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The Key Role of Color Doppler Ultrasound in the Work-up of Hemodialysis Vascular Access

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ABSTRACT

Vascular access (VA) is the lifeline for the hemodialysis patient and the native arterio-venous fistula (AVF) is the first-choice access. Among the different tests used in the VA domain, color Doppler ultrasound (CD-US) plays a key role in the clinical work-up. At the present time, three are the main fields of CD-US application: (i) evaluation of forearm arteries and veins in surgical planning; (ii) testing of AVF maturation; (iii) VA complications. Specifically, during the AVF maturation, CD-US allows to measure the diameter and flow volume in the brachial artery and calculate the peak systolic velocity (PSV) of the arterial axis, anastomosis and efferent vein, to detect critical stenosis. The borderline stenosis, revealed by the discrepancies between access flow rate and PSV, should be followed up with subsequent tests to detect progression of stenosis; the cases with significant changes in brachial flow should be referred to angiography. In conclusion, clinical monitoring remains the backbone of any VA program. CD-US is of utmost importance in a patient-centered VA evaluation, because it allows the appropriate management of all aspects of VA care. These are the main reasons why we strongly advocate the adoption of a VA surveillance program based on CD-US.

Duplex ultrasound scanning in the assessment of arterio-venous fistulas (AVFs) was suggested more than 25 years ago by Tordoir et al. (1). Subsequent studies have shown that ultrasonographic evaluation may have a key role in the evaluation of AVF maturity and adequacy for dialysis (2) and for a global dialysis access assessment (3). The development of digital technology in the 2000s has greatly improved the spatial resolution and sensitivity of color Doppler ultrasound (CD-US), making it more reliable, simple, and rapid in the analysis of Doppler parameters and blood flow rate. To date, CD-US is able to provide noninvasive and reproducible data on the morphology and flow dynamics in the arterial and venous limbs of an AVF in a short time (4). At the present time, three are the main fields of application of CD-US in the management of hemodialysis vascular access (VA): (i) planning of VA construction by evaluating veins and arteries of the upper arm; (ii) the AVF maturation period; (iii) VA complications.

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The Role of CD-US in Planning VA Construction

Early vascular surgical referral is recommended in stage 5 chronic kidney disease patients (5). In the routine practice, vessel suitability for the fistula placement is always determined by means of an accurate clinical examination. However, we have now adequate tools in the preoperative period to provide reliable information for the first access operation. CD-US may provide useful data on the preoperative morphological and functional characteristics of the vessels used for AVF construction. Vessel mapping has been highly encouraged and current international guidelines support the routine use of CD-US before AVF surgery (5,6). This had led to an increased use of CD-US examination of veins and arteries prior to access creation. The goal was to achieve satisfactory arterial inflow and a compliant outflow vein by selecting the optimal location of the arterio-venous anastomosis, especially in patients with diabetes mellitus, obesity, in the elderly, and in patients with compromised vasculature. Several anatomic parameters, including feeding artery internal diameter, resistance index, arterial blood flow before and after reactive hyperemia test, and internal diameter of the vein before and after proximal vein compression, have been proposed to evaluate vessel suitability (7). Presurgical evaluation of these parameters has made

possible a rising number of AVF constructions. Although vessel mapping has many potential benefits, there is still no evidence that presurgical evaluation leads to an increase in the primary patency of AVFs. Our opinion is that the gap between the value of preoperative evaluation and the missing maturation mainly depends on the experience of the vascular access surgeon (8). A very recent randomized controlled trial (RCT), comparing a selective and a routine policy of CD-US before AVF surgery, found no significant differences in primary patency and complication rates (9). On the contrary, another RCT supported the use of CD-US over physical examination alone (10). Finally, CD-US parameters may be relevant in the construction of a patient-specific hemodynamic computational model. This innovative approach may help the vascular access surgeon to plan the most appropriate fistula configuration to optimize access blood flow rate (Qa) for hemodialysis, potentially reducing the incidence of VA dysfunctions (11).

In conclusion, we think that CD-US preoperative evaluation represents a real advantage in patients who require complex procedures and in patients with risk factors for central vein stenosis or with previously failed access surgery.

The Role of CD-US in the AVF Maturation Period

VA maturation is a dynamic process characterized by the acute drop of the resistance and consequently an increase in the blood flow rate. Both conditions modify the hemodynamic wall shear stress and promote remodeling and blood vessel dilation (12). All the conditions that alter the inflow (atheroma and critical stenosis in the feeding artery, anastomotic problems) as well as the outflow (venous compliance, torsion, surgical traction, bridles, periadventitial fibrosis, and fibrotic valves) during the maturation period, predispose to AVF failure or complications. Therefore, the evaluation of AVF maturation should be the first step of any surveillance program (Table 1). The access flow measurement in the brachial artery has a prognostic value for adequate dialysis and the access patency, predicts AVF maturation, and/or the timing to intervene for stenosis (13). Assessment of AVF by CD-US may allow the clinician to visualize anatomy suitable for cannulation and verify a threshold volume flow adequate for dialysis. A blood flow greater than 600 ml/minute, a diameter greater than 0.6 cm, and a depth of approximately 0.6 cm (the rule of Sixties characteristics) have been recommended in the NKF-K/DOQI clinical practice guidelines for the AVF maturity (5).

In conclusion, CD-US can be considered a very important diagnostic tool together with physical examination in the maturation period, as it can help to check for AVF maturity parameters and to identify nonmatured AVFs (2,14).

TABLE 1. CD-US parameters in evaluating AVF maturation

CD-US parameters	Significance
Brachial artery • Diameter (Ø, mm) (B-Mode and TM-Mode) • Blood flow rate (ml/minute)	Direct hallmarks of successful maturation
Radial artery • Blood flow rate of distal stump (ml/minute)	Quantification of the reverse flow from the palmar arches
V/t curve of feeding artery (brachial, radial) and anastomotic tract • PSV and EDV (cm/s)	Rule out stenosis of inflow
Efferent vein • Diameter (Ø, mm) • PSV and EDV (cm/s)	Rule out stenosis of outflow

TM-Mode, time-motion mode; PSV, peak systolic velocity; *V*/*t*, velocity over time; EDV, end-diastolic velocity.

The Role of CD-US in VA Surveillance Programs

In evaluating the validity and usefulness of a surveillance strategy, it is useful to examine its four components by applying globally recognized criteria for screening tests according to the World Health Organization (WHO): (i) the undesired condition (the underlying natural history of stenosis leading to thrombosis and VA loss remains unclear); (ii) the screening test (Qa or the venous pressure measurement may not be accurate and reliable); (iii) the intervention (angioplasty and stenting: the benefits versus potential harm remain unclear); (iv) the outcome (the strong evidences from RCTs are lacking) (15).

According to some authors, an ideal program of noninvasive stenosis surveillance should fulfill three criteria: (i) the test should have a high positive predictive value for hemodynamically significant stenosis; (ii) it should be able to distinguish between stenosed VA destined to thrombose and those that will remain patent; (iii) preemptive angioplasty of stenosis detected by surveillance should reduce the likelihood of VA thrombosis (16). VA surveillance in the hemodialysis population remains a highly uncertain issue, mainly because RCTs published until now failed to give strong evidences and also because results have often been conflicting (17–19). In a recent meta-analysis, Tessitore and coworkers reviewed the available literature data and analyzed reproducibility, sensitivity, and positive predictive value of the surveillance methods checking for different Qa criteria (20). The study showed that Qa surveillance fulfills the WHO criteria for a screening test, and Qa measured with the ultrasound dilution method has a good reproducibility, with a within-session coefficient of variation of $5.5 \pm 3.8\%$ (21). The diagnostic performance of Qa measurements with the ultrasound dilution method is very accurate in detecting inflow stenoses located upstream the needling area, but not discriminative for outflow

stenoses located downstream from the needling area, which can be detected by physical examination and derived static venous pressure measurement (20). Therefore, Qa surveillance with the ultrasound dilution method becomes more sensitive when higher thresholds (Qa 600–700 ml/minute) are combined with a drop in Qa >25%, or when a Qa ranging between 750 and 900 ml/minute is associated with a positive physical examination (20). The validity of this screening strategy was tested by the same authors in a RCT, in which they enrolled patients bearing AVFs with stenoses which were identified by highly sensitive screening criteria and defined as subclinical stenosis (Qa <900 ml/minute and/or physical examination and/or high static venous pressure) (22). These AVFs were randomized either to elective stenosis repair or to intervention according to the NKF-K/DOQI clinical practice guidelines (a hemodynamically significant stenosis is when Qa <400–500 ml/minute) (5). It must be pointed out that, according to the latter guidelines, a functionally significant stenosis is defined as a decrease >50% of the normal vessel diameter, accompanied by hemodynamic or clinical abnormality (5). The study demonstrated that the adoption of highly sensitive criteria for stenosis and elective repair provided a significant three-fold lower risk of thrombosis and VA loss. The trade-off of this strategy implies 16–32% of unnecessary imaging procedures; however, according to the authors, this unwanted effect does not influence the beneficial effect of the strategy (20). The combination of physical examination, venous pressure, and access flow might provide a better indicator of the need for intervention and reduce the risk of AVF thrombosis and access loss (23).

Duplex ultrasound scanning in the assessment of AVF was suggested by Tordoir et al. in a study that compared ultrasound findings with digital subtraction angiography (1). The authors showed that, based on the determination of PSV in the spectral curve, the diagnosis of stenosis of the feeding artery, anastomotic tract, and the efferent vein was very reliable (sensitivity 95%; specificity 97%). Afterward, a prospective study conducted in 2792 hemodialysis patients showed that the most significant predictor of VA failure was the decreased Qa as measured by CD-US (24). Recently, Bandyk proposed a VA surveillance program based on an algorithm with diagnostic criteria and interpretation of several CD-US parameters (13). The author emphasized the role of the measurement of volume flow from brachial artery, which may have a prognostic significance for the dialytic adequacy and conduit patency. Indeed, Bandyk proposed a precannulation assessment in which, to evaluate AVF adequacy for hemodialysis, parameters such as Qa, PSV, and end-diastolic velocity (EDV) should be evaluated, and at the same time, complications as steal syndrome and venous central stenosis should be ruled out (13). Once the patient is on a regular dialysis program and the AVF is well functioning, then a surveillance program based on CD-US for the access dysfunction should be selectively performed for documented medical indications based on signs or symptoms of access dysfunction, inadequate dialysis, and cannulation difficulties. It offers the advantage of being a noninvasive bedside procedure with low costs and no need for radiocontrast agents. It should be kept in mind that the maintenance of high-quality performances of these methods requires trained vascular technicians (25) or nephrologists skilled in CD-US, with a substantial learning curve (26).

The definition and assessment of access stenosis is rather problematic when using CD-US. Very recently, complex criteria have been proposed to define a critical stenosis, and the concept of borderline stenosis has been introduced: they are the stenoses with a very low thrombosis risk and a good prognosis (Table 2) (26,27). Of note, the attempt of finding additional criteria for stenosis led to change indication of intervention from 50% to >70%, similar to the indications for coronary or peripheral arterial intervention (27).

The diagnosis of arterial critical stenosis is quite simple when using CD-US. It is based on the encoded criteria, as in the other arterial districts (PSV >250 cm/s, spectral dispersion, doubling of PSV compared to upstream).

More difficult is the diagnosis of venous outflow stenosis, which requires the combination of morphologic and functional criteria. B-Mode vein diameter measurement has several drawbacks: the neointimal hyperplasia is hypo- or anechoic, so it is not always evident, as well as venous valves and periadventitial fibrosis (28). Conversely, the segmental increase of PSV >400 cm/s associated with a flow rate reduction (Qa <600 ml/minute, or a decrease >25% from previous measurements) are valid criteria for significant stenosis. Both criteria are necessary to distinguish the true stenosis from borderline stenosis. If the flow rate in brachial artery is normal, the increase in PSV in the efferent vein has the meaning to support the continuity of blood flow downstream. If the flow rate diminishes while PSV increases in the efferent vein, this means that the stenosis is becoming critical (28). The diagnostic accuracy of CD-US compared with angiography for detection of >50% diameter-reducing stenosis is approximately 80% (13) with a pooled estimated sensitivity of 91% and positive predictive value of 98% (20). Other access abnormalities, such as aneurysms or false aneurysms, and

TABLE 2. CD-US criteria of hemodynamically significant stenosis

Main criteria	1. >50% diameter reduction
	2. >Two-fold increase of PSV
Additional criteria	1. Qa decrease by >25%
	2. Qa <600 ml/minute
	3. Residual diameter <2 mm

Stenoses without any additional criteria are called borderline (modified from ref. 26,27).

PSV, peak systolic velocity; Qa, access blood flow.

access-induced ischemia can be easily detected by CD-US. Indeed, several guidelines (5,6) emphasize the role of CD-US in the surveillance of VA. The NKF-K/DOQI clinical practice guideline 4 for VA (detection of access dysfunction) recommends as preferred the surveillance with CD-US in both AVF and arterio-venous graft. Furthermore, guideline 5 (treatment of fistula complication) states that CD-US is the preferred diagnostic method because it avoids any diagnostic cannulation of the newly created AVF and thereby avoids iatrogenic damage (5). Finally, guideline 3.2 (maturation and cannulation of fistulae) focuses on the rule of Sixies characteristics that clearly refers to CD-US measurements (5). However in the real world, things are different and the access to CD-US may be limited in some cases (20,29). Thus, the VA surveillance program may depend on the availability of special instruments and staff competence. Given the wide dissemination of surveillance tools integrated in the dialysis machines, the screening tests for VA assessment are mainly based on Qa measurement. Moreover, Qa measurement based on the ultrasound dilution technique (21) may require an increase in workload for dialysis staff, needs the interruption of dialysis treatment, and is costly. Also, Qa screening test based on the ultrasound dilution technique (21) may be unsuitable in the AVF with noncommunicating branches and is absolutely not applicable in the nonmature AVFs (20).

VA Surveillance: is it Time to Change Mind?

The ongoing controversy in VA surveillance and the risk of unwanted procedures associated with higher sensitivity criteria for diagnosis of stenosis prompted us to a more cautious attitude toward screening test programs, as the uncertain benefits of surveillance do not warrant the associated extra-costs and workload, as pointed out by one of the leading groups in the VA surveillance field (22). On the other hand, to some extent, Qa surveillance based on the ultrasound dilution technique (21) can be considered blinded with respect to stenosis location. On the contrary, CD-US method allows a detailed morphological and functional assessment, and the combination of these parameters offers the most complex stenosis examination available *in vivo* (27). Although angiography was considered the gold standard for VA dysfunction imaging, CD-US may be superior in some aspects as it provides information both on the morphology and function of VA (30). If it is true that no convincing evidences of the benefits related to the VA surveillance by CD-US are available, it is also true that, due to technology progress in devices and standardized measurements, we can expect a great benefit in relevant clinical aspects as the predialysis access care, the access maturation period, and the access complications. In the attempt to optimize VA care, training in ultrasonography should be *a must* in the curriculum of nephrologists, physicians, vascular surgeons, and dialysis nurses (27).

In conclusion, clinical monitoring remains the backbone of any VA program. CD-US is of utmost importance in a patient-centered VA evaluation, because it allows the appropriate management of all aspects of VA care. These are the main reasons why we strongly advocate the adoption of a VA surveillance program based on CD-US.

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