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Surveillance and monitoring of early failing arteriovenous fistula using Doppler assessment in children on regular hemodialysis

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Abstract

Background: A well-functioning vascular access is a mainstay to perform an efficient hemodialysis procedure. Limited lifespan of arteriovenous accesses is one of the major challenges of the current long-term hemodialysis therapy. Vascular access-related morbidity accounts for up to 50% of total dialysis patient's costs. The pediatric vascular access clinical guidelines published by the National Kidney Foundation Kidney Disease Outcome Quality Initiative recommend establishing a surveillance strategy to detect access stenosis and direct patients for early intervention. The aim of this study was to test the role of using the color Doppler ultrasonography (CDU) as a surveillance method for arteriovenous fistulae in children on regular hemodialysis and its value for detecting the early vascular access failure or dysfunction to avoid access loss.

Results: During 10-month duration, we prospectively conducted surveillance for 30 patients on regular hemodialysis through arteriovenous fistulae (AVF) as a vascular access, clinical assessment of AVF and radiological examination using CDU of the upper limbs. Their ages were ranging from 2 to 18 years with 1:1 male: female ratio. Doppler indices were measured in the afferent arteries, at the site of anastomosis, and the draining veins. AVF stenosis was the highest among all the detected complications ($n=9$, 30%), aneurysm and pseudoaneurysmal formation ($n=8$, 26%) anastomoses diameter reduction in 16.6%, and it was correlated with the dialysis adequacy measured through the Kt/v. Other complications were thrombosis ($n=2$, 6.7%), central venous stenosis ($n=2$, 6.7%), steal syndrome ($n=1$, 3.3%) and calcifications in ($n=1$, 3.3%). In total, 26% of the patients have more than one malfunction. Only one case has access failure a month after CDU examination.

Conclusion: In conclusion, among pediatric patients CDU can detect early stenosis of AVF in children, which can affect the dialysis adequacy.

Keywords: Children, Surveillance, Arteriovenous fistula, Complications, Doppler, Hemodialysis

Background

When hemodialysis was introduced as an effective workable treatment in 1943, the outlook for patients with advancing kidney failure suddenly changed from anticipation of impending death to indefinite survival [1].

Currently, there are three modes of renal replacement therapy: peritoneal dialysis, hemodialysis and kidney transplantation. In spite of renal transplant being the best renal replacement, the choice of the most appropriate method will depend on various factors, with respect to the child age and the available resources and staff experiences [2].

Different vascular accesses for hemodialysis include central venous catheters, arteriovenous fistulae (AVF) and arteriovenous grafts. Arteriovenous fistulae are

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associated with better clinical outcomes and quality of life and lower costs compared with arteriovenous grafts and central venous catheters [3]. Also, it showed reduced risk for all-cause mortality, fatal infections and cardiovascular events in comparison with the use of central venous catheters [4].

Various AVF screening methods have been proposed, including physical examination, measurement of access blood flow, access recirculation, either direct or derived static dialysis pressure and Doppler ultrasonography [5].

Doppler ultrasonography can diagnose access stenosis and the measurement of residual diameter. Moreover, the advantage over angiography is more precise explanation of stenosis etiology [6]. It allows for a detailed morphological and functional assessment, and the combination of these parameters offers the most complex stenosis examination available in vivo [7].

As the AVF acts as a life line for the hemodialysis patients, establishing a non-invasive screening through Doppler ultrasonography can define access stenosis or dysfunction to allow for early intervention or pre-emptive correction if needed to prevent complications or access loss, saving our patients from the undesired risks [7].

The aim of this study was to test the role of using the color Doppler ultrasonography as a surveillance method for arteriovenous fistulae in children on regular hemodialysis and its value for detecting the early vascular access failure or dysfunction to avoid access loss.

Methods

The Institutional Review Board of our Radiology Department approved the design of the study and the use of clinical data. Written consent was obtained from the patients or their parents prior to the procedures.

This study was conducted on patients receiving hemodialysis sessions at our Children Hospital from October 2019 to July 2020.

Inclusion criteria

- Age: from 2 to 18 years old.
- Children on regular hemodialysis with matured AVFs as a vascular access for hemodialysis.
- Patients were eligible for enrollment into the study if they had been on maintenance hemodialysis for at least 3 months.

Exclusion criteria

- Patients with AVFs before maturation time.
- Patients were excluded if they had severe or unstable medical illness (class IV congestive heart failure; chronic pulmonary disease requiring home oxygen; hepatic encephalopathy or active malignancy being treated with chemotherapy or radiation therapy).

A clinical evaluation of the dialysis access was performed in all patients before Doppler examination:

- Access patency was determined by the presence of a palpable thrill, in addition to the strength and consistency of a thrill throughout the access.
- Visual inspection of the limb and access site to detect areas of swelling, redness as well as the presence of dilatation, collateral vessels, palpable prominent localized areas of pulsations (suggesting pseudoaneurysm) and the presence of ischemic manifestations.
- Response to arm elevation.

Doppler examination

CDU examinations were performed using LOGIQ B5 Premium from GE. Linear arrays transducers (5–10 MHz) were usually chosen for superficial vascular imaging and the access itself. However, curved transducers (3.5–5 MHz) were utilized for deeper vascular imaging, such as central veins in the shoulder or the neck, the inflow arteries or in obese patients.

During the examinations, the patient positioning supine, with the arm relaxed and extended out to the side, with the area to be evaluated closest to the sonographer. Examination included the afferent artery, site of anastomosis, the draining veins as far as the subclavian vein as well as the arterial tree distal to the AVF in cases experiencing steal syndrome.

All vessels were examined in both transverse and longitudinal planes using gray-scale and color images. At first, the vessels were examined by B-mode to determine the site and type of the fistula, detection of wall echo pattern and dilatations, and measurement of the vessel's diameter. Then color images were obtained to assess the direction of blood flow. Finally, Doppler studies were performed, in the longitudinal orientation, and the sample size was maintained below 5 mm and was located at the center of each vessel. The spectral waveform was angle corrected, and the Doppler angles of incidence were less than 60°. Then spectral waveforms were obtained at each level.

The following parameters were measured by CDU: diameter of the fistula, peak systolic velocity (PSV) and end diastolic velocity. Then examination of proximal, mid and distal outflow vein for diameters, patency, and peak and mean velocities was performed.

Stenosis was diagnosed when there was reduction of the anastomosis diameter of below 2 mm and an increase in PSV, PSV >300 cm/sec and ratio of PSV (PSV in the stenotic area/PSV upstream the stenotic area in the venous outflow) greater than 2.

Statistical analysis

Data were coded and entered using the Statistical Package for the Social Sciences (SPSS) version 25 (IBM Corp., Armonk, NY, USA). Data were summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (%) for categorical data. Comparisons between quantitative variables were made using the nonparametric Mann–Whitney test [8]. For comparing categorical data, Chi-square test was performed. Exact test was used instead when the expected frequency is less than 5 [9]. Correlations between quantitative variables were done using Spearman correlation coefficient [10]. *P*-values less than 0.05 were considered as statistically significant.

Results

We conducted a prospective observational study on 30 patients to investigate the role of CDU screening in early detection of failing AVFs in children on regular hemodialysis. The median age of the included patients was 10 (5–18) years with 1:1 male: female ratio.

The mean age of onset of dialysis was 6.75 years old (3–13 Y), while the mean duration of regular HD was 3.95 (0.5–14 Y). In total, 46% of the cases have previously failed AVFs. The AVF type was brachiocephalic in most of the cases ($n=24$, 80%) and the rest brachiobasilic ($n=6$, 20%). Left arms are the predominately used, accounting for 66.7% of the total cases. The mean fistula age was 20.26 months (1.9–61.9) Table 1.

The primary renal disease was cystinosis in 20% of cases, focal segmental glomerulosclerosis in 10%, bilateral hypoplastic kidneys in 10%, glomerulonephritis in 6.7%; urological stones and tumors were accounting for 6.7% for each and unknown cause in 13.3%.

As regarding the laboratory results, the blood urea mean was 69.17 (41–134), creatinine mean was 6.48 (3–11.7), calcium mean was 9.77 (6.5–13), phosphorus mean was 4.47 (2.00–8.9), serum sodium mean was 139.73 (134–148), serum potassium mean was 5.32 (3.5–7.2), and alkaline phosphatase mean was 394.33 (71.00–1835).

We conducted clinical examination of the fistulae for all the cases. Abnormality in thrill was found in 12 (40%), abnormal bruit in 10 (33.3%), abnormal response to arm elevation in 5 (16.3%). Aneurysmal dilatation was seen in 10 cases (33.3%), while focal aneurysms were present in 2 cases (6.7%). Hand ischemia manifestations were present in 1 case (3.3%) in the form of peripheral coldness, cyanosis and pains. Three cases complained of peripheral upper limb edema (10%). Difficult needling has been found in 3 cases (10%), while prolonged postdialysis bleeding was a complaint in 2 cases (6.7%). Dilated veins were found in 2 cases (6.7%) (Fig. 1).

Color Doppler examination was done for all cases, fistula diameter was less than 2 mm in 5 cases, the PSV was more than 400 cm/sec and PSV ratio was >2 in 3 of them, and one case showed hemodynamic affection in the form of reduced volume flow (Qa) below 500 ml/min (=408 ml/min). PSV at the anastomosis site was >400 cm/sec in 9 cases, and PSV ratio was >2 in 10 cases (Table 2) (Fig. 2).

In this study, 8 (26%) patients had aneurysm and pseudoaneurysm, 6 at the venous side of the AVF, two have pseudoaneurysms, and one of them has mural thrombus. CDUS was useful to determine the extent of aneurysm and evaluate the presence of luminal thrombus as well as to determine if the patient requires surgery or not. Only 2 (6.7%) patients had thrombosis in this study; the thrombi were mural based and not occluding the AVF lumen or causing a hemodynamic effect (Fig. 3). Only 1 (3.3%) patient had calcification in this study (Fig. 4) (Table 3).

One case has steal syndrome; clinically, there is distal edema and weak pulsation in the radial artery and manifestations of distal ischemia in the form of peripheral coldness and pain. By CDU, the AVF has a very high Qa and decreased Qa in the radial artery and retrograde flow toward the brachiocephalic AVF, confirming the diagnosis of steal syndrome (Fig. 5). This case was sent for further intervention.

Fistula failure event has been shown only in one case. There was access flattening on clinical assessment with absence of thrill and bruit over it. The remarked

Table 1 Dialysis and AVF onset and duration

	Mean	Standard deviation	Median	Minimum	Maximum
Age of onset of HD (years)	6.75	2.64	7.00	3.00	13.00
Duration of HD in years	3.95	3.28	3.00	0.50	14.00
AVF age months	20.26	14.20	17.23	1.97	61.90
Duration of maturation in weeks	8.20	1.03	8.00	7.00	12.00

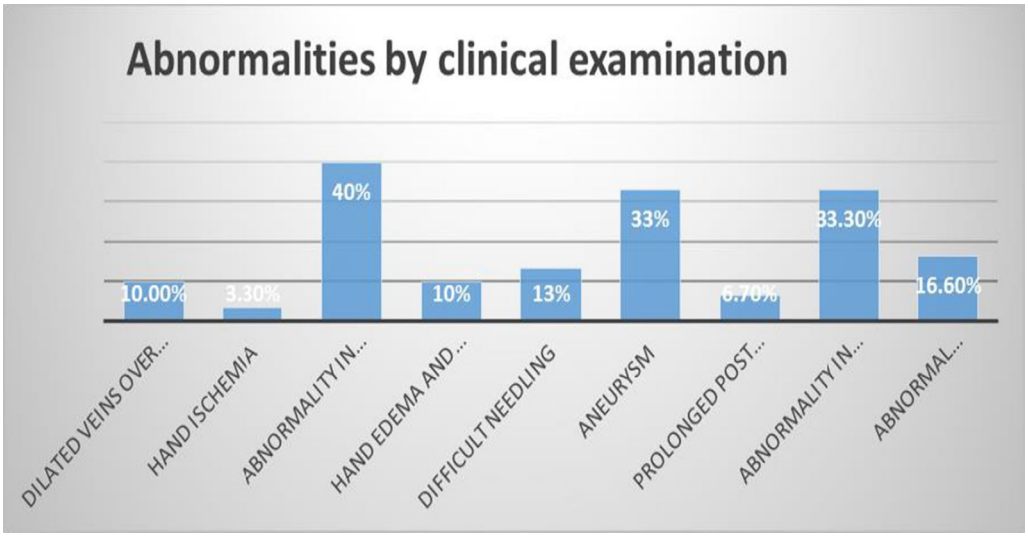

Fig. 1 Abnormalities by clinical examination

Table 2 CDU examination parameters in the study group

	Mean	Standard deviation	Median	Minimum	Maximum
Fistula diameter	0.47	0.17	0.46	0.22	0.80
Fistula PSV ml/sec	328.49	164.18	290.00	63.80	773.00
OUTLET diameter	1.64	0.66	1.46	0.50	2.90
OUTLET PSV ml/sec	188.82	110.97	156.50	25.00	462.00
PSV ratio	2.70	3.03	1.82	0.35	13.44

abnormality in CDU examination of that case was fistula diameter which was 0.23 mm.

Regarding the relation between CDU examination parameters of AVFs and dialysis adequacy (KT/v), the correlation was positive as regarding the fistula diameter in the first assessment and in the follow-up with correlation coefficient 0.56 and 0.38, respectively ($P=0.001$, 0.0.038) (Table 4).

There was no significant statistical association between the clinical findings of thrill, bruit, presence of aneurysms and the dialysis adequacy in the first examination nor in the follow-up after 3 months. The statistical association

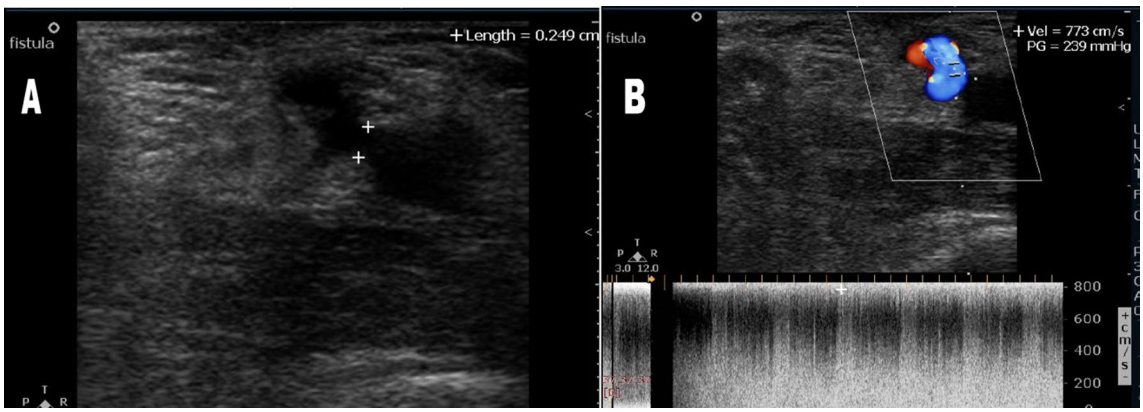

Fig. 2 Fistula stenosis. **A** Sonographic examination of the fistula revealed reduced diameter (0.249 cm). **B** Color Doppler examination of the fistula showed high PSV 773 cm/s

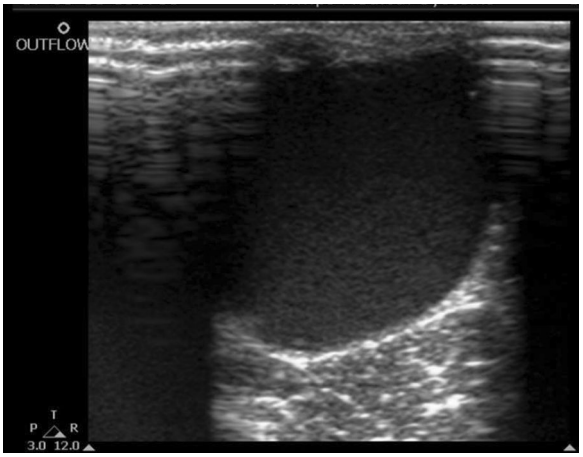

Fig. 3 Sonographic examination at site of the AVF showed pseudoaneurysm

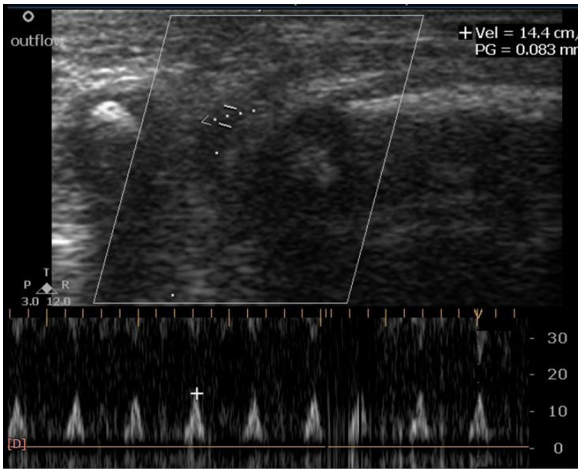

Fig. 5 Radial artery CDU in steal case

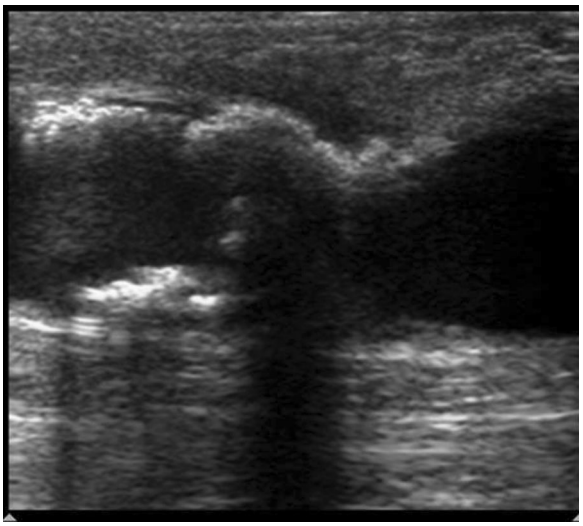

Fig. 4 Calcifications in the AVF

Table 3 The abnormal findings in AVFs CDU examination

Finding	Count	%
Doppler abnormal findings		
Central venous stenosis	2	6.7
Thrombus	2	6.7
Calcification	1	3.3
Pseudoaneurysm	2	6.7
Dilated venous outflow	6	20
Steal syndrome	1	3.3
Stenosis	9	30
Low Qa	3	10

was only significant for arm elevation test and the first dialysis adequacy reading with ($p=0.018$).

Regarding the association between the clinical examination findings and the CDU measurements, there was statistical association between aneurysms and venous outflow diameters ($p=0.003$); also there was statistical association between arm elevation test results and outflow diameter and PSV, the volume flow and with ratio of fistula PSV/ outflow PSV ($p=0041$, 0.028, 0.018 and 0.009). There was no statistical association between the CDU parameters with the other clinical examinations as thrill, bruit, arm edema, ischemic manifestations peripherally in the examined limb, difficult needling, prolonged postdialysis bleeding and dilated veins (Table 5).

Regarding the dysfunctions found through CDU examinations as presence of thrombi, calcifications, central venous stenosis, pseudoaneurysms, outflow dilatation or steal syndrome, there was a statistical association found between dilatation of outflow and aneurysmal dilatations with $p<0.001$. There was also association between the ischemic manifestations peripherally in the examined limb and steal syndrome by CDU examination $p=0.033$ and the presence of dilated veins with central venous occlusion $p=0.007$ (Table 6).

Discussion

A well-functioning vascular access (VA) is a mainstay to perform an efficient hemodialysis (HD) procedure. AVF, described by Brescia and Cimino, remains the first choice for chronic HD. It is the best access for longevity and has the lowest association with morbidity and mortality, and for this reason AVF use is strongly recommended by guidelines from different countries [11].

Table 4 Relation between AVF Doppler examination parameters and dialysis adequacy index (Kt/v)

	Fistula diameter	Fistula PSV ml/sec	Outlet diameter	Outlet PSV ml/sec	Stenosis index
KT/V 1st					
Correlation coefficient	0.560	− 0.191	0.266	− 0.016	− 0.359
P value	0.001	0.313	0.156	0.931	− 0.359
N	30	30	30	30	30
KT/V 2nd					
Correlation coefficient	0.380	− 0.100	0.192	0.156	− 0.086
P value	0.038	0.598	0.311	0.410	0.652
N	30	30	30	30	30

Table 5 Association between the clinical examination results and CDU measurements

	Fistula diameter	Fistula PSV	Outflow diameter	Outflow PSV	Ratio of PSV
Aneurysm	0.502	0.120	0.003	0.422	0.055
Thrill	0.917	0.787	0.662	0.819	0.950
Bruit	0.713	0.650	0.914	0.746	0.650
Arm elevation test	0.138	0.777	0.041	0.028	0.018
Arm edema	0.791	0.245	0.837	0.220	0.536
Ischemic manifestations	0.600	0.400	0.133	0.933	0.533
Difficult needling	0.271	0.702	0.328	0.576	0.976
Prolonged bleeding	0.966	0.074	0.460	0.717	0.506
Dilated veins	0.600	0.897	0.226	1.000	0.897

Table 6 Association between the clinical examination results and CDU AVF dysfunctions

	Central venous stenosis	Thrombus	Calcification	Pseudoaneurysm	Dilated outflow	Steal syndrome
	P value (Chi-square test)					
Aneurysm	1	1	0.333	1	< 0.001	1
Thrill	1	0.503	0.400	0.503	0.139	0.400
Bruit	0.540	0.540	1	0.540	0.690	0.333
Arm elevation test	1	1	1	1	0.540	1
Arm edema	0.253	1	1	1	0.584	0.133
Ischemic manifestations	1	1	1	1	0.333	0.033
Difficult needling	1	0.253	1	1	1	1
Prolonged bleeding	1	1	1	1	0.540	1
Dilated veins	0.007	1	1	1	0.251	1

Limited lifespan of arteriovenous accesses (AVFs and AVGs) is one of the major challenges of the current long-term hemodialysis therapy. Vascular access-related morbidity accounts for up to 50% of total dialysis patient's costs [7].

The performance of color Doppler ultrasonography in the regular surveillance of AVF patency has been widely described in the literature [12]. This safe, non-invasive and reproducible technique has been found useful for pre-operative vascular mapping, evaluation of AVF maturation and surveillance of AVF flow, providing direct evidence for the presence, localization and severity of stenosis [13]. Moreover, it permits assessment of VA patency by measuring the flow rate. Over the last two decades, there is growing evidence that CDU may potentially replace fistulography [14].

The pediatric vascular access clinical guidelines published by the National Kidney Foundation Kidney Disease

Outcome Quality Initiative (KDOQI) recommends establishing a surveillance strategy to detect access stenosis and direct patients for early intervention. The CDU is minimally invasive, while fistulography was costly, required radiation exposure and, in younger children, sedation and anesthesia [15].

In our study the median age was 10 (5–18) and mean BSA 0.83 m2. The median age of onset of dialysis was 10 years (5–18), median age at ESRD was 7 years (3–13), while the median duration of regular HD was 3 years (0.5–14 Y). In particular, 46% of the patients have previously failed AVFs. The mean fistula age was 20.26 months (1.9–61.9). The AVF type was brachiocephalic ($n=24$, 80%) and ($n=6$, 20%) brachiobasilic. Left arms are the predominately used, accounting for 66.7% of the total. The gender of the study population was 50% for each males and females.

Karava et al. [14] conducted a single-center study on 16 cases (11 males), and the median age was 15, weight 39, age at ESRD 14.1 and duration of dialysis 0.9 years. Localization of AVF was in the upper arm in 5 patients and in the forearm in 11 patients.

Ashoor et al. [15] conducted a study on 31 children into 2 groups (baseline and intervention groups), gender were 50% males in each group, the median age at ESRD was 14 and 15.5 years, median weight was 57 and 50.6 kg. Duration on dialysis was 24 and 8 months in each group, respectively.

Stenosis of HD vascular access is common and may lead to thrombosis and the loss of the access. Thus, detection of stenosis in AVF before thrombosis could offer a strategy to improve AVF survival by early intervention [16]. More than 50% stenosis is associated with more than 50% risk of access thrombosis within 6 months [7].

In our study, we used fistula diameter, PSV measurements and PSV ratios to diagnose access stenosis. The detected stenosis was ($n=9$, 30%). Overall, AVF with stenosis had a lower flow rates, although it did not reach the statistical significance ($p=0.128$). The mean fistula diameter was 0.47 cm (0.2–0.8), and the mean PSV ratio was 1.82 (0.35–13.44).

In Karava et al. [14] study, there was a significant stenosis detected by CDU in 43% of cases, with low flow rates in stenosis cases reaching to statistical significance ($p=0.008$).

In our study 2 patients (6.7%) have VF/PSV less than 2, and we found that the Kt/v was dropped below 1.2 (with exclusion of other causes) in these patients. The decreased fistula diameter was correlated with the drop of Kt/v (CC = 0.56, $p=0.001$), and this finding agreed with Campos et al. [17] as patients of stenosis diagnosis had significant lower Kt/v (1.15 + 0.20) when compared with patients with negative diagnosis (1.33 + 0.16; $p<0.0001$) [17].

Only 2 (6.7%) patients had thrombosis in this study, and this low thrombosis rate could be explained by the fact that most of the patients were asymptomatic. In Karava et al. [14] study, the thrombosis rate was 1 (6.2%). Thrombosis events were reduced from 13.5 per 100 patient-months on HD in the baseline group to 3.5 per 100 patient-months on HD ($p<0.04$) in the intervention group in Ashoor et al. [15] study.

Pseudoaneurysms occur at the site of puncture or at the anastomoses. The clinical finding of a pulsatile mass and a systolic murmur usually allows correct diagnosis of aneurysms and pseudoaneurysms. However, CDUS is of the most importance as it allows better estimation of the extent of aneurysm (less or more than 5 mm) size of its neck and degree of mural thrombosis. Additionally, CDUS can differentiate pseudoaneurysm from hematomas as they have a typical 'to-and-fro' pattern [18].

In this study, 8 (26%) patients had aneurysm and pseudoaneurysm: six at the venous side of the AVF, two have pseudoaneurysms, one of them has mural thrombus. CDUS was useful to determine the extent of aneurysm and evaluate the presence of luminal thrombus as well as to determine whether the patient requires surgery or not.

The value of physical examination in the detection of AVF stenosis has recently been compared with angiography and Doppler ultrasound [5]. Asif et al. [19] and Campos et al. [17] determined the accuracy of physical examination in the detection of stenosis in AVFs, with excellent results. In addition, Campos et al. determined the accuracy of physical examination in the detection of AVF stenosis in comparison with Doppler ultrasound. Tessitore et al. [5] reported that the level of agreement of physical examination in the detection of AVF stenosis was fair-to-moderate among nephrologists with different expertise on vascular access monitoring.

In our study, there was an association between physical examination and CDU stenosis diagnosis through arm elevation test $p=0.041$ with outflow diameter, $p=0.028$ with outflow PSV, $p=0.018$ with PSV ratio and with regard presence of aneurysms and outflow diameter $p=0.003$. Ischemic manifestations in the form of weak distal pulse, peripheral coldness and fingers cyanosis were associated with the CDU steal syndrome diagnosis $p=0.033$. Presence of dilated veins and collaterals over the chest, neck and upper part of the arm was associated with central venous stenosis by CDU $p=0.007$. That complies with the results of Vladimir et al. [20].

The limitations of our study included the small number of patients. Large-scale studies on pediatric population are needed to confirm our results.

Conclusion

The current study demonstrated the role of CDU as a non-invasive surveillance method for detection of AVF different dysfunctions. Among pediatric patients, CDU can detect early stenosis of AVF which can affect the dialysis adequacy.

In presence of abnormal physical examination of the AVF as absence of response to arm elevation test, peripheral ischemic manifestations, non-propagating thrill, appearance of pseudoaneurysms or unexplained drop in Kt/v, CDU examination should be considered.

Abbreviations

HD: Hemodialysis; KDOQI: Kidney Disease Outcome Quality Initiative; CDU: Color Doppler ultrasonography; AVF: Arteriovenous fistulae; PSV: Peak systolic velocity; SPSS: Statistical Package for the Social Sciences; Qa: Vascular access flow; ESRD: End-stage renal disease.

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Author contributions

EF formulated the research goals, designed the study methodology and supervised/actively participated in the research activity planning/execution. AS conducted/actively participated in the research process, performed the data collection/data analysis and wrote the initial draft of the manuscript. SM assisted in data analysis, largely contributed in reviewing the manuscript and contributed in follow-up of the patients. SH assisted in clinical assessment of the patients, data analysis, contributed in follow-up of the patients. MG assisted in performing Doppler studies, data analysis, contributed in reviewing the manuscript and contributed in follow-up of the patients. All authors have read and approved the manuscript.

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Availability of data and materials

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

Declarations

Ethics approval and consent to participate

The Institutional Review Board of our Radiology Department approved the design of the study and the use of clinical data. Ethics Committee reference number is not available (was not provided). Written consent was obtained from the patients or their parents prior to the procedures.

Consent for publication

All patients (or their parents) included in this research gave written informed consent to publish the data contained within this study.

Competing interests

The authors declare that they have no competing interests.

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