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Research Article

Comparison of Clinical Evaluation with Duplex Ultrasound Parametersin Predicting Early Hemodialy Sisarteriovenous Fistula Failure

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ABSTRACT

Introduction:This observational study aimed to compare the diagnostic accuracy of physical evaluation (PE) and duplex ultrasound (DUS) parameters in predicting early arteriovenous fistula (AVF) failure in patients undergoing hemodialysis, as well as identify risk factors associated with early AVF failure. Early AVF failure, defined as inadequate development or failure within the first three months, can often be salvaged with prompt percutaneous interventions. ***Methods:*** The study was conducted at the Department of Nephrology, Govt. T D Medical College, Alappuzha, and included various patient demographic and laboratory variables, such as age, sex, smoking, blood pressure, diabetes, dyslipidemia, coronary artery disease, hemoglobin, lipid profile, HbA1C, serum calcium, serum phosphorus, intact parathormone (iPTH), and serum ferritin. Physical examination of AVFs and DUS were performed immediately postoperatively and at 2 weeks, 6 weeks, and followed up for 3 months, with DUS serving as the gold standard for validation. ***Results:*** The study outcomes showed that among 29 cases predicted as successful by PE, 24 were ultimately successful, while 5 were incorrectly predicted as failures by DUS. Among the 31 cases predicted as failures by PE, 25 indeed failed, but 6 were incorrectly predicted as successful by DUS. PE exhibited a sensitivity of 83.3%, specificity of 83.3%, positive predictive value of 82.8%, and negative predictive value of 80.6%, with an overall accuracy of 81.6%. ***Conclusions:*** This study highlights the importance of early identification and salvage of non-maturing AVFs to support dialysis. It suggests that while PE can be a reasonably accurate method, DUS plays a crucial role in improving the diagnostic accuracy for early AVF failure. Further research could help refine these diagnostic approaches and enhance the success rates of AVF in hemodialysis patients.

INTRODUCTION

Patients with an end stage renal disease who are hemodialysis dependent are required to maintain a patent vascular access. While an arteriovenous fistula (AVF) is the best available form of hemodialysisaccess, a significant number of fistulae (28 to 53%) fail to mature adequately to support dialysis therapy.Early AVF failure is defined as an AVF that never develops adequately to support dialysis or fails with in the first 3 months of its use[1]. Venous stenosis and the presence of accessory veins are the two main causes of early failure.Recent data have demonstrated that a great majority of such AVFs can be successfully salvaged by percutaneous interventions[2]. This can minimize catheter use and its associated complicatio-ns. Henceidentification of a non-maturing AVF is important. Secondly, access stenosis is a progressive process and eventually culminates in complete occlusion, leading to access thrombosis. In this context, the opportunity to salvage the AVF that fails early may be lost if not identified early[3, 4]. Arteriovenous Fistula is shown in **figure 1.** There is no universal definition for a mature AVF; the one adopted in the updated NKF-KDOQI guidelines has been widely in use. KDOQI introduced the role of 6s to define maturation (Flow of 600 ml/min, an AVF located less than 6 millimetres from the skin surface to facilitate successful repeated cannulation by HD staff and finally a minimal diameter of 6 millimetres. In most successful fistulae, these parameters are met within first 4 to 6 week, so the assessment of a newly created AVF and identification of candidates with early AVF failure should be-

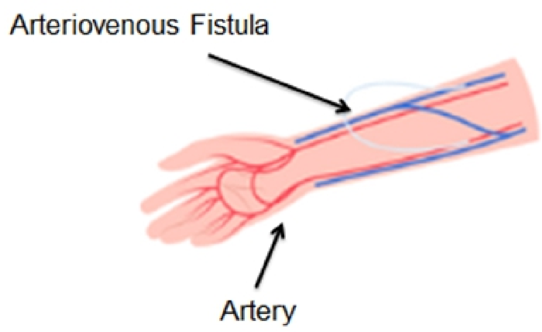

Figure 1: An Arteriovenous Fistula, is an abnormal connection between an artery and a vein.

begin early[5, 6].

Duplex Ultrasonography can successfully identify candidates who are likely to develop early AVF failure. It is not readily available in all centers and adds to the medical care expenses, so physical examination of AVF has been highlighted as a convenientand economic method to monitor early AVF dysfunction. Most commonly encountered problems such as vascular stenosis and presence of accessory veinsthat result in early AVF failure can be diagnosed easily with skillful physical examinationand that can be taught to nephrology trainees and nurse. Early detection of dysfunction would lead to timely intervention to correct the problem and prolong the life of the access[7, 8].

Various patient factors have been suggested to be associated with poor AVF maturation, including diabetes mellitus (DM), female sex,advanced age, some comorbid conditions (cardiovascular disease, peripheral artery disease, diabetes, needing assistance, or institutionalized status), and obesity. Dialysis vintage longer than 1 year, and catheter or arteriovenous graft use at ESRD incidence were also associated with lower rates of successful AVF maturation. In contrast, hypertension and prior AVF placement at ESRD incidence were associated with higher rates of successful AVF maturation[9, 10].

Clopidogrel has been shown to significantly reduce the incidence of early AVF thrombosis; however, it failed to increase the number of fistulae suitable for haemodialysis use in 3–4 months. A history of stroke or transient ischemic attack, and dependence on dialysis at the time of access placement were associated with lower probabilities of maturation[11, 12].

We designed this study to compare the diagnostic accuracy of clinical evaluation and duplex ultrasound parameters in predicting early arteriovenous fistula failure in patients undergoing hemodialysis and to find out the risk factors associated with early AVF failure.

MATERIALS AND METHODS

This is an observational, prospective longitudinal study conducted in wards and OP of Department of Nephrology in a tertiary care centre in South India in patients of age above 18 ye-ars, of both genders with chronic kidney disease with new arteriovenous fistula creation, both brachiocephalic fistula and radio cephalic fistula. Patients with non-functioning fistula immediately after surgery were excluded from the study. After getting informed consent, subjects underwent a history and physical examination with detailed review of past medical history. Physical examination of AVF was done at immediate postoperative period and at 2 weeks, 6 weeks and followed up for 3 months. The criteria include an easily palpable superficial AVF with adequate diameter for cannulation and a uniform thrill to palpation. The accessible draining vein needed to be relatively straight and at least 10 cm in length. These patients also underwent duplex ultrasound examination of the AVF for diameter and blood flow. Ultrasound examination of the AVF was performed with the patient in an upright seated position at 2weeks, 6 weeks and followed upto 3 months. The arm was be positioned at 45° from the body and comfortably supported by towels on a mobile instrument stand. An initial overview of the AVF feeding artery, draining vein, and anastomotic region was obtained. Gray-scale examination of the vessel diameter was performed in both the transverse and longitudinal planes. The diameter of the draining vein was measured in the anteroposterior dimension in the transverse plane by using gentle transducer pressure. Draining venous diameter was measured at the caudal, middle, and cranial portion of the draining vein in the forearm if a forearm fistula or in the upper arm if an upper arm fistula. Three to five blood flow measurement were obtained in the draining vein of the AVF using colour Doppler. To decrease the possibility of encountering turbulent flow, these measurements were obtained in the middle of the forearm for a forearm AVF or the middle of the upper arm for an upper arm AVF, locations where stenosis or extremely curvy draining veins are rarely seen. Blood flow was evaluated in straight non tapering venous segment**(Figure 2).**

OBSERVATION AND RESULTS

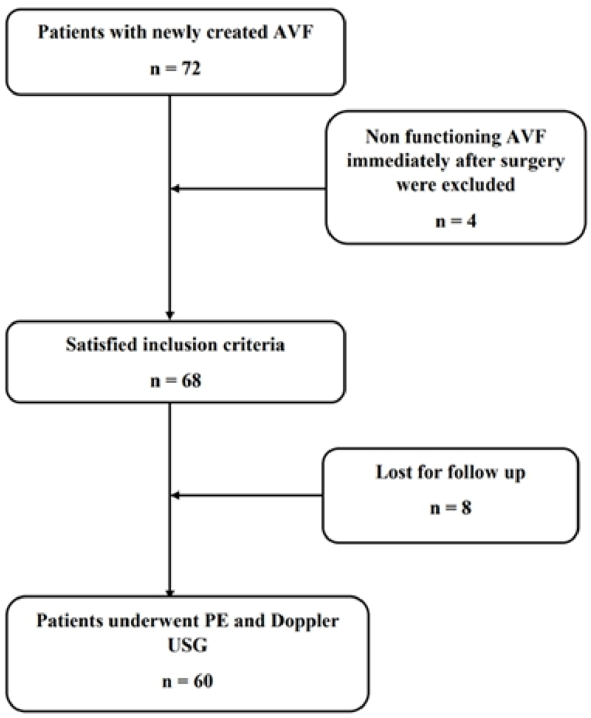

Figure 2: Representing the blood flow evaluated in straight non tapering venous segment

All the data collected were coded and entered in Microsoft Excel sheet which was re-checked and analysed using SPSS statistical software version 22. Categorical variables were represented using frequency and percentage. Pearson Chi-square test and Fisher's Exact test were used for comparing categorical variables between groups.

Early AVF failure is defined as an AVF that never develops adequately to support dialysis or fails with in the first 3 months of its use. Association of variables with early AVF failure were analysed.Diagnostic characteristics of physical examination were found out by comparing it with Doppler ultrasound. A p value of <0.05 was considered statistically significant.

RESULTS

Baseline demographic characteristics

The baseline demographic characteristics are given in **Table 1.** The male female ratio of the study population was 1:1. Diabetic nephropathy was the most common cause of chronic kidney disease in our study group.19 patients had a history of coronary artery disease and were already on antiplatelets, while 12 patients gave a history of POVD.All the patients were on hemodialysis and 10 patients had a previous history of failed AVF. Brachiocephalic arteriovenous fistula was the most common type of fistula created **(Figure 3).**31 patients had a history of central venous catheter insertion.

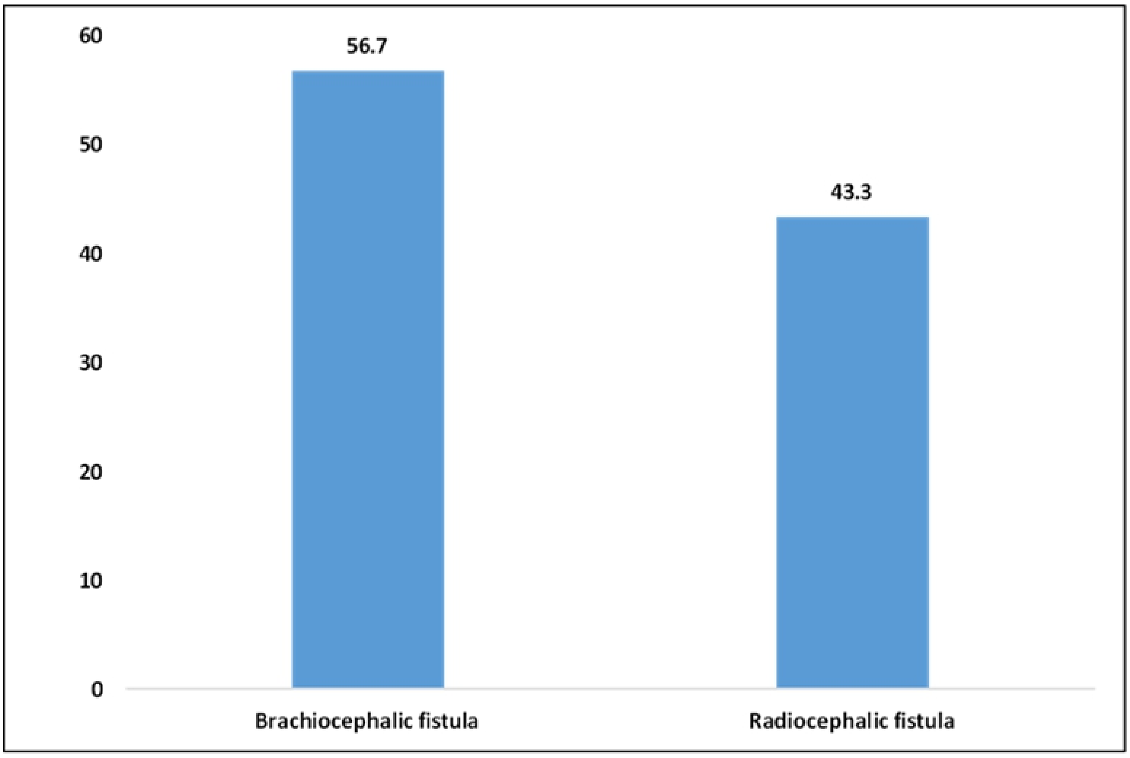

Figure 3: Shows that brachiocephalic arteriovenous fistula was the most common type of

Table1: Demographic characteristics of study subjects

Age	No(%)
18-30years	10(16.7)
30-45years	20(33.3)
45-60years	9(15)
>60years	21(35)

Causes of CKD	No(%)
Diabetic nephropathy	40(66.7)
Ischemic nephropathy	1(1.7)
Chronic glomerulonephritis	12(20)
Reflux nephropathy	5(8.3)
Obstructive nephropathy	2(3.3)

Hypertension	No(%)
YES	60(100)
NO	0(0)
Duration of hypertension	**No(%)**
<5years	20(33.3)
5-10years	16(26.7)
>10years	24(40)
Coronary artery disease	**No(%)**
YES	19(31.7)
NO	41(68.3)
Peripheral occlusive arterial disease	**No(%)**
YES	12(20)
NO	48(80)
Already on antiplatelet therapy	**No(%)**
YES	19(31.7)
NO	41(68.3)
Smoker	**No(%)**
YES	15(25)
NO	45(75)
Previous history of failed AVF	**No(%)**
YES	10(16.7)
NO	50(83.3)
Whether on dialysis	**No(%)**
YES	60(100)
NO	0(0)

Central venous catheters	No(%)
YES	31(51.7)
NO	29(48.3)

Factors associated with early AVF failure.

Demographic factors:

In this study**(Table 2)** demographic factors such as increased age, female sex, duration ofdiabetes mellitus for more than 10 years, presence of coronary artery disease and use of central venous catheters, were associated with increased failure rate. The type of fistula, previous history of AVF failure and dialysis vintage were not found to be associated with early AVF failure.

Table 2: Factors associated with early AVF failure Demographic factors

Variable	Final status of AVF		P value
	Success (N=30)	Failure (N=30)	
Age			
18-30years	5(50)	5(50)	0.012*
30-45years	15(75)	5(25)	
45-60years	5(55.6)	4(44.4)	
>60years	5(23.8)	16(76.2)	
Sex			
Male	20(66.7)	10(33.3)	0.010*
Female	10(33.3)	20(66.7)	

Variable	Final status of AVF		Pvalue
	Success (N=30)	Failure (N=30)	
Diabetes mellitus			
Yes	20(50)	20(50)	1.000
No	10(50)	10(50)	
Duration of diabetes	**N=20**	**N=20**	
5-10years	15(100)	0(0)	<0.001*
>10years	5(20)	20(80)	

Variable	Final status of AVF		P value
	Success (N=30)	Failure (N=30)	
Coronar yartery disease			
Yes	5(26.3)	14(73.7)	0.012*
No	25(61)	16(39)	
Peripheral occlusive arterial disease			
Yes	3(25)	9(75)	0.053
No	27(56.2)	21(43.8)	
Already on antiplatelet therapy			
Yes	5(26.3)	14(73.7)	0.012*
No	25(61)	16(39)	
Smoker			
Yes	5(33.3)	10(66.7)	0.136
No	25(55.6)	20(44.4)	
Type of AVF			
Brachiocephalicfistula	15(44.1)	19(55.9)	0.297
Radiocephalicfistula	15(57.7)	11(42.3)	
Previous history of failed AVF			
Yes	5(50)	5(50)	1.000
No	25(50)	25(50)	

Variable	Final status of AVF		Pvalue
	Success (N=30)	Failure (N=30)	
Duration of dialysis			
<6 months	25(55.6)	20(44.4)	0.136
6-12months	5(33.3)	10(66.7)	
Central venous catheters			
Yes	10(32.3)	21(67.7)	0.004*
No	20(69)	9(31)	

Biochemical parameters: Increased AVF failure rate was also found to be associated with severe anemia (Hb< 7 gm/dl), hypo--albuminemia, Hyperparathyroidism, high serum ferritin (>500 ng/ml) and HBA1C >7 **(Table 3).**

Table 3: Factors associated with early AVF failure (Pathological and biochemical values)

Variable	Final status of AVF		P value
	Success (N=30)	Failure (N=30)	
Hemoglobin			
>10 gm/dl	15(78.9)	4(21.1)	<0.001*
7-10 gm/dl	15(57.7)	11(42.3)	
< 7 gm/dl	0(0)	15(100)	
Serum albumin			
>3.5 gm/dl	15(78.9)	4(21.1)	0.007*
2- 3.5 gm/dl	15(37.5)	25(62.5)	
< 2 gm/dl	0(0)	1(100)	
Serum calcium			
8.6 – 10.3 mg/dl	15(62.5)	9(37.5)	0.114
< 8.6 mg/dl	15(41.7)	21(58.3)	

Serum phosphorus			
> 5.5 mg/dl	5(19.2)	21(80.8)	<0.001*
3- 5.5 mg/dl	25(92.6)	2(7.4)	
< 3 mg/dl	0(0)	7(100)	

Variable	Final status of AVF		P value
	Success (N=30)	Failure (N=30)	
Serum iPTH			
> 600 pg/ml	0(0)	25(100)	<0.001*
< 300-600 pg/ml	10(66.7)	5(33.3)	
< 300 pg/ml	20(100)	0(0)	
Serum ferritin			
> 500 ng/ml	10(71.4)	4(28.6)	0.009*
300-500 ng/ml	15(60)	10(40)	
< 300 ng/ml	5(23.8)	16(76.2)	
LDL cholesterol			
<100 mg/dl	0(0)	5(100)	0.052
>100 mg/dl	30(54.5)	25(45.5)	
HBA1C	**N=20**	**N=20**	
<7	15(88.2)	2(11.8)	<0.001*
>7	5(21.7)	18(78.3)	
MPV			
6.7 -7.5 fl	20(100)	0(0)	<0.001*
7.5 -9 fl	10(100)	0(0)	
9-11.5 fl	0(0)	30(100)	

Physical examination and doppler ultrasound parameters: Presence of AVF thrill, collapsibility, pulse augmentation were associated with good fistula outcomes, but presence of water hammer pulse, accessory vein (present in 15% of cases) were associated with poor outcome. Pre procedure cephalic vein diameter > 2 mm, radial artery diameter > 1.8 mm and brachial artery diameter > 3.5 mm were associated with increased success rate. Post operative vein diameter>6 mm and average blood flow of 600ml/min at 2 weeks and at 6 weeks were associated with successful outcomes. (Table 4). Failure to mature was the most common cause of AVF failure. Hematoma, thrombosis, stenosis and infection were the other common causes. (Table 5).

Table 4: Factors associated with early AVF failure (PE & DUS Parameters)

Variable	Final status of AVF		P value
	Success (N=30)	Failure (N=30)	
AVF pulse thrill			
Present	24(82.8)	5(17.2)	<0.001*
Absent	6(19.4)	25(80.6)	
Thrill			
Present	24(82.8)	5(17.2)	<0.001*
Absent	6(19.4)	25(80.6)	
Collapsibility			
Present	24(82.8)	5(17.2)	<0.001*
Absent	6(19.4)	25(80.6)	
Water hammer pulse	**N=30**	**N=5**	
Present	0(0)	5(100)	<0.001*
Absent	30(100)	0(0)	
Pulse augmentation			
Present	24(82.8)	5(17.2)	<0.001*
Absent	6(19.4)	25(80.6)	
Accessory vein			
Present	0(0)	9(100)	0.002*
Absent	30(58.8)	21(41.2)	
Radial artery diameter	N=15	N=16	
<1.5 mm	0(0)	11(100)	<0.001*
1.6-2 mm	0(0)	5(100)	
2- 3 mm	15(100)	0(0)	
Brachial artery diameter	**N=15**	**N=14**	
<3.8 mm	0(0)	14(100)	<0.001*
>3.8 mm	15(100)	0(0)	

Variable	Final status of AVF		P value
	Success (N=30)	Failure (N=30)	
Cephalic vein diameter			
<1.5 mm	0(0)	16(100)	<0.001*
1.6-2 mm	0(0)	5(100)	
2- 3 mm	30(76.9)	9(23.1)	
Post-operative vein diameter at 2 weeks			
<6 mm	0(0)	30(100)	<0.001*
>6 mm	30(100)	0(0)	
Average blood flow at 2 weeks			
<600 ml/min	0(0)	30(100)	<0.001*
>600 ml/mim	30(100)	0(0)	
Post-operative vein diameter at 6 weeks			
<6 mm	0(0)	30(100)	<0.001*
>6 mm	30(100)	0(0)	
Average blood flow at 6 weeks			
<600 ml/min	0(0)	30(100)	<0.001*
>600 ml/min	30(100)	0(0)	

Table 5: Cause of AVF failure (N=30)

Cause of AVF failure	No (%) (N=30)
Failure to maturation	16(53.3)
Hematoma	4(13.3)
Thrombus	3(10)
Stenosis	5(16.7)
Infection	2(6.7)

Comparison of physical evaluation with duplex ultrasound parametres

In this study physical evaluation (PE) was validated with gold standard test Doppler ultrasound. Out of the 29 cases which were predicted as successful by PE, 24 of them were finally successful. 5 of those 29 cases (predicted as successful by PE) which were predicted failure by DUS finally failed. Out of the 31 cases which were predicted as failure by PE, 25 of them finally failed. 6 of those 31 cases (predicted as failure by PE) which were predicted successful by DUS, were finally successful **(Table 6).** Physical examination has a sensitivity of 83.3 %, specificity of 83.3 %, positive predictive value of 82.8 %, and negative predictive value of 80.6%. Overall accuracy of the test was 81.6 % **(Table 7).**

Table 6: Comparison of physical examination with final status of AVF

Physical examination inference	Final status of AVF	
	Success	Failure
Success	24	5
Failure	6	25

Table 7: Diagnostic characteristics of Physical Examination

Sensitivity	Specificity	PPV	NPV	Accuracy
80	83.3	82.8	80.6	81.6

Table 8: Comparison of PE of the AVF with angiography and DUS examination

Study	n	Gold standard	Location	Sen.%	Spec.%	Kappa
Asif et al.[75]	142	Angiogram	Outflow	92	86	0.78
			Inflow	85	71	0.55
Leon and Asif[79]	45	Angiogram	Outflow	76	68	0.63
			Inflow	100	78	0.56
Campos et al.[80]	84	DUS	Overall	96	76	-
			Inflow	70	76	0.46
Tessitore et al.[81]	119	Angiogram	Outflow	75	93	0.63
			Inflow	98	88	0.84
Coentrão et al.[78]	177	DUS	Outflow	97	92	0.92
			Inflow	-	-	0.86
Maldonado-Carceles et al.[82]	99	Angiogram	Outflow	70	67	0.37
			Inflow	82	67	0.50

Table 9: Vessels diameters associated with successful AVF - DUS Parameters

Parameter	Brimble et al [90]	Malvorh [91]	Wilmink et al [92]	This study	P value
Cephalic Vein	>2 mm	>1.6 mm	-	>2 mm	<0.001
Radial Artery	>1.6 mm	>1.8 mm	-	>2mm	<0.001
Brachial Artery	-	-	> 3mm	>3.8mm	<0.001

DISCUSSION

In this study demographic factors such as increased age, female sex, presence DM, presence of CAD, presence of CVC, use of antiplatelet drugs for other diseases were associated with increased failure rate. Similar findings were noted in favoured study[13, 14]. Pre-existing CVC had a negative impact on the successful maturation of the newly created AVF. The mechanisms by which preexisting CVCs affect AVF maturation remain elusive. One proposed explanation is that the CVC impedes the maturation of its ipsilateral AVF via mechanisms of hemodynamic changes as a consequence of catheter-induced central venous stenosis. Another hypothesis, systemic inflammation, a common condition occurring in the setting of CVC placement, has been proposed as a pathogenic mechanism underlying neointimal hyperplasia which is a foundation of AVF failure[15, 16]. Presence of diabetes mellitus and history of atherosclerotic vascular disease were associated with increased AVF failure which may be due to the increased systemic inflammatory status as well as the poor quality of vessels due to increased vascular calcification observed in these conditions. Infavoured study peripheral occlusive vascular disease was associated with increased failure rate, but such difference was not recorded in this study[17, 18].

Increased AVF failure rate was found in cases of low Hb (< 7 gm/dl), low albumin (5.5 gm/dl), high serum iPTH(>600 pg/ml), high serum ferritin (>500 ng/ml) and HBA1C >7. Similar findings were noted in Favoured study. Increased MPV (> 9 fl) was associated with high AVF failure rate, similar finding was noted in Gulden Bilican *et al.* [19].

Presence of AVF thrill, collapsibility, pulse augmentation was associated with good fistula outcomes, but presence of water hammer pulse and accessory vein was associated with poor outcome. Of all the parameters studied venous diameter and blood flow across the fistula are the two main factors determining success of the fistula[20].

In the two studies mentioned, **(Table 8)** blood flow is measured on post procedure day 1 which is found to be half of the blood flow measurement after two weeks. Hence this study findings are comparable with those studies, ie>600 ml blood flow across AVF is associated with increased fistula success rate. In this study blood flow measurement at 2 weeks is almost equal to blood flow measurements at 6 weeks. So a fistula with parameters suggestive of failed fistula at 2 weeks will be a failed fistula at 6 weeks also (if no interventions are made) [21].

In 1992, Migliacci *et al.* showed that the results of physical examination in detecting stenosis had similar sensitivity (>80%) and positive predictive value (>80%) as continuous-wave Doppler ultrasound. Six prospective observational studies **(Table 8)** have compared the detection of stenosis by physical examination of the AVF to the gold standard tests, namely Doppler ultrasound (two studies) and angiogram (four studies) [22-26].

The PE was done by nephrologists, nephrology fellows or interventional radiologists. The accuracy of the PE was compared to the gold standard test using Cohen's kappa coefficient in the detection of inflow and outflow stenosis. A score of 1 indicated complete accuracy, whereas a score of 0 indicated total inaccuracy of the examination. The majority of kappa scores were greater than 0.5 for inflow and outflow stenosis in all the above studies suggesting that PE of the AVF is good alternative at detecting stenosis. Repetitive PE (monitoring) over a defined time span has not been compared to surveillance in detecting AVF dysfunction in observational or randomized studies. A meta-analysis of four randomized controlled studies in which blood flow measurements done at intervals of 1–3 months were compared to standard care, which showed that blood flow measurements were superior **(Table 9)[27-30]**. Blood flow surveillance significantly decreased the risk of thrombosis but not the risk of AV fistula loss.Based on these studies, regular perhaps, a monthly PE of AVF together with other clinical indicators is sufficient to detect AVF stenosis. Coentrão *et al.* have shown that the majority of general nephrologists have inadequate skills in AVF examination[31]. A total of 177 patients with AVFs, PE examination results were compared with 11 general nephrologists and a nephrology resident skilled in PE for evaluation. The results of their PE were compared with the gold standard of angiography[32]. The nephrology resident scored significantly better than the general nephrologists (inflow stenosis kappa 0.84 vs 0.49 and outflow stenosis kappa 0.92 vs 0.58). Leon and Asif showed that following 1 month of training in AVF examination, a nephrology fellow performed just as well as an interventional nephrologist. Experienced HD nurses can diagnose AVF immaturity and dysfunction with PE of the vascular access, although the length of time spent taking care of HD patients did not seem to improve these skills[33, 34].

Physical examination of arteriovenous fistula will be a convenient simple economic tool in predicting early arteriovenous fistula failure. Most commonly encountered problems (stenosis and accessory veins) that result in early AVF failure can be diagnosed easily with skillful physical examination[35]. Duplex ultrasound measurements at 6 weeks will be highly predictive of fistula maturation and adequacy of dialysis. A blood flow of 600ml/min and a venous diameter of at least 6 mm will be the most important predictors needed for an AVF to be adequate to support dialysis therapy. Combining venous diameter and flow volume will increase fistula adequacy predictive value[22].

CONCLUSION

Regular physical examination of the vascular access is a cost-effective and straightforward method to monitor dysfunction in arteriovenous fistulas (AVF), comparable to gold standard tests. Success of AVF largely depends on a cephalic vein diameter greater than 6 mm and a blood flow across the AVF exceeding 600 ml/min at 6 weeks. The "fistula first approach" is preferred for CKD patients. Several factors like the presence of a central venous catheter, low hemoglobin levels, increased mean platelet volume, and high iPTH levels can hinder AVF maturation. Advanced age, female gender, diabetes mellitus, and coronary artery disease are associated with early AVF failure. If ultrasound parameters indicate AVF failure at 2 weeks, it is likely to persist at 6 weeks without intervention. All healthcare providers involved in hemodialysis care should be adept at AVF examination to detect complications early.

LIMITATIONS

This study was limited by a small sample size, making it difficult to achieve statistical significance. Additionally, the absence of brachio-basilic fistula cases hindered a comprehensive analysis. The COVID-19 pandemic situation constrained the ability to perform interventions to salvage malfunctioning AVFs in all cases. Patient follow-up was restricted to only two visits at 2 weeks and 6 weeks post-surgery due to the pandemic, limiting the depth of review and monitoring.

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