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A novel duplex ultrasound-based classification of outflow stenosis in native arterio-venous fistulas for hemodialysis

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Abstract

Background Stenoses of the outflow tract can compromise the function of arteriovenous fistulas (AVFs) used for haemodialysis. Limited data exists to differentiate stenosis types and understand their underlying causes. This study aims to develop a new classification system for AVF stenoses based on the morphology and location of the lesions as assessed by duplex ultrasound (DUS).

Materials and methods A multicenter, cross-sectional cohort study was conducted in four hospitals from October 2017 to February 2024. After exclusions, 1122 patients with dysfunctional AVFs were evaluated. The DUS variables studied were intimal-media thickness (IMT), venous valve calcifications (VVC), and stenosis location. The stenosis location was classified as follows: juxta/post anastomotic tract; middle tract; proximal tract; arm cephalic vein tract; cephalic arch; and arm basilic vein tract.

Results Intimal hyperplasia (corresponding to IMT ≥ 0.4 mm) was present in 718 AVFs (64%; 95% CI 0.61–0.67), with an average thickness of 0.72 ± 0.14 mm (95% CI 0.71–0.73); no intimal hyperplasia (corresponding to IMT < ≥≥0.4 mm) in 354 AVFs (32%; 95% CI 0.29–0.34), and valve calcification in 50 AVFs (4%; 95% CI 3–6). Stenoses were classified in 4 types: Type A, dominant IMT with thickness ≥ 0.6 mm; Type B, IMT 0.4 mm to 0.6 mm; Type C, IMT < 0.4 mm; and Type D, with calcifications of the venous valves. Most of the stenosis fell within Type A and C (79.5%). Type A stenosis was in 80% found in the juxta/post-anastomotic segments. The middle and proximal tract segments showed a similar distribution of all four types of stenosis. Type C and D stenosis were prevalent in the distal segments.

Conclusion DUS reveals distinct characteristics of AVF stenoses, suggesting different underlying causes. This classification system may facilitate the development of targeted interventions for preventing and treating AVF stenosis.

Clinical trial number Not applicable.

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Keywords Arterio-venous fistula, AVF, Ultrasound, Haemodialysis, Vascular access, Ultrasound, B-mode, Stenosis, Complications

Introduction

International guidelines endorse native arterio-venous fistulas (AVFs) as the optimal vascular access for haemodialysis (HD) [1], owing to their lower infection rates, reduced acute thrombosis, superior cost-effectiveness, and enhanced long-term patency compared with arterio-venous grafts and tunnelled dialysis catheters [2–4]. However, stenosis remains the most prevalent complication in AVFs, occurring both perioperatively and during long-term follow-up. Subclinical stenoses may even be present in patients with well-functioning AVFs [5]. Neointimal hyperplasia, observed in 55% to 75% of venous stenoses at the juxta-anastomotic region, is a significant contributor [6]. The aetiology of these stenoses is multifactorial, encompassing surgical trauma, blood flow dynamics, low shear forces at the arterial-venous junction, compliance mismatch, turbulence at collateral side branches, and uraemia [7]. Additionally, stenoses distal to the anastomosis in the outflow veins may arise from needle insertion trauma, thus generating aneurismatic dilatation, scarring and fibrosis, and venous valve calcification (VVC) [8]. Digital Subtraction Angiography remains the gold standard for determining the site and severity of stenoses, although it provides limited characterization of the stenosis. In contrast, Duplex ultrasound (DUS) is pivotal in vascular access surveillance strategies [9] and may guide angioplasty, serving as an alternative to conventional angiography [10]. DUS also offers potential in evaluating different stenosis types, the presence or absence of neointimal hyperplasia, puncture scarring, and compression of adjacent structures. Current international guidelines provide DUS criteria for stenosis severity, but there is a gap in knowledge regarding DUS's ability to differentiate the morphology and characteristics of stenosis linked to different aetiologies [11]. This study aims to bridge this gap by developing a novel classification system for AVF stenoses based on their morphological and topographical features identified through DUS.

Methods

Patient population

This multicentre cross-sectional cohort study was conducted across several tertiary general hospitals, including Cannizzaro Emergency Hospital, San Giuseppe Moscati Hospital, Pederzoli Hospital, and C. and G. Mazzoni Hospital, spanning from October 2017 to February 2024. All consecutive HD patients referred for DUS examination due to AVF dysfunction were enrolled. The study complied with institutional ethical guidelines and the 1964 Helsinki Declaration and its subsequent revisions. Informed consent was obtained from all participants. AVF dysfunction was diagnosed based on clinical and screening tests such as upper arm oedema, pain, difficult venipuncture, difficult haemostasis, and low Kt/V due to recirculation, assessed by Access Flow Monitor technology®, echo-colour-Doppler ultrasound, or Transonic®. Inclusion criteria included patients aged 18 or older, undergoing HD three times a week with a native AVF for at least six months, and exhibiting DUS evidence of hemodynamically significant stenosis. Hemodynamically significant stenosis was defined as a venous diameter reduction greater than 50%, a peak systolic velocity ratio between stenotic and pre-stenotic areas over 2, and/or an access blood flow reduction exceeding 25% from prior measurements. Exclusion criteria encompassed heart failure or arrhythmias, inability to maintain a stable position during ultrasound examination, vascular abnormalities such as bifurcation of the radial or ulnar artery from the axillary artery, surgical complications at AVF creation, congenital or acquired thrombophilia, a tortuous AVF outflow vein, and lack of informed consent.

Duplex ultrasound examination

Patients were examined in an outpatient setting before dialysis while in a supine position. The ultrasound equipment used included the Sequoia S3000™ (Acuson-Siemens, Mountain View, CA, USA), MyLabTM-Omega™ (Esaote, Genova, Italy), and Venue GO™ (GE Healthcare, Chicago, Illinois, USA). Linear array probes with frequencies of 4–9 MHz, 3–15 MHz, and 8–12 MHz were used as appropriate for the circumstance. DUS examinations were conducted by nephrologists with at least five years of experience in AVF imaging. During the examination, both the arterial and venous vascular axes of the arm were studied, with a particular focus on the venous axis in cases of stenosis. The following parameters were evaluated: intima-media thickness (IMT), measured as the distance between the blood-intima and media-adventitia interfaces using a longitudinal approach; VVC, defined by the presence of hyperechoic 'white' spots on the intimal and/or medial layer eventually accompanied by a posterior acoustic shadow, and the location of stenoses in relation to the arterio-venous anastomosis. The stenosis location was classified in: juxta/post anastomotic tract (involving the vein within 4 cm from the anastomosis), middle tract (adjacent to the juxta/post anastomotic region, but beyond 4 cm from the anastomosis), proximal tract (adjacent to the elbow, regardless of the type of vein used cephalic, cephalic median and basilic median), arm cephalic vein tract (the cephalic vein between the elbow

and the cephalic arch), cephalic arch (the central perpendicular portion of the cephalic vein, as it traverses the deltopectoral groove and joins the axillary vein), and arm basilic vein tract (the basilic vein between the medial side of the elbow and the origin of the axillary vein).

Statistical analysis

Data were entered into a common database. Continuous variables are presented as mean and standard deviation and categorical variables as cumulative results and proportions, with 95% Confidence Interval (95% CI). One-way ANOVA was conducted to compare the IMT among three types of stenosis, Type A, Type B, and Type C, with Tukey-Kramer post-hoc analysis for pairwise comparisons between groups. Fleiss's kappa for multiple readers was used to calculate agreement, on a sample of 30 cases read by three ultrasonographers [12]. Statistical analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA.).

Results

A total of 1925 patients were screened, with 803 (41.7%) excluded for various reasons: severe atherosclerotic artery disease of the inflow (257; 13.4%), arrhythmias (241; 12.5%), involuntary tremor or inability to cooperate (46; 2.4%), tortuous vein course (91; 4.7%), lack of informed consent (19; 1%), and others (149; 7.7%) (Fig. 1). Consequently, 1122 patients were included in the study. Demographic data and comorbidities are detailed in Table 1, while Table 2 outlines the types of AVFs and anastomosis. Among these patients, 895 (80%) had a primary AVF, with no prior surgical revisions or angioplasty performed on the AVF evaluated. The average longevity of the AVFs was 2.4 ± 1.7 years. Specifically, 203 patients (18%) had AVFs lasting less than one year, 637 patients (57%) one to three years, and 282 patients (25%) more than three years. Inter-rater agreement for DUS results was good (k = 0.67), as per the empirical evaluation of Landis & Koch [13]. Significant intimal hyperplasia (corresponding to IMT ≥ 0.4 mm) was found in 718 AVFs (64%; 95% CI 0.61–0.67), with an average thickness of 0.72 ± 0.14 mm (95% CI 0.71–0.73); no intimal hyperplasia (corresponding to IMT < 0.4 mm) in 354 AVFs

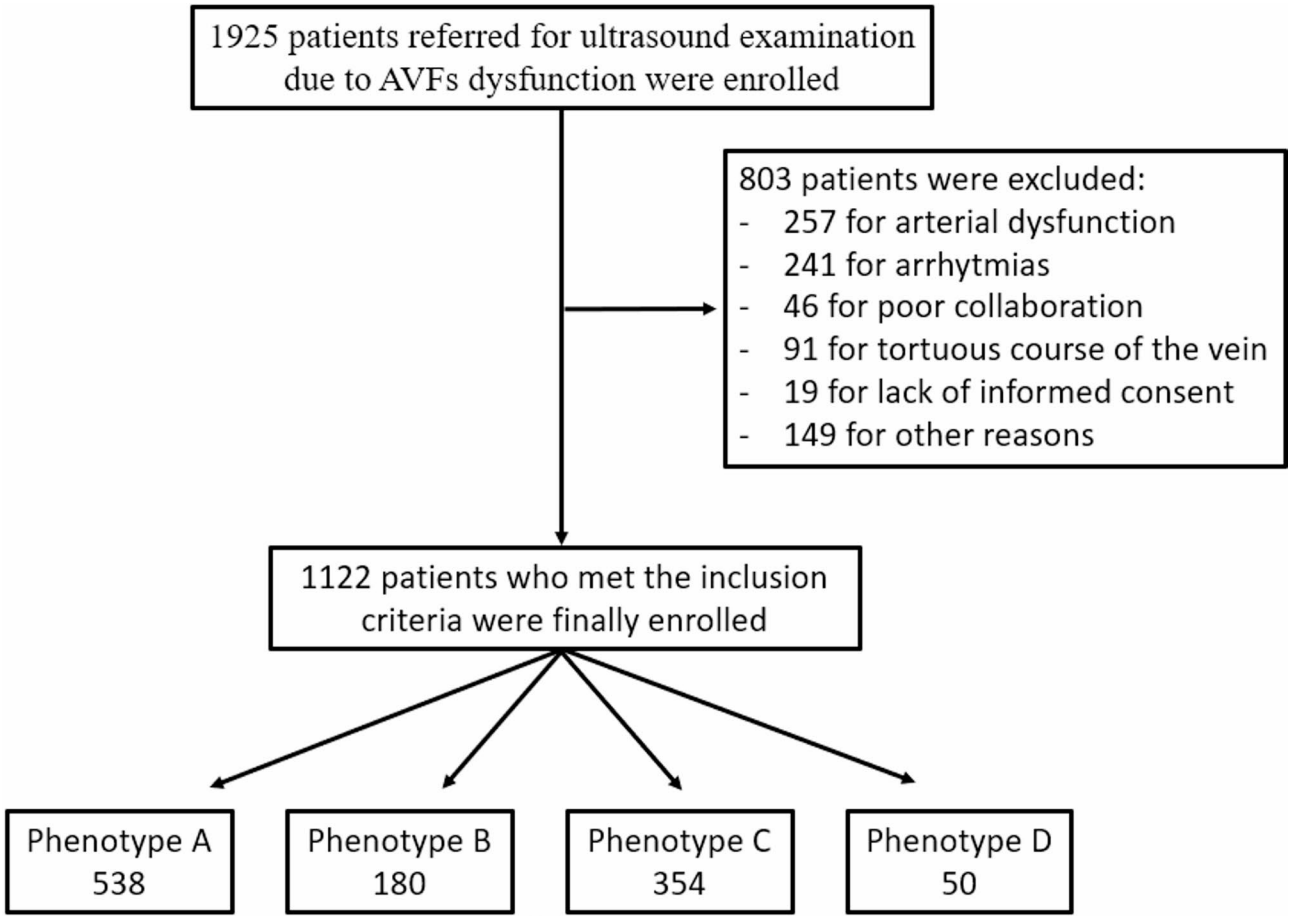

Fig. 1 study flow diagram

Table 1 Patients demographics and comorbidities

TOTAL (*N* = 1122)	*N* (%)
Age, 64.7 ± 14.3 y	
Male sex	658 (58.6)
Primary diseases	
Chronic glomerulonephritis	138 (12.3)
Chronic tubulointerstitial nephritis	86 (7.6)
Ischemic nephropathy	74 (6.6)
Inherited nephropathy	102 (9)
Other	149 (13.2)
Unknown	165 (14.7)
Comorbidities	
Hypertension	945 (84.2)
Diabetes Mellitus type 1 and 2	239 (21.3)
Atherosclerotic nephropathy	154 (13.7)
Other	16 (1.4)
Patients on antiplatelet therapy	947 (84.4)

Table 2 Type of vascular access

	N (%)
Left arm	974 (86.8)
Type of anastomosis	
Side to side	506 (45.1)
Artery side to vein end	613 (54.6)
End to end	3 (0.3)
Type of AFVs	
Distal radio-cephalic fistula	442 (39.3)
Mid-arm radio-cephalic fistula	392 (35)
Proximal radio-cephalic fistula	123 (11)
Brachial-cephalic fistula %	72 (6.4)
Brachial-basilic fistula	86 (7.7)
Ulnar-cephalic distal fistula and other	7 (0.6)

(32%; 95% CI 0.29–0.34); and VVC in 50 AVFs (4%; 95% CI 3–6). Based on these findings and the variable IMT, stenoses were classified into four types: Type A (dominant intimal hyperplasia) IMT ≥ 0.6 mm (Fig. 2); Type B (intermediate intimal hyperplasia) IMT ≥ 0.4 mm but ≤ 0.6 mm (Fig. 3); Type C (minimal intimal hyperplasia) IMT < 0.4 mm (Fig. 4); and Type D (VVC) (Fig. 5). Table 3 stratifies the four types of stenosis according to AVFs, while Table 4 details the types of stenosis by AVF type and lesion site. Out of 1122 AVFs examined, the distribution was as follows: 442 distal radio-cephalic (39.4%), 392 middle-arm radio-cephalic (35%), 123 proximal radio-cephalic (11%), 72 brachial-cephalic (6.4%), 86 brachial-basilic (7.6%), and 7 ulnar-cephalic distal and others (0.6%). The distribution of stenosis types was: Type A 538 (48%; 95% CI 45–50), Type B 180 (16%; 95% CI 14–18), Type C 354 (32%; 95% CI 29–34), and Type D 50 (4%; 95% CI 3–6). The mean IMT for Type A stenosis was 0.76 ± 0.14 mm (N = 538), for Type B 0.46 ± 0.07 mm (N = 180), and for Type C 0.24 ± 0.03 mm (N = 354). There was a statistically significant difference in IMT among the three groups (F [df 2, 2143] = 128, p = 0.001). Post hoc analysis indicated that the mean IMT for each type of stenosis was significantly different from the others (p < 0.01). These results suggest that the thickness of IMT significantly discriminated the three groups, with Type A stenosis showing the highest mean of IMT and Type C stenosis the lowest. Among the 477 juxta/post anastomotic segments there were 350 type A (73%, 95% CI 69–77), 29 type B (6%, 95% CI 4–9), 98 type C (21%, 95% CI 17–24) and no type D lesions. Among the 141 middle tract segments there were 57 type A (40%, 95%CI 32–49), 28 type B (20%, 95% CI 14–27), 49 type C (35%, 95% CI

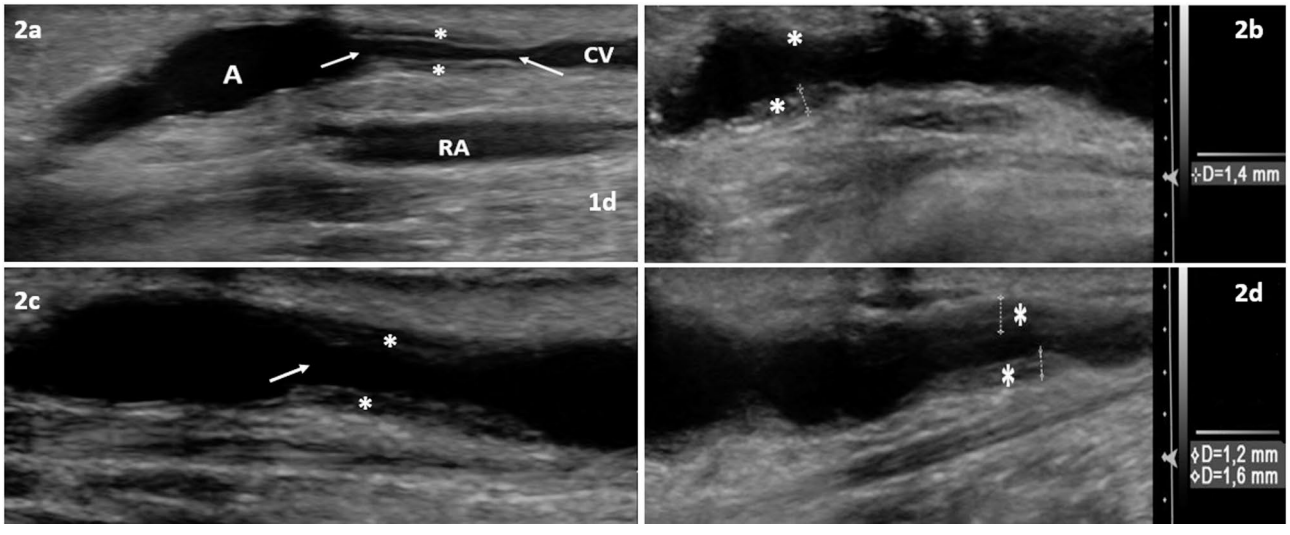

Fig. 2 type A stenosis: 2**a**) juxta-anastomotic region of a distal radio-cephalic fistula; 2**b**) proximal tract of a mid-arm radio-cephalic fistula; 2**c**) post-anastomotic tract of a brachial-cephalic fistula; 2**d**) juxta-anastomotic region of a mid-arm radio-cephalic fistula. A: anastomosis; RA: radial artery; CV: cephalic vein; arrows: stenotic tract; *: neo-intimal hyperplasia

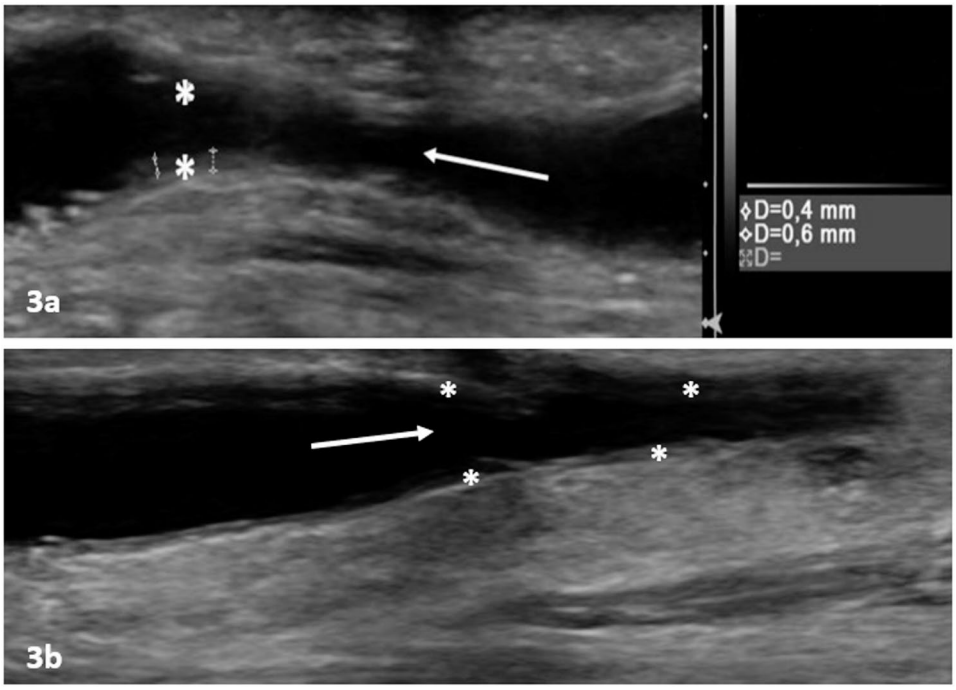

Fig. 3 type B stenosis: 3**a**) basilic tract of a proximal radio-cephalic fistula; 3**b**) cephalic arch of a mid-arm radio-cephalic fistula. Note the presence of stenosis with modest neo-intimal hyperplasia. CV: cephalic vein; *: neo-intimal hyperplasia; arrows: stenotic tract

27–43), and 7 (5%, 95% CI2-10) type D lesions. In the 223 proximal tract segments there were 86 type A (39%, 9%% CI 32–45), 56 type B (25%, 95%CI 20–31), 80 type C (36%, 95%CI 30–43) and 1 type D lesions (0.4%, 95% CI 0.01–2.5). Among the 140 arm cephalic vein tract/cephalic arch segments there were 16 type A (11%, 95% CI 7–18), 26 type B (19%, 95%CI13-26), 81 type C (58%, 95% CI 49–66) and 17 type D lesions (12%, 95% CI 7–19). In the 141 arm basilic vein tract there were 29 type A (21%, 95% CI 14–28), 41 type B (29%, 95% CI 22–37), 46 type C (33%, 95% CI 25–41) and 25 type D lesions (18%, 95% CI 12–25). The sub-group analysis confronting AVFs with prior endovascular or surgical intervention to AVFs without prior intervention did not evidence significant differences between stenosis location and type.

Discussion

Modern DUS diagnostic techniques enable a more detailed definition of the characteristics of vascular stenoses and their topographic localization. Our study demonstrates the potential of DUS for detailed characterization of AVF stenosis morphology and localization. We propose a new classification system based on these features, identifying four distinct stenosis types (A-D) with varying prevalence depending on their location relative to the anastomosis. This classification highlights the possible link between stenosis morphology and underlying pathophysiology and might have the potential to guide different interventions according to distinct types of lesions. Stenoses associated with AVFs exhibit variable representation of IMT and/or VVC depending on the location of stenoses. Most of the stenosis fell within Type A and C (79.5%, Table 3). The prevalence reaches 73% in the juxta/post-anastomotic segments for Type A. Moving further away from the AVF anastomosis, the prevalence of Type A decreases, whereas of Type C and D increases progressively. The DUS type and location of the stenosis may reflect different pathophysiological mechanisms: intimal hyperplasia, expressed as increased IMT, in the venous tract of the juxta-anastomotic areas suggests that the cause may be found in sudden decreases in vascular resistance, changes in vessel geometry, turbulent flow, and unfavourable local anatomy. Type C and D lesions, found predominantly distal to the anastomotic region, may represent the expression of traumatic damage caused by needle insertion for dialysis or media/perivascular fibrosis and vessel calcification.

From an opposite point of view about 20% of the stenosis in the juxta/post-anastomotic segments cannot be explained only by intima-media thickening, respectively 40% in the middle tract segments, 36% in the proximal tract segments, 70% in the arm cephalic vein tract/cephalic arch segments and 50% in the arm basilic vein tract. That means that other causes of stenosis than intima-media thickening have to be analysed and discussed. This fact is supported by the histologic analysis of stenotic versus non-stenotic venous segments in 2-stage arterialized vein transposition interventions of proximal upper arm AVFs

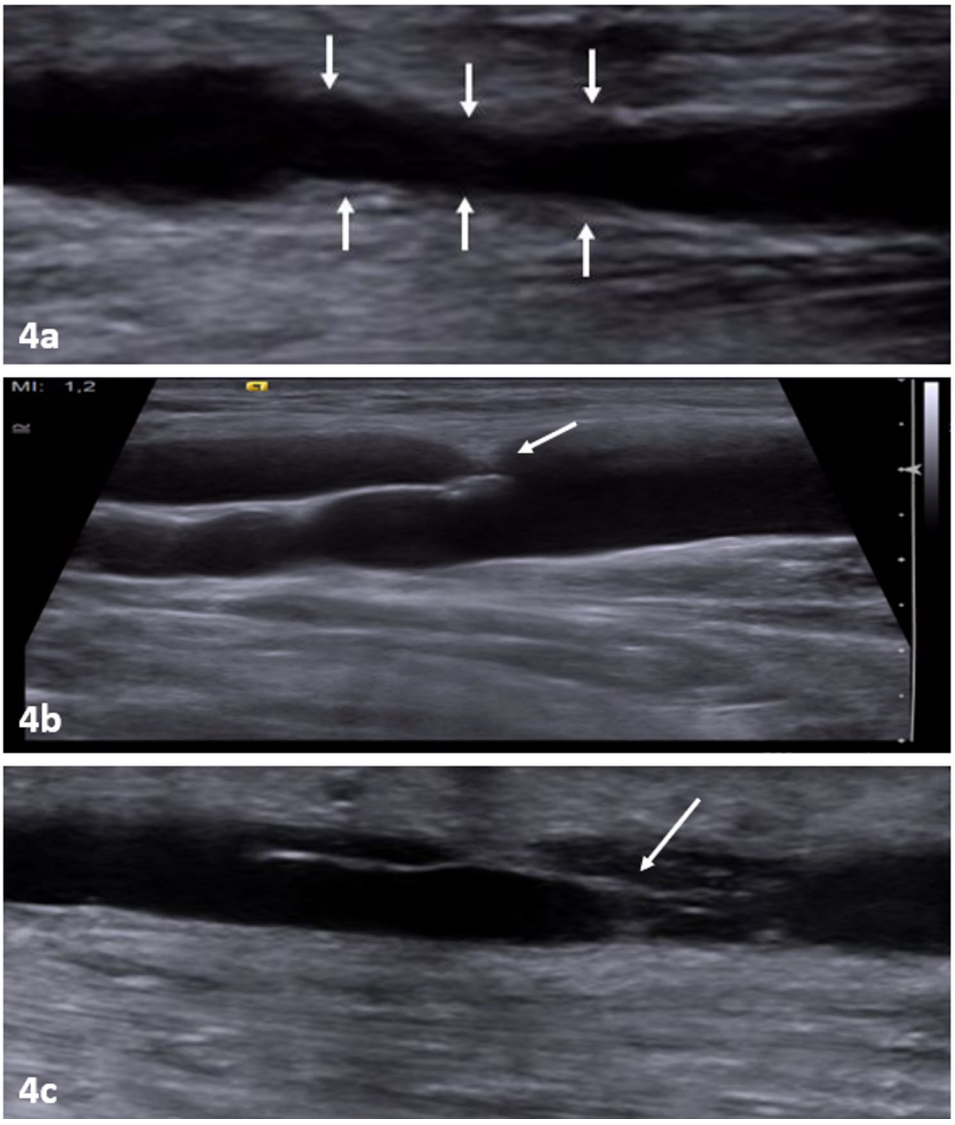

Fig. 4 type C stenosis: 4**a**) forearm tract of a mid-arm radio-cephalic fistula; 4**b**) cephalic arch of a proximal brachial-cephalic fistula; 4**c**) traumatic stenosis due to vessel dissection. Arrows: stenotic tract

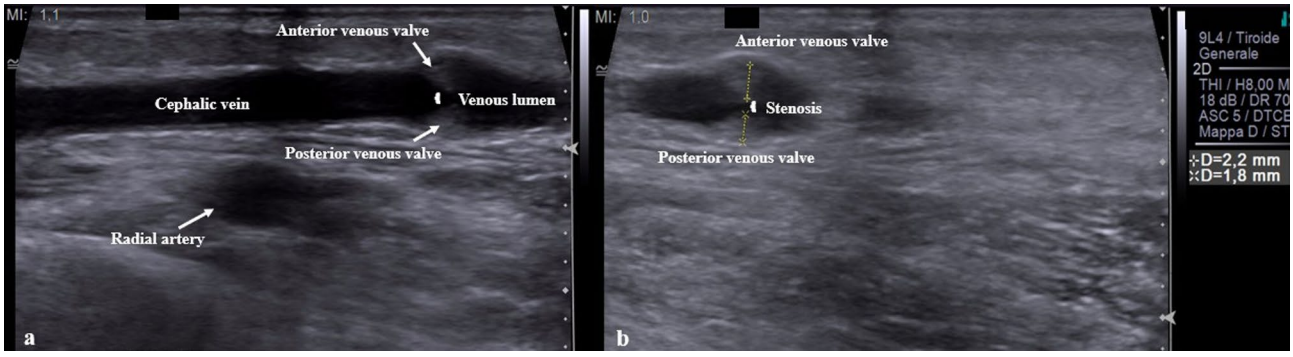

Fig. 5 B-mode ultrasound of the outflow (cephalic vein of the forearm). **a**) The valve leaflets (white arrows) appear finely hyperechoic (calcified) and demonstrate reduced mobility on dynamic ultrasound; **b**) Increased hyperechogenicity of the valve leaflets with poor mobility on dynamic ultrasound. In both cases, a significant stenosis is observed

Table 3 Types of lesions stratified according to types of AVFs

Type of AVF		Type of lesion			
		A	B	C	D
	N	N (%)			
Distal radio-cephalic fistula	442	255 (57.7)	55 (12.4)	122 (27.6)	10 (2.3)
Middle-arm radio-cephalic fistula	392	187 (47.7%)	72 (18.4)	129 (32.9)	4 (1)
Proximal radio-cephalic fistula	123	46 (37.4)	17 (13.8)	50 (40.7)	10 (8.1)
Brachial-cephalic fistula	72	20 (27.8)	16 (22.2)	27(37.5)	9 (12.5)
Brachial-basilic fistula	86	29 (33.7)	19 (22.1)	23 (26.7)	15 (17.5)
Ulnar-cephalic distal fistula and other	7	1 (14.3)	1 (14.3)	3 (42.8)	2 (28.6)

Table 4 Different types of stenosis stratified by site of lesion and type of AVF

Type of fistula	Site of lesion	Type of stenosis				
			A	B	C	D
		N	N (%)			
Distal radio-cephalic		442				
	Juxta/post-anastomotic	208	168 (80.7)	-	40 (19.3)	-
	Middle	67	31 (46.3)	10 (14.9)	19 (28.4)	7 (10.4)
	Proximal	119	47 (39.5)	30 (25.2)	42 (35.3)	-
	Arm cephalic vein /cephalic arch	16	4 (25)	3 (18.8)	7 (43.7)	2 (12.5)
	Arm basilic vein	32	5 (15.6)	12 (37.5)	14 (43.8)	1 (3.1)
Middle-arm radio-cephalic		392				
	Juxta/post-anastomotic	154	112 (72.7)	17 (11.1)	25 (16.2)	-
	Middle	71	26 (36.6)	17 (23.9)	28 (39.5)	-
	Proximal	103	39 (37.9)	26 (25.2)	38 (36.9)	-
	Arm cephalic vein/cephalic arch	21	1 (4.8)	1 (4.8)	18 (85.6)	1 (4.8)
	Arm basilic vein	43	9 (20.9)	11 (25.6)	20 (46.5)	3 (7)
Proximal radio-cephalic		123				
	Juxta/post-anastomotic tract	56	37 (66)	6 (10.7)	13 (23.3)	-
	Proximal	-	-	-	-	-
	Arm cephalic vein/cephalic arch	41	2 (4.9)	4 (9.8)	31 (75.6)	4 (9.7)
	Arm basilic vein	26	7 (27)	7 (27)	6 (23)	6 (23)
Brachial-cephalic		72				
	Juxta/post-anastomotic	30	16 (53.3)	3 (10)	11 (36.7)	-
	Arm cephalic vein tract/cephalic arch	27	3 (11.1)	7 (25.9)	12 (44.5)	5 (18.5)
	Arm basilic vein tract	15	1 (6.6)	6 (40)	4 (26.7)	4 (26.7)
Brachial-basilic		86				
	Juxta/post-anastomotic tract	27	16 (59.3)	3 (11.1)	8 (29.6)	-
	Arm cephalic vein tract/cephalic arch	34	6 (17.6)	11 (32.4)	13 (38.2)	4 (11.8)
	Arm basilic vein tract	23	7 (30.4)	5 (21.7)	2 (8.7)	9 (39.2)
	Distal tract (near axillary vein)	2	-	-	-	2 (100)
Ulnar-cephalic distal and others		7				
	Juxta-postanastomotic	2	1 (50)	-	1 (50)	-
	Middle tract	3	-	1 (33.3)	2 (66.7)	-
	Proximal tract	1	-	-	-	1 (100)
	Arm cephalic vein tract/cephalic arch	1	-	-	-	1 (100)
	Arm basilic vein tract	-	-	-	-	-

showing that intimal area was similar, as well as maximal intimal thickness, maximal IMT, maximal intima/media ratio. Only the higher extend of medial fibrosis determined the risk of stenosis and AVF maturation failure [14–16].

It has to be taken into consideration that US cannot differentiate between intima and media compared to histology, thus intimal hyperplasia based only on IMT measurements assumes that only the intima thickness increases leaving unchanged or even reduced the media thickness.

This is in contrast with morphometric classifications based on histology, which clearly define intimal hyperplasia based on intima/media area ratio, intima/media thickness ratio, intimal thickness, and/or intimal area

measurements [17]. IMT measured by US may also remain stable or unchanged when intima hypertrophy is accompanied by medial atrophy, which seems to be a result of smooth muscle cell migration into the intima or of cell death replaced by extracellular matrix fibrosis [17]. Therefore, IMT by US cannot be a real description of histologic changes in the AVF wall.

DUS provides real-time access to AVF anatomy and haemodynamics, with high sensitivity and specificity in detecting IMT [18, 19]. A recent prospective 2-year longitudinal study showed that the incidence of AVF stenosis or thrombosis detected by DUS was 32% [20]. Another study reported a prevalence of stenosis of 14% at 1 day, 28% at 2 weeks and 30% from 2 to 6 weeks after AVF creation [21]. In proximity of an AVF, factors such as loss of vasa vasorum, shear stress, and high blood flow contribute to the development of stenosis and intimal hyperplasia [17, 22, 23]. Moreover, an anastomotic angle greater than 30°, causing secondary and recirculation eddies, can result in low and oscillatory wall shear stress on endothelial cells [24]. Some studies suggest that this type of injury leads to the expression of atherogenic and thrombogenic genes, promoting neo-intimal hyperplasia through mechanisms such as inflammation, platelet activation, apoptosis, and the migration of myofibroblasts from the adventitia to the intima [16, 25, 26]. Conversely, repeated venipunctures over weeks to months in the same area, as opposed to the "rope-ladder" or buttonhole cannulation strategies [1, 27], can lead to aneurysmatic dilatation and stenosis [28]. The vessel wall injury associated with needle placement and the altered access geometry due to hematomas from vessel piercing promotes flow obstruction and increases the risk of thrombosis and access loss, even without neo-intimal hyperplasia [27, 29]. Hsiao et al. analysed the role of imaging techniques in quantifying the mechanical and hemodynamic trauma related to needle insertion in the venous outflow tract of AVFs [30]. The Authors described vascular dilatation of the arterial and venous puncture segments with intimal changes in 42% and 40% of cases, respectively, albeit without significant luminal stenosis. In addition to haemodynamic, other risk factors, smoking, hypertension, hyperhomocysteinemia, and hypercholesterolemia, may cause endothelial dysfunction and transformation of vascular smooth muscles cells into osteoblast-like cells. These cells then play a critical role in the recruitment and production of mediators that lead to calcium deposition. Venous calcifications and medial/perivascular fibrosis may reduce the vein's capacity to vasodilate and promote the onset of type C and D stenosis [8, 14–16, 31]. The study by Wang et al. [32] categorized AVF stenosis based on DUS characteristics into five groups: intima-dominant, non-intima-dominant, valve obstruction, vascular calcification, and mixed groups. Additionally, they classified stenoses by location into four types: Type I (juxta-anastomotic area), Type II (region of the draining vein), Type III (venous confluence site), and Mixed type (presence of two or more types of stenosis). Their findings indicated that diabetes was most commonly associated with intima-dominant lesions, and Type III location was linked to lower post-PTA primary patency. Using Cox proportional-hazards model analysis, they identified that the number of PTA procedures performed, the presence of vascular calcification, calcification at the lesion site requiring PTA, and serum parathyroid hormone levels are independent risk factors for lower post-intervention primary patency. The authors suggested that tailored approaches based on the type of lesion could improve outcomes. Chen et al. conducted a retrospective study to assess the impact of different morphological types of AVF lesions on patency rates post-PTA [22]. They identified three types of AVF stenosis: Type I (neointimal hyperplasia), Type II (non-neointimal hyperplasia), and Type III (mixed). The study found that Type I lesions were a significant risk factor for poor primary and secondary patency rates post-PTA. Both studies underscore the importance of understanding the morphological characteristics and specific locations of AVF stenosis. These factors are crucial for predicting patient outcomes and tailoring interventions to enhance the efficacy of treatments like PTA. Tailored treatment approaches based on the lesion type and location can lead to better management of AVF stenosis and improved patient outcomes in HD. Our classification system aligns with the current studies by capturing the different types of stenosis based on location [], but offers a more comprehensive framework encompassing both IMT, ultrasound morphological features, and lesion topography. The large, multicenter design with standardized procedures by experienced ultrasonographers strengthens the generalizability of our findings. However, our work focuses only on a DUS-based classification of AVFs stenosis occurring at or after the arterio-venous anastomosis without considering other relevant factors. For instance, DUS-IMT measurements of the radial artery have been studied as a potential predictor of early AVF failure [33, 34]. Other potential limitations of this work include reporting bias due to non-controlled data analysis and the absence of a control group with functioning AVFs. Additionally, the lack of follow-up data hinders our understanding of stenosis progression and treatment effectiveness over time. Furthermore, it has to be taken into consideration that B-mode US and CDUS are 2-dimensional examinations, but stenosis have a 3-dimensional often excentric configuration. That is why 2-dimensional imaging might even underestimate the extend or hydrodynamic impact of AVF stenosis [35].

IMT remains one of the major culprits in AVF stenosis, especially in proximity of the anastomosis, driven by a complex interplay of hemodynamic and biological factors. Other factors like scarring, fibrosis and VVC might block the physiological dilatation of the venous out-flow tract, thus causing stenosis only infrequently accompanied by IMT. The quantification of fibrosis or microscopic calcifications is difficult to be performed by B-mode ultrasound and CDUS with the probe frequencies and settings actually in use. Shear wave elastosonography, as a measure of fibrosis, is even difficult to be applied as it has to be synchronized to the heart rate to measure shear stress of the vessel wall [36]. Gray scale distribution analysis might be helpful to quantify fibrosis, but there remains a problem of standardization. A promising approach might be intravenous US and high frequency-high resolution US [35–37]. Intravascular US of AVF showed a high eccentricity index and homogeneity index of the stenotic vessel wall indicating an abnormal excentric remodeling with intimal hypertrophy and at the same time a homogeneous wall due to fibrosis [37]. A preliminary study of high-resolution elasticity imaging evidenced lower strain values at the AVF stenosis site corresponding to a higher local wall stiffness compared to non-stenotic sites [36].

Stenosis location also plays a crucial role, with various segments within the AVF susceptible. Current treatment strategies for AVF stenosis include PTA as the gold standard, often guided by DUS [1, 10]. Other options include cutting balloons, stents (medicated or non-medicated) [38, 39], and surgical revisions depending on the specific stenosis characteristics. The future of AVF stenosis treatment lies in personalization based on factors like location, inflammatory stage, and stenosis type. Our classification system can potentially guide this approach. For example, lesions with thick IMT might benefit from antiproliferative drugs delivered via balloons or stents. Conversely, fibrotic or calcified stenoses (type C and D) might respond better to cutting balloons, stent grafts, or surgery. This personalized approach has the potential to improve intervention effectiveness and reduce recurrence rates. Advancements in imaging, molecular profiling, and bioengineering hold promise for targeted therapies based on specific characteristics of stenotic lesions. Additionally, integrated care models and the use of artificial intelligence can further enhance our ability to predict, detect, and treat AVF dysfunction. Establishing a common nomenclature for AVF stenosis, like the one proposed here, will facilitate research efforts by enabling standardized reporting, guiding appropriate treatment selection, and paving the way for future discoveries. Future research may focus on evaluating stenoses in AVFs dysfunction to validate our findings and creating convergence evidence that would increase the robustness of our proposal, including a more diverse participant population in terms of age, gender, and diverse geographic locations, reporting results with long periods of follow-up, allowing to define the history of the stenoses; and conducting randomized controlled trials of different types of interventions according to the different types of stenoses as defined by our classification.

Conclusions

DUS is valuable for assessing stenosis and morphology in AVFs, allows for close surveillance and potentially pre-emptive interventions before stenosis becomes clinically apparent. While current guidelines focus on treating symptomatic stenoses [1, 40], our proposed classification system holds promise for a more nuanced approach. By categorizing stenoses based on the extent and location of intima-media alterations, fibrosis and VVC, this system can provide clinicians with a deeper understanding of the underlying pathophysiology. This, in turn, could lead to more precise diagnoses and personalized treatment plans. Tailoring interventions to the specific stenosis type has the potential to improve patient outcomes and reduce complications associated with AVF dysfunction. Overall, this DUS-based classification system for AVF outflow stenosis may represent a significant step forward in managing patients with AVFs for HD.

Author contributions

All authors have all read and approved the manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All participants have signed an informed consent to participate in and publish the study. The study was submitted to and approved by the Catania Local Ethics Committee 1 (https://www.policlinicorodolicosanmarco.it/azienda/organizzazione/comitato-etico-catania-1.aspx). The study adhered to the Declaration of Helsinki.

Compliance with ethical standards

All authors have all read and approved the manuscript. The results presented in this paper have not been published previously in whole or part, except in abstract format.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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