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Outcomes of arteriovenous fistula and role of duplex ultrasound for its assessment in pre-dialysis patients; a single center longitudinal study

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ABSTRACT

Introduction: Arteriovenous fistula (AVF) is the preferred vascular access for hemodialysis; however, it has a primary failure rate of 20%–60%. Analyzing the factors associated with AVF failure is crucial for planning appropriate management strategies.

Objectives: We aimed to identify the AVF outcomes and associated factors along with the role of duplex ultrasound (DUS) in preoperative and postoperative AVF assessment at a tertiary care hospital.

Patients and Methods: This prospective observational study was conducted on pre-dialysis patients who underwent AVF creation between January 2020 and December 2021.AVF outcomes and associated clinical and vascular factors were analyzed using pre- and post-operative DUS.

Results: Of 171 patients, males were predominant (83.6%), and diabetic nephropathy (42.7%) was the predominant cause of chronic kidney disease (CKD). AVF outcomes showed, 109 (63.7%) had unassisted mature AVF and 29 (16.9%) had AVF failure wherein early dialysis suitability failure was predominant (17; 9.94%). Among clinical factors, only a history of smoking correlated with AVF failure ($P=0.04$). On pre-and post-operative DUS assessment, the absence of distensibility and immediate post-operative vein diameter strongly correlated with AVF failure ($P<0.001$). A unit increase (1 mm) in outflow vein diameter immediately after surgery emerged as an independent predictor of AVF outcome in both univariate (OR 0.98, 95% CI: 0.35-3.99; $P<0.001$) and multivariate analysis (OR: 0.313, 95% CI: 0.148-0.663; $P<0.001$).

Conclusion: Most patients in our setting had unassisted AVF fistula. We additionally found that smoking correlated with AVF failure. Predominant factors determining AVF success were cephalic vein diameter, distensibility, and increase in draining vein diameter and flow volume at six weeks. This study highlights using DUS in pre- and post-operative periods, along with conventional examination to improve AVF outcomes.

Implication for health policy/practice/research/medical education:
The quality of life and survival of patients on hemodialysis depends on the placement of an appropriate access and maintaining well-functioning arteriovenous fistula (AVF) remains a great challenge. This study emphasizes the use of duplex ultrasound (DUS) in both the pre- and postoperative periods in addition to conventional physical examination to enhance the success of favorable AVF outcomes.

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Introduction

Hemodialysis is the most prevalent modality of renal replacement therapy for patients with end-stage kidney disease (1). The quality of life and survival of patients on hemodialysis depends on the placement of appropriate access. By construction of an arteriovenous fistula (AVF),

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the high-pressure arterial blood is diverted into the high-capacity venous system, thus as a result of the pressure drop, the blood velocity increases, which causes the vein to dilate and develop thickened walls supporting enough blood flow to carry out an effective dialysis. Multiple factors are involved in the functional maturation of AVFs which include demographic (age, gender, race/ethnicity), clinical (ischemic heart disease, peripheral vascular disease, diabetes mellitus, obesity), hemodynamic (size of the vein and feeding artery as well as blood flow) or technical (experience of the surgeon creating the AVF and the care of AVF). However, creating and maintaining well-functioning vascular access remains the greatest challenge(2).

With a primary failure rate of up to 40%, achieving functional AVF remains difficult, and hence strategies that establish and maintain adequate vascular access are imperative(3,4). Current practice for the evaluation and maturation of AVF involves clinical acumen as well as duplex ultrasound (DUS) assessment. DUS is essential for pre-operative vascular mapping, assessing AVF maturation, and monitoring AVF over time. It provides both morphological and functional data on the AVF. This tool can be used by nephrologists to assess the maturity of AVF post-creation, determine the optimal timing for AVF puncture, detect complications, and select the most appropriate therapeutic procedures for AVF management (5).

Since the AVF is known to be superior to AV grafts and central venous catheters due to its longer lifespan and lower risk of complications, every effort should be made to increase the number of fistulae in both incident and prevalent chronic kidney disease (CKD) patients (3). Fistula failure (1) can be classified as "early failure" denoting instances where the AV fistula doesn't mature sufficiently for use or fails within the initial three months of creation, and "late failure," indicating failures occurring after successful usage for more than three months (4). Although there is considerable overlap, the typical causes for failure in these two groups differ.

Objectives

This study aims to identify the AVF outcomes and its predictors along with the role of DUS in preoperative and postoperative AVF assessment at a tertiary care hospital.

Patients and Methods

Study sample

A prospective, single-centre, observational study was conducted at a tertiary care hospital. All patients aged below18 years diagnosed with CKD stage 5 (as per standard definitions) planned for upper limb AVF construction were included. Those with lower limb fistula, arteriovenous grafts, tunneled catheters, and those on peritoneal dialysis were excluded (Figure 1).

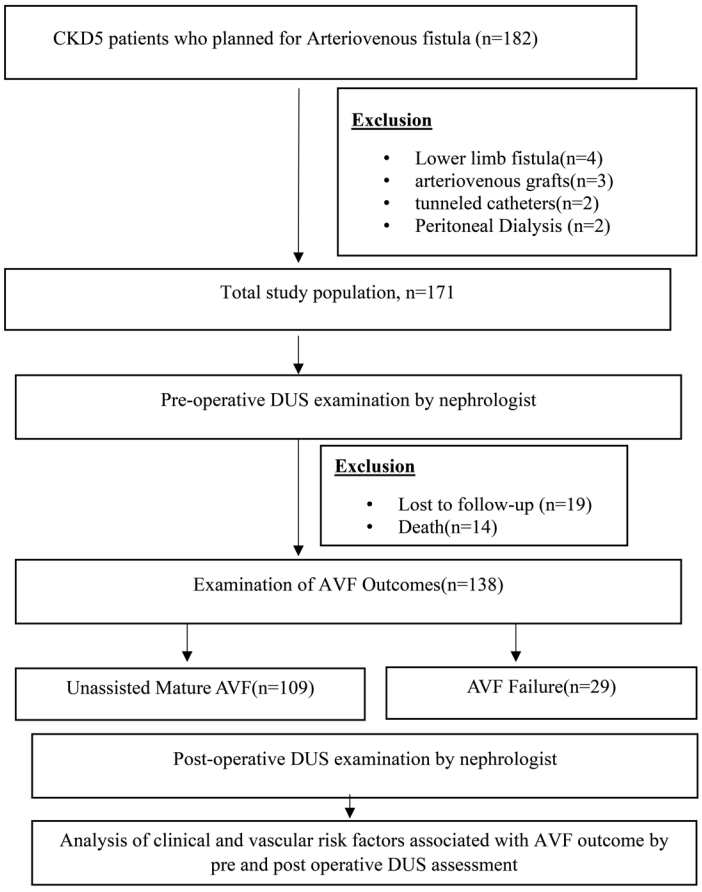

Figure 1. Sampling algorithm.

Data collection

Data was collected using a pre-designed proforma which included demographic details, comorbidities, etiology of CKD, and physical examination which included Allen's test and assessment of distensibility of veins. To look for venous distensibility, a tourniquet was used to induce venous congestion on the upper arm to check for it in the superficial arm veins.

Pre-operative DUS protocol

A preoperative DUS mapping and assessment of the upper limb vasculature was conducted by a single nephrologist using the standardized protocol for hemodialysis vascular access. As shown in Figure 2, the DUS was performed using Phillips®, HD 5 with a 5-12 MHz variable frequency linear transducer (6).

In a warm, comfortable environment, the patient was examined in the supine position, with a moderately elevated trunk to avoid elbow flexion using armed gel to prevent vasoconstriction of vessels. The arterial and venous districts were evaluated sequentially, with transverse and/or longitudinal scans of the veins (from the periphery to the thorax) and the arteries (from the root of the arm towards the hand). Then a B-mode assessment of morphological aspects along with color and DUS evaluations of venous and arterial blood flow was performed. The vein was considered distensible if its size increased by 30% of the initial size after the tourniquet application.

After ensuring normal physical examination and after a preoperative DUS, the nondominant hand with the best anatomical site for AVF creation was suggested to the surgeon and a single surgeon performed all the fistulas with an end-to-side anastomosis of the vein and the artery using 6-0 or 7-0 polypropylene sutures according to the vessel diameter.

Post-operative DUS protocol

Post-AVF creation patients were advised regular isometric hand grip exercises underwent DUS assessment in the first and sixth weeks and were followed up clinically.

Unassisted mature AVF

An AVF that facilitates prescribed dialysis, allowing both needles to be used for over two-thirds of dialysis sessions within a four-week period, and is suitable for dialysis without requiring endovascular or surgical interventions (7).

Immediate AVF failure

Access that has either no appearance of or a loss of thrill or bruit within 72 hours of its creation (8).

Early AVF failure

An access that despite radiological or surgical intervention, cannot be successfully used for hemodialysis by three months following its creation (8).

Figure 2. Device used for DUS and preoperative DUS mapping.

Outcomes

The outcomes analyzed were the predictors of AVF by comparing operative and post-operative DUS between unassisted mature AVF and early AVF failures.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD), median (interquartile range, IQR), and range according to normality. Categorical data were summarized in terms of frequencies and percentages. The chi-square test was conducted to compare proportions, while the T-test was conducted to compare continuous data. Binary logistic regression was used to identify the predictors of AVF outcomes. The statistical analysis (IBM Corp., Armonk, NY, USA) was done using SPSS version 20.

Results

Baseline characteristics

During the study period, a total of 171 patients underwent AVF construction. The mean age was 51.7 ± 13.84 years, males were 143 (83.6%), the mean body mass index (BMI) of the study was 22.60 ± 2.85 kg/m^2, the most common cause of CKD was diabetic nephropathy 73(42.7%), 156 (91.2%) had hypertension and 51 (29.8%) had ischemic heart disease. The blood pressure of both arms was measured and a difference of <10 mm Hg was noted. All 171(100%) had a negative Allen's test and 80% had the presence of distensibility of vein clinically apparent after tourniquet application (Table 1).

Pre-operative and post-operative DUS assessment

The pre-operative DUS revealed a mean cephalic vein diameter of 2.09 ± 0.64 mm and 2.87 ± 1.05 mm at the wrist and elbow respectively. The basilic vein diameter was found to be 3.26 ± 1.13 mm. The radial artery and brachial artery diameters were found to be 2.33 ± 0.63 mm and 4.54 ± 1.12 mm respectively, whereas their peak systolic velocities (PSVs) were 60.13 ± 19.35 cm/s and 77.75 ± 19.64 cm/s respectively. Around 94.2% of the patients had

Table 1. Baseline characteristics

Characteristics	n=171 (%)
Mean age (y)	51.7±13.84
Males	143 (83.6)
Mean BMI (kg/m^2)	22.60±2.85
Etiology of CKD	
Diabetes	73 (42.7)
Chronic glomerulonephritis	50 (29.2)
Chronic interstitial nephritis	32 (18.7)
Polycystic kidney disease	10 (5.8)
Multiple myeloma	2 (1.2)
Others	4 (2.3)
Hypertension	156 (91.2)
Ischemic heart disease	51 (29.8)
Negative Allen test	171 (100%)
Presence of distensibility of veins	137 (80.1%)

BMI, Body mass index; CKD, Chronic kidney disease.

normal vascular anatomy while vascular anomalies were noted in the rest. They included high branching of the brachial artery in 8 patients and absent cephalic vein in two patients. Calcification in the vessel wall was seen in 33 patients (19.3%), thrombosis (vein/artery) in five patients (2.9%), calcification with thrombosis in two patients (1.2%), and narrow caliber in three patients (1.8%). Vein distensibility was observed in 137 patients (80.1%), with mean distensibility of 30.5% and reactive hyperemia was observed in 169 (98.8%) of the patients.

Of the 171 patients who underwent AVF, 147 (85.9%) of the AVFs were in the upper arm, and 24 (14.1%) were forearm AVFs. The post-procedural means flow volumes and vein diameter at week 0 and week 6 were conducted. AVF blood flow and diameter were found to be increased progressively from day one to six weeks after construction (Figures 3 and 4). An increase in the flow volume and average vein diameter was seen in 78.9% of the patients.

AVF outcomes

A total of 109 (63.7%) had a functioning unassisted mature fistula. Early Access failures including immediate failure, immature fistula, and thrombotic and non-thrombotic complications (early dialysis suitability failure) occurred in 29 (16.9%) patients (Table 2). About 10 (10.1%) of the mature AVFs were pre-emptively constructed and were not used for dialysis till the completion of the study.

We additionally compared the clinical factors among mature AVF and failed AVF and observed the patients with smoking history were statistically higher in failed fistula groups ($P=0.04$). However, gender, BMI, and comorbidities such as diabetes, hypertension, or ischemic heart disease did not exhibit any statistical difference (Table 3).

Pre-operative and post-operative DUS comparison between unassisted matured AVF and failed AVF

The pre-operative DUS revealed that the cephalic vein diameter and presence of distensibility differed significantly between both groups. Flow rates in feeding arteries in the functioning group ranged from 650 to 1550 mL/min with an average of 1020.71 ± 252.78 mL/min. In the failure group, flow volumes in the feeding artery ranged from 150 to 325 mL/min with an average of 392.9 ± 128.08 mL/min. The average diameter of the vein which had a good adaptation to hemodialysis was 6.08 ± 0.99 mm and those patients who did not adapt to hemodialysis had an average diameter of 3.7 ± 1.57 mm. The increase in the immediate post-op vein diameter at six weeks between the groups was significant ($P<0.001$). Flow rates in the feeding artery between the groups in the immediate post-operative period as well as at six weeks were significant ($P<0.001$). We also found that the absence of distensibility strongly correlated with failure ($P<0.001$; Table 4).

In our study, the immediate post-operative vein diameter independently predicted the possibility of failure. A unit increase (1 mm) in outflow vein diameter immediately

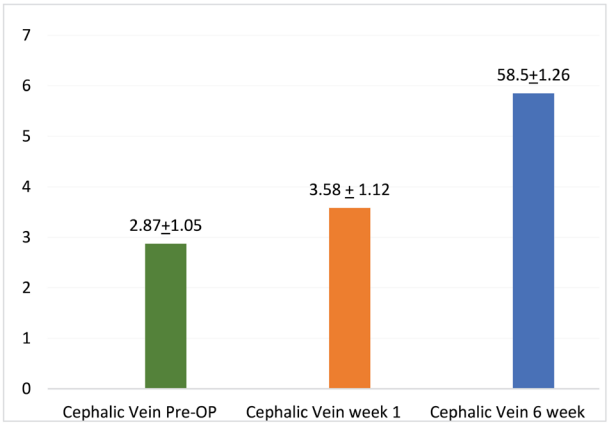

Figure 3. Progressive increase in cephalic vein diameter.

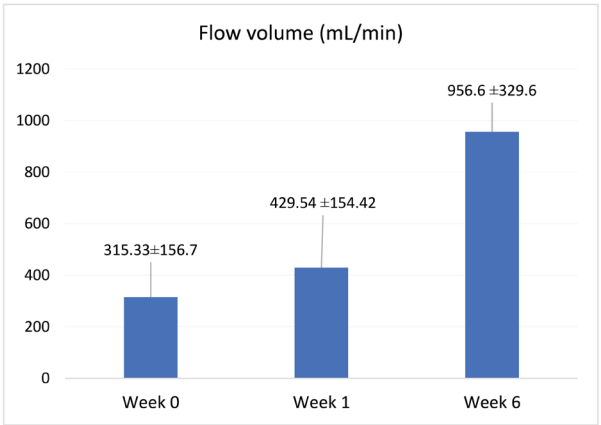

Figure 4. Progressive increase in AVF flow volume.

Table 2. Outcomes of AVF

Outcomes	n (%)
Unassisted mature AVF	109 (63.7)
AVF failure	29 (16.9)
Immediate failure	12 (7)
Early dialysis suitability failure (≤3 months)	17 (9.94)

AVF, Arteriovenous fistula.

after surgery showed significance in both univariate analyses (OR: 0.98, 95% CI: 0.35-3.99; $P<0.001$), and multivariate analysis (OR: 0.313, 95% CI: 0.148-0.663; $P<0.001$).

Discussion

The challenge for a patient with end-stage kidney disease is to achieve functioning vascular access. AVF when compared to grafts and catheters has a reduced incidence of infections and longer survival, at equivalent flow rates (1). DUS is utilized not just for examination of the arterial and the venous anatomy before the surgery, but also for postoperative monitoring of AVF maturation and ongoing AVF surveillance. Preoperative DUS shows promise in lowering primary AVF failure rates, however, its use as a routine screening tool for AVF remains debated. Based on level II evidence, the "KDOQI and European Best Practice Guidelines" recommend routine pre-operative ultrasonography, despite the lack of conclusive evidence (9). The present study analyzed the demographic factors, comorbidities, and physical examination prior to vascular access creation as well as compared the preoperative and postoperative DUS comparison between matured and failed AVF.

In this study, a total of 109 (63.7%) had a functioning unassisted mature fistula. AVF failure was seen in 29 (16.9%) patients of which 12 (7%) had an immediate

Table 3. Comparison of clinical characteristics between AVF outcomes

Clinical parameters	Unassisted mature (n=109)	Failed AVF (n=29)	*P* value[a]
Gender, n (%)			
Male	90 (82.5)	23 (79.3)	0.812
Female	19 (17.4)	06 (20.6)	0.502
BMI (kg/m^2)	22.7+2.7	21.67±3.03	0.083
Diabetes, n (%)	48 (44)	17 (58.6)	0.214
Hypertension (%)	99 (90.8)	26 (89.6)	0.818
Smoking (%)	30 (27.8)	14 (48.3)	0.004*
Ischemic heart disease (%)	33 (30.2)	5 (17.2)	0.223

BMI, Body mass index; AVF, Arteriovenous fistula.
[a] Chi-square test; * Significant.

Table 4. Pre-operative and post-operative DUS comparison between unassisted matured AVF and failed AVF

Vessels	Characteristics	Comparison between groups		*P* value[a]
		Unassisted mature AVF (n=109)	Failed AVF (n=29)	
		Pre-operative DUS		
Brachial artery	Diameter (mm)	4.54 ± 1.15	4.39 ± 1.25	0.557
	PSV (cm/s)	78.58 ± 20.2	75.21 ± 21.19	0.434
Radial artery	Diameter (mm)	2.39 ± 0.64	2.21 ± 0.6	0.712
	PSV (cm/s)	60.47 ± 20.54	61.29 ± 19.34	0.847
Cephalic vein	Wrist (RC AVF)	2.11 ± 0.64	1.76 ± 0.6	<0.001*
	Elbow (BC AVF)	2.99 ± 1.06	2.19 ± 0.7	<0.001*
Distensibility of veins		101 (92.7)	7 (24.1)	<0.001*
Reactive hyperemia		108 (99.1)	28 (96.6)	0.794
		Post-operative DUS		
Out flow vein diameter(mm)	0 weeks	3.77 ± 1.08	2.27 ± 0.41	<0.001*
	6 weeks	6.08 ± 0.99	3.72 ± 1.51	<0.001*
Average blood flow (mL/min)	0 weeks	466 ± 120.96	154.3 ± 55.85	<0.001*
	6 weeks	1020.71 ± 252.78	392.9 ± 128.08	<0.001*

AVF, Arteriovenous fistula; RC, Radiocephalic; BC, Brachiocephalic; PSV, Peak systolic velocity.
[a] Independent *t* test; * Significant.

failure and early dialysis suitability failure (≤3 months) was seen in 17 (9.9%) patients. Consistent with these findings, a lower rate of immediate failure was reported by Ferring et al (10) which was seen in 4% of patients and primary failure in 11%.

The mean age was 51.7 ± 13.84 years and it had no significant difference between mature AVF and failed AVF in our study. This is unlike other studies, wherein the elderly group had a significantly higher incidence of non-maturing fistulas, doubling the risk for failure (OR: 2.23; 95% CI: 1.25 to 3.96) (11). Increasing age is related to a decline in the ability to maintain adequate vessels, which occurs with normal aging and is further exacerbated by concurrent disease (comorbidities like diabetes, hypertension, and peripheral vascular disease) (11). In this study, the mean BMI was 22.60 ± 2.85 kg/m^2 with no significant difference in the AVF outcomes of our study groups. Diabetes was the most common etiology of end-stage kidney disease in the present study, which was consistent with the findings by Ferring et al (10).

Various factors affecting AVF maturation in terms of the presence of diabetes mellitus, hypertension, ischemic heart disease, and smoking were analyzed in this study. Studies have suggested that maturation is negatively affected by the presence of diabetes (11). Diabetes manifests itself as pro-thrombotic conditions; also causes endothelial damage, altered growth factors, and increased extracellular matrix deposition thus interfering with the maturation of AVF (12). Farber et al (13) and Joseph et al (14) showed that control of diabetes has a positive impact on preventing fistula thrombosis and was a predictor of patency in their studies. Holland et al (8) found that with careful preoperative assessment of vessels by DUS, diabetes did not impact the AVF outcomes. Though 65 patients of our study population had diabetes, it had no impact on AVF outcome ($P = 0.21$) which emphasizes the need for careful assessment of the vessels. Manne et al (15) study showed that hypertension was a major factor that profoundly affects vascular access patency. The significance of hypertension could not be assessed in the present study as the number of non-hypertensive patients was small when compared with those with hypertension. Also, no correlation between the presence of ischemic heart disease and the outcomes of the AVF was seen, which was consistent with Dasari et al (16). However, smoking was found to be more prevalent in those with failed fistulas, with a statistically significant difference between the groups ($P = 0.04$). Similar findings were reported by Griffin et al (17) who found that the rate of fistula failure was significantly higher ($P = 0.001$) in smokers compared to ex-smokers and non-smokers combined.

In our study, all were found to have a negative Allen test indicating a patent palmar arch and a blood pressure difference of less than 10 mmHg between the upper limbs with 137 (80.1%) of them having clinically distending veins. Although in our study we did not divide the patients into groups all the patients underwent a thorough physical examination and a DUS in the preoperative period. Harduin et al (18) and Smith et al (19) hypothesized that impaired distensibility is related to failures and found that forearm venous distensibility is a predictor of AVF success and it was absent (90%) in all patients who had an unsuccessful AVF. The clinical data required to make any recommendations on minimum lumen size is limited due to the heterogeneity in reported metrics. A study by Mat Said et al (20) showed that the physical examination with preoperative DUS significantly improves the short-term patency and the suitability of AVF for dialysis which is similar to our study.

In this study, 147 (85.9%) of the AVFs were in the upper arm and 24 (14.1%) forearm AVFs. An increase in the flow volume and average vein diameter was seen in 78.9% of the patients from day one to 6 weeks after construction. Calcification in the vessel wall was seen in 33 patients (19.3%), thrombosis (vein/artery) in five patients (2.9%), calcification with thrombosis in 2 patients (1.2%), and narrow caliber in three patients (1.8%). Similarly, in a study by Nguyen et al (21), wrist AVF was conducted in 80% of participants. Early complications, such as bleeding and anastomosis, occurred in only one (1%) and two (2%) cases, respectively. The radial artery and brachial artery diameters found in our study were consistent with Srivastava et al (22) wherein 173 patients' analysis revealed mean radial artery and cephalic vein diameter to be 2.27 ± 0.66 mm (range;1.4–3 mm) and 2.24 ± 0.33 mm (range;1.6–3.7 mm), respectively with a mean PSV in radial artery being 54.76 ± 17.6 cm/s (range 15.7–92.5 cm/s).

In our study, the difference in the cephalic vein diameters for AVF at the wrist and elbow were statistically significant ($P < 0.001$) as well as a significant difference in the distensibility of veins between mature and failed AVF. The average vein diameter in the mature AVF group was 6.08 ± 0.99 mm was significantly better when compared to 3.72 ± 1.51 mm in the failed AVF group ($P < 0.001$). Even the mean flow rate of 1020.71 ± 252.78 mL/min in the mature AVF group was significantly better when compared to 392.9 ± 128.08 mL/min ($P < 0.001$).

In this study, other than vein and artery diameter we also considered vein distensibility and the presence of reactive hyperemia and found a statistical difference between groups in terms of the presence of distensibility ($P < 0.001$) which is identical to the study by Malvorh et al (23) wherein they described the significance of characteristics such as distensibility, the thickness of the arterial wall, and the resistance index, in preoperative assessment of AVF for better outcomes.

In our study, we found primary unassisted patency rates of 78.98% at 6 weeks and the primary AVF failure rate was 17 %, which is similar to results from various centers across the world (23 to 40%) (24). The role of arterial diameter in predicting AVF success remains controversial. Farrington

Study Highlights

Maintaining well-functioning AVF remains the greatest challenge. This study emphasizes the use of DUS in both the pre and postoperative periods in addition to conventional physical examination to enhance the success of favorable AVF outcomes.

et al (25) found arterial diameter to be a major predictor of unaided AVF development, whereas vessel diameter did not predict AVF functionality, according to Wilmink et al (26). However, in our study, there was no significant difference in the arterial diameter between those with an unassisted patency and failure in both radiocephalic and brachiocephalic AVF. This could be explained by the fact that the majority of the fistulas in the present study were BC AVF and currently no recommendations are available regarding the brachial artery diameter and there are very few studies comparing the outcomes of brachiocephalic AVF with diameters, pointing out that it is less important to the surgical procedure's success. Our findings suggest that diameter should not be a reason to avoid the construction of AVF. In our study, there is an increase in the arterial flow volume and diameter of the draining vein, and these are important factors in the maturation of a fistula. An increase of draining vein diameter by an average of 56% and flow volume by 55% between the completion of the first DUS exam and the second at six weeks was seen and this was seen in 80% of our patients. Malovrh et al(23) reported similar findings when they observed that venous diameter increased by 48% in patients who had a successful 83 fistula.

In our analysis, 78.9 % of the study population had an arterial flow volume of ≥600 mL/min and the diameter of the vein >6 mm at week 6-8 following construction of AVF, fulfilling criteria for mature AVF according to NF-KDOQI.

Conclusion

The majority of the patients in our settings had unassisted AVF fistula. The diameter of the cephalic vein, the presence of distensibility, and the increase in both the draining vein diameter and flow volume in the artery at six weeks were the predominant factors determining the success of AVF. The history of smoking was found to be the only clinical factor associated with AVF failure. Our study emphasizes the use of DUS in both the pre and postoperative periods in addition to conventional physical examination to enhance the success of favorable AVF outcomes. Therefore, we recommend the use of DUS for pre- and post-operative assessment in nephrology practice.

Limitations of the study

The study has several limitations, including a significant proportion of brachiocephalic fistulas, a small sample size for immediate failures that prevented separate assessment of predictive risk factors, the absence of long-term follow-up, and the lack of calculation of the artery's resistive index, which may impact the outcomes of AVF.

Authors' contribution

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Writing–original draft: All authors.
Writing–review & editing: Mohan V Bhojaraja, Shankar Prasad Nagaraju, Dharshan Rangaswamy, Ravindra Prabhu Attur and Srinivas Vinayak Shenoy.

Conflicts of interest

The authors declare no competing interests.

Ethical issues

The research conducted in this study followed the principles outlined in the Declaration of Helsinki and received approval from the Kasturba Medical College and Kasturba Hospital Institutional Ethics Committee (#IEC-438) as well as registration with the Clinical Trial Registry of India (CTRI) under REF#2020/10/037880, with informed consent obtained from all participants. The authors have fully complied with ethical issues, such as plagiarism, data fabrication, and double publication.

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