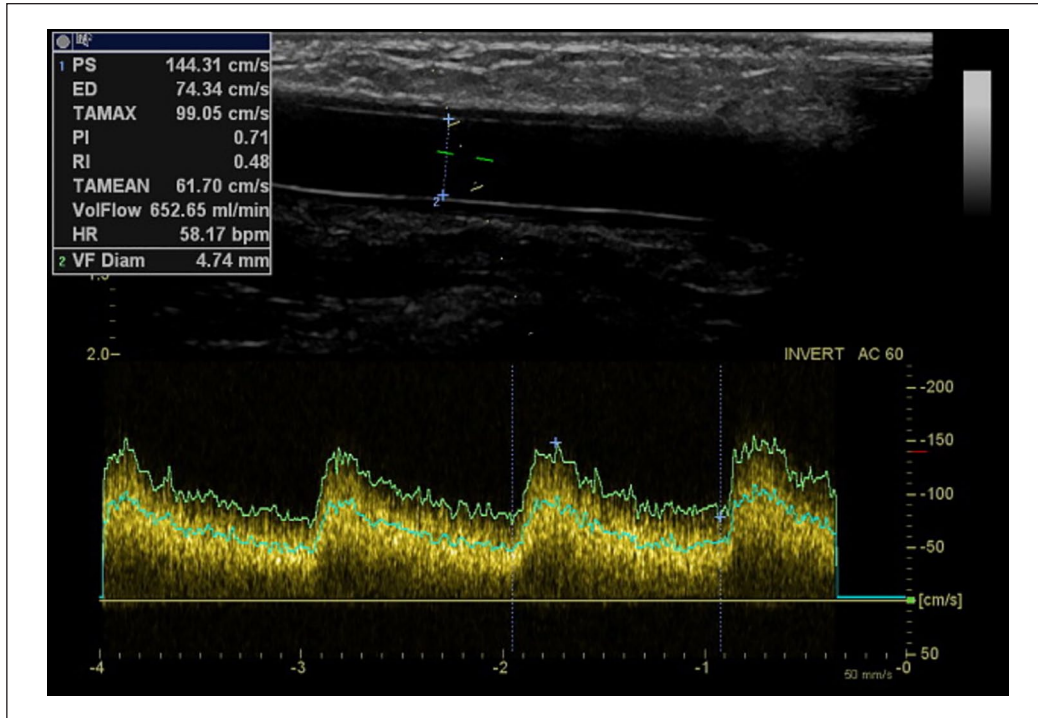


Figure 4. Calculation of arteriovenous access blood flow by DUS.

Blood flow measurement of AVG in graft is performed along longitudinal axis in the middle of the lumen, far from any stenosis or arch. Minimal variations in diameter translate into major variations in flow volume (indeed, the formula used to calculate flow volume entails squaring the vessel radius). The sample volume is oriented parallel to the direction of blood flow, positioned at the center of graft and the angle of insonation maintained at 60°.

three consecutive flow measurements should be reported, in case of arrhythmias at least five calculations are recommended.

In AVGs we measure the vascular access flow volume directly in the graft (Figure 4). The vascular access flow in native AVFs should be measured in brachial artery no matter which artery is a feeding artery of the vascular access. The distal AVF (i.e. RC AVF) is fed by both forearm arteries (radial and ulnar) via palmar arches, collateral circulation represents up 25% to 30% of flow.⁸⁰ We do not measure Q_a in an efferent vein, although the blood vessel is arterialized, due to easy compressibility of veins, variations in diameter and collateral veins. In presence of high brachial bifurcation, we measure both afferent arteries and count up values.

We avoid sites with turbulent flow that is anastomosis, stenosis, or dilation. These aforementioned irregularities should be at least 5 cm away from sample volume. DUS of hemodialysis access should be provided during interdialysis period, more than 24 h after the termination of a dialysis session. Shortly after dialysis, the ultrasonographer is limited by the presence of hemostatic tampons, there could be hemodynamic instability (hypotensive phenomena) and Q_a underestimated due to fall in plasma volume after ultrafiltration. Twenty-four hours after ultrafiltration, a further refilling of plasma volume is observed in most patients.⁸¹

Most common reasons of incorrect calculation the vascular access flow:

- Wrong settings of ultrasound machine (the angle of interrogation more than 60°, unsuitable sample volume)
- Unsuitable vascular site of calculation (nearby stenosis, anastomosis, dilatation or in a curvature)
- Ultrasound technique (vein compression by a probe)
- Hemodynamic instability (arrhythmia, tachycardia, hypotension)
- Wrong timing of DUS examination (less than 24 h after dialysis session)

Interventions in hemodialysis vascular access with maturation failure

An immature dialysis fistula that cannot be punctured during dialysis is difficult to access even by an interventional radiologist. Therefore, it is very useful first to perform angiography of AVF by puncture of the brachial artery in the cubital fossa. Cheung et al.⁸² have shown that postoperative stenosis of the outflow vein was associated with AVF maturation failure. Likewise, anastomosis and/or arterial stenosis can also cause a maturation

failure. Percutaneous transluminal balloon angioplasty could not be done without the puncture of the outflow vein and the introduction of a 4F- or 5F-wide sheath, which is especially tricky soon after access creation. In most patients, the intervention on an immature AVF can be performed under X-ray control, using a low dose iodinated contrast agent. In patients with residual diuresis, as well as in patients in pre-dialysis and in patients allergic to the contrast agent, the use of the iodine contrast agent should be avoided. Thanks to the superficial position of the vessels, ultrasound can be used to navigate the PTA. Some centers have extensive experience with ultrasound-guided PTA. Evidence of this is the work of Japanese authors, Wakabayashi et al.,⁸³ who published their experience with 4869 PTAs of dialysis fistula in 1011 patients. In most cases, stenosis was the indication for the procedure, where the authors report an early success rate of 97.1%. Of the total number of procedures, 455 were performed due to thrombosis, where the early success rate was 97.4%. The primary patency after a month was 94.4% for stenosis and 91.9% for thrombosis. Only 55 procedures were required for fluoroscopy with iodine contrast administration, and complications occurred in only 12 cases (0.2%).

Also other authors⁸⁴⁻⁸⁶ reported the implementation of the ultrasound-guided PTA. Gorin et al.⁸⁴ disclosed the performance of 55 procedures (48 because of maturation failure and 7 because of later stenosis) on AVFs in 30 patients. In 85% of patients with maturation failure of the arteriovenous fistula, a functional AVF was achieved. Ascher et al.⁸⁵ reported 32 procedures in 25 patients, with 27 procedures performed on an immature AVF, while 5 procedures on AVF failed.

Instead of an iodine contrast agent, carbon dioxide can also be used for angiography of the dialysis fistula.⁸⁷ According to Ehrman,⁸⁸ the use of CO₂ for vascular access angiography has a sensitivity of 94% and a specificity of 58%, compared to angiography of vascular access using an iodine contrast agent as the golden standard. The use of CO₂ is safe for i.v. administration, but arterial anastomosis cannot be visualized by the "reflux technique".

Advantages of ultrasound-guided procedures are as follows: (1) avoiding of ionizing radiation for patients and staff; (2) avoiding of nephrotoxicity of contrast agent, which is especially important in patients with residual diuresis, in pre-dialysis patients and in patients after kidney transplantation; (3) avoiding of anaphylactic reaction to iodine contrast agent; (4) possibility of immediate functional evaluation of the PTA effect and self-indication for PTA by blood flow measurement.

As with any method, there are some drawbacks to ultrasound navigation. A major disadvantage is the problem of ultrasound examination of the central vein from the subclavian vein to the superior vena cava, because of their placement behind the bones and the pulmonary

parenchyma.⁸⁹⁻⁹¹ Some authors⁸³ use a micro convex probe to visualize the subclavian and brachiocephalic veins and display these veins from a subclavian or intercostal approach. If central veins cannot be reliably examined by ultrasound and the central vein stenosis is highly suspect, the alternative is to perform CO₂ angiography, as mentioned above, or possibly magnetic resonance venography) of the central veins, as reported by some authors.⁹²⁻⁹⁵

Quality assessment of vascular access procedure for hemodialysis: Patency rate

Quality assessment in vascular access procedures for hemodialysis and quality indicators are not clearly defined in angioaccess surgery. A position paper of the Vascular Access Society, by Fila et al.⁹⁶ is based on the analysis of existing guidelines, trying to find out the recommendations for quality control in VA procedures, especially regarding the quality assessment of VA surgeons.

Some of possible measurable criteria could be as follows: specific education in VA surgery and license; number of procedures per year; the percentage of autologous fistula/AVG and CVCs in prevalent HD patients; primary patency, primary failure rate, maturation time et cetera.

Primary patency (intervention-free access survival) is defined as the interval from time of vascular access placement to any intervention to maintain or re-establish patency or to access thrombosis.

Primary functional patency refers to the useful duration of AVF/AVG function from initiation of successful dialysis at that site until the first intervention (surgical or endovascular).

Assisted primary patency (thrombosis-free access survival) is defined as the interval from time of vascular access placement to access thrombosis.

Secondary patency (access survival until abandonment) is defined as the interval from time of access placement to access abandonment, including intervention (surgical or endovascular).

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