Original Article

Primary Failure of Autogenous Arteriovenous Fistula: Critical Analysis

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Abstract

Introduction: Permanent vascular access is an essential intervention in patients with advanced chronic kidney disease (CKD) and its success depends on various non-modifiable and modifiable factors. Considering the element of unpredictability and failure, we attempted to analyze various factors responsible for primary arteriovenous fistula (AVF) failure in presumed high-risk groups. **Materials and Methods:** We conducted an observational study of newly created AVFs at a tertiary referral government hospital in Eastern India between January 2014 and June 2015. All adult CKD patients undergoing AVF creation were included. Primary AVF failure was assessed at 12 weeks and total follow-up was 24 weeks in presumed high-risk groups of females, patients aged ≥65 years and those with diabetes mellitus. **Results:** Female gender was at a higher risk of primary AVF failure if aged ≥65 years (P = 0.0026), second AVF creation (P = 0.03), loupe magnification not used (P = 0.03), arterial plaque (P = 0.028), absent immediate thrill, and with radiocephalic AVF (P = 0.02). Absent immediate thrill (<0.0001) and AVF size ≤5 mm (P = 0.002) were important independent risk factors for primary failure. Diabetes or elderly age did not have additional risk, except with uncontrolled hypertension and female gender. **Conclusion:** Female gender was at a higher risk of poor unassisted AVF patency if their age was ≥65 years, had second AVF creation, loupe magnification not used or if arterial plaque was present. An absence of thrill immediately or at 24 hours or an AVF diameter ≤5 mm were independent intraoperative factors for poor outcome. On the contrary, diabetics, elderly males and intimal thickness were essentially noncontributors for AVF failure, except in few subsets.

Keywords: *Arteriovenous fistula, chronic kidney disease, factors, primary failure*

Introduction

The incidence of chronic kidney disease (CKD) is progressively increasing in our country, and it is estimated that the yearly incidence of end-stage kidney disease is approximately 150–200 patients per million population.[1] Preparation for renal replacement therapy includes the creation and maintenance of permanent vascular access, which acts as a lifeline for these patients when they become dialysis-dependent. The history of arteriovenous fistula (AVF) is closely associated with the history of dialysis. Georg Haas, Willem Kolff, Nils Alwall, and William Thalheimer played important roles in creating practical hemodialysis using glass cannula and cellophane.[2] In 1943, venipuncture needles were used by Kolff for blood acquisition from the femoral artery and its reinfusion to the patient by venipuncture.[3] World over, medical professionals will always be thankful for the wonderful and practical work published by Brescia and Cimino in 1966, detailing creation of AVF in the forearm. Their work laid the foundation for safe and permanent vascular access for hemodialysis and established it as a standard procedure even after 50 years.[4]

AVF is the preferred permanent venous access for hemodialysis, by virtue of ease of creation, the safety of procedure, ease of maintenance, and lesser complications. Failure of AVF could be termed as primary when it never functioned or secondary when it has been functional for some period prior to occlusion. Various factors contribute to the primary failure of the AVF. Female gender, advanced age, and diabetes or hypertension are presumed high-risk groups for primary failure.[5-14] In the present study, we critically analyzed the preoperative, intraoperative, and postoperative factors responsible for primary failure of AVF in these high-risk groups.

How to cite this article: Venkatnarayanan R, Dogra PM, Bavdekar R, Singh SK, Mondal AK. Primary failure of autogenous arteriovenous fistula: Critical analysis. Indian J Nephrol 2020;30:382-90.

Received: 17-06-2019
Revised: 05-09-2019
Accepted: 10-11-2019
Published: 11-11-2020

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Access this article online

Website: www.indianjnephrol.org

DOI: 10.4103/ijn.IJN_214_19

Quick Response Code:

Materials and Methods

We conducted an observational study at the departments of plastic surgery and nephrology of a tertiary referral government hospital in Eastern India. The study included 197 patients with CKD (Stage 5) aged between 15 and 80 years who underwent AVF creation at this center between January 2014 and June 2015. Exclusion criteria were AVF (functional or nonfunctional) created at other centers, thrombosed veins, uncooperative patients, and patients with gross uremic symptoms unable to tolerate the surgery time. Informed consent was obtained from all patients prior to enrolment in the study. Prior approval from the institutional ethical committee of the hospital was taken in December 2013.

The study parameters were divided into preoperative, intraoperative, and postoperative parameters. The considered preoperative parameters were patient characteristics like age, sex, the onset of CKD, associated comorbid conditions, availability of patent cephalic vein, Allen's test, hemodialysis requirement (HD) and condition of the overlying skin. A single radiologist (trained in intervention radiology) assessed the intima–media thickness (IMT) of radial and brachial artery (≤0.25 mm and ≥0.26 mm) and cephalic vein diameter using ultrasound (USG) with a 10 MHz linear transducer of GE LogiqP5, selecting veins with >2 mm diameter. The following were the intraoperative parameters:

- Site of AVF [radiocephalic AVF (RCAVF) vs brachiocephalic AVF (BCAVF)]
- Type of AVF created [end-to-side (E-S) vs side-to-side (S-S)]
- Presence of palpable thrill over the vein after the release of clamps
- Pulsatile flow in the vein
- Thickness of arterial wall measured by ophthalmic calipers
- Presence of atherosclerotic plaques in the arterial intima
- Vascular suture size
- Use of loupe magnification
- Difficulty in the closure of skin after fistula creation.

The following were the post-operative parameters:

- Size of AVF by USG at 24 hours (h)
- Presence of persistent palpable thrill over the venous segment at 24h after surgery
- Pulsatile flow in the venous segment.

All the AVF surgeries were conducted by a team of three plastic surgeons, one nephrologist, and one general surgeon in different combinations. A standard surgical technique was used for doing AVF creation. An ophthalmic caliper was used to measure the diameter of the vessels in vivo. E-S AVF was created with an end vein to side artery anastomosis, whereas for S-S AVF, distal end of vein beyond AVF was ligated. Non-absorbable sutures of different sizes were used for anastomosis. Clinical evaluation of AVF was done at 24 h. Patients and their relatives were given relevant instructions about the care of the operated arm. Written instructions about how to feel for the thrill were given, and the patients were asked to report any coldness, numbness, ulcers, and discoloration at fingertips. Handball exercises were taught to patients before discharge. Patients were under follow-up of the surgeon in the initial week and the nephrologist thereafter. Hemodialysis with heparin was avoided in the initial 48 h to avoid inadvertent episodes of hemodynamic instability and prevent a remote possibility of surgical site bleeding.

The analysis was done to assess the influence of preoperative, operative, and postoperative factors in causing primary AVF failure in three presumed high-risk groups, i.e., female gender, higher age group (≥65 years), and diabetic patients. The primary objective was assessment of the above parameters on primary AVF failure at 24 weeks. The secondary objective was to analyze the effect of various factors on primary AVF failure at 12 weeks and the mechanical and infective complications. We defined primary AVF failure in our study as an AVF that could never be utilized for hemodialysis or fails within 12 weeks of use. The mechanical complications considered were thrombosis of AVF, bleeding, and hematoma at surgery site within 1 week. The infective complications considered were local cellulitis and abscess formation, dehiscence of wound because of subcutaneous infective collection and features of systemic bacteremia.

The statistical technique applied was the Chi-square test or Fischer's exact test for comparing two qualitative or categorical variables and student's 't' test or Mann–Whitney test wherever applicable for continuous data. Relative risk (RR) and odds ratio (OR) were calculated for specific multivariate analysis. RR was calculated to ascertain the attribution of primary AVF failure in either of the three risk groups (female gender, age ≥65 years, and diabetes) with AVF site (RCAVF vs BCAVF), type of AVF (E-S vsS-S), IMT of radial/brachial artery, diameter of AVF, and duration of hemodialysis. OR was calculated to ascertain the attribution of either of these three high-risk groups with the opposite gender, diabetes status, hypertension control categories, previous nonfunctional AVF, presence of arterial plaque, use of loupe magnification, and presence of intraoperative thrill and thrill at 24 h of surgery. The Statistical Package for the Social Sciences (SPSS) Software (version 18.0, SPSS, Chicago, IL, USA) was used for statistical analyses. A $P < 0.05$ was considered statistically significant.

Results

Data were collated for 197 patients suffering from Stage 5 CKD who had undergone AVF creation for permanent vascular access for hemodialysis. The standard surgical technique was used for the creation of AVF and patients were followed up for the initial 7 days by the operating

surgeon and then by the treating nephrologist. The surgical teams comprised of three plastic surgeons, one nephrologist, and one general surgeon. As per protocol, all patients were followed up until 24 weeks. The results were analyzed for determining the primary failure rate of AVF among the three presumed high-risk groups (females, age ≥65 years, and diabetes) in these patients and were analyzed in three subgroups: according to gender (male vs female), age (<65 years vs ≥65 years) and presence of diabetes (yes vs no).

Correlation of general variables and intraoperative variables on overall AVF success and primary AVF failure

The male to female ratio was 1.4:1, whereas, the ratio of age <65 years to ≥65 years was 3.3:1, and the ratio of diabetics to nondiabetics was 0.8:1. The mean age of males was 48.22 ± 18.62 years, whereas females averaged 45.43 ± 17.82 years [Table 1]. Diabetes was the most common etiology of CKD (44.2%). The female gender dominated the chronic tubulointerstitial nephritis (CIN) etiology (39% vs 28.6%, males), whereas the male gender dominated all the other etiologies, though this was statistically non-significant (NS). 38.1% patients were on hemodialysis for ≥2 weeks and 18.3% had history of previous AVF failure. 71.6% of males required ≥3 antihypertensives for blood pressure control as against 28.3% females (P = 0.001). Though mean serum albumin was comparatively less in males, it was not associated with an increased risk of primary AVF failure (RR = 0.69, 95% confidence interval [CI] = 0.23–1.65, P = 0.28).

The primary unassisted patency rate was 91.4% (93.2% males and 89% females); whereas, it reduced to 88.3% (88.8% males and 87.8% females) at 12 weeks and 85.8% (86.9% males and 84.1% females) at 24 weeks of follow-up. Primary AVF failure was seen on the table in 8.6% patients whereas it increased to 11.7% at 12 weeks [Figure 1].

During the follow-up period of 24 weeks, five fistulas became nonfunctional, whereas six patients with functional AVFs expired. The nonfunctional AVF were re-explored and an attempt to achieve primary assisted patency was done, but this subset has not been included in this study. Various preoperative factors were analyzed gender wise for relation to failure/success of AVF at different intervals for 24 weeks [Table 2]. The presence of diabetes did not increase the risk of primary AVF failure (RR = 1.10, 95% CI = 0.70–1.73, P = 0.65). The use of ≥3 antihypertensive medications did not have any negative impact on the primary failure of AVF (RR = 0.94, 95% CI = 0.59–1.50, P = 0.82). Thirty-six patients included in the study had previously nonfunctional and failed AVFs and 86% of patients in this subset had a good primary unassisted patency, which was functional at 24 weeks. However, previously failed AVFs did not have any negative attributive value on the outcome of second AVF creation (RR = 0.88, 95% CI = 0.47–1.66, P = 0.70). Seventy-five patients were already on hemodialysis for more than two weeks and only 14.7% of these patients had primary failure of AVF. However, there was no increased risk of AVF failure among those already on hemodialysis for >2 weeks duration at the time of AVF creation (RR = 0.89, 95% CI = 0.55–1.41, P = 0.66), despite hemodynamic variability because of ultrafiltration removal during the process, thereby risking intradialytic hypotension and eventual AVF failure.

The success rates of S-S anastomosis was significant compared with E-S anastomosis (P = 0.04). BCAVFs and

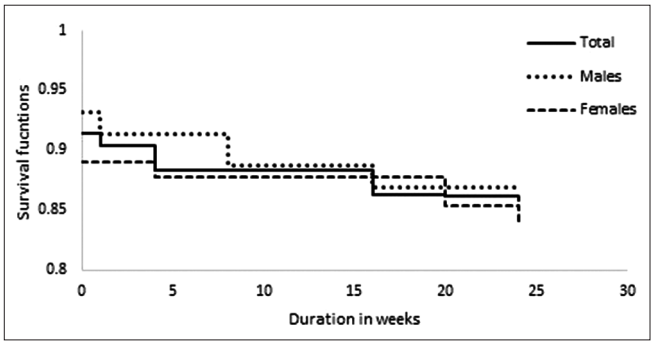

Figure 1: Kaplan–Meier plot showing AVF survival over the duration of 24 weeks

Table 1: Baseline characteristics detailed genderwise

Variable	Male (n=115)	Female (n=82)	P
Age (in years)	48.22±18.62	45.43±17.82	0.3
DM, n (%)	52 (45.2)	35 (42.6)	0.38
CGN, n (%)	29 (25.2)	14 (17.1)	0.45
CIN, n (%)	33 (28.6)	32 (39)	0.39
ADPKD, n (%)	1 (0.9)	1 (1.2)	1
Dialysis, n (%)	49 (42.6)	26 (31.7)	0.1
Hypertension (≥3 drugs)	86 (74.7)	34 (41.4)	0.0001
Hemoglobin (g/dL), mean±SD	9.45±3.24	8.98±2.73	0.45
S. creatinine (mg/dl), mean±SD	5.42±3.34	5.73±3.02	0.01
S. albumin (g/dl), mean±SD	3.29±1.97	3.51±1.73	0.56

DM=Diabetes Mellitus, CGN=Chronic glomerulonephritis, CIN=Chronic tubulointerstitial nephritis, ADPKD=Autosomal dominant polycystic kidney disease, SD=Standard deviation

Table 2: Influence of gender with pre- and intraoperative variables on AVF success

Variable ↓	Functional AVF→	Males				Females			
	Subgroup↓	Baseline (*n*=115)	24 h (*n*=107)	12 week (*n*=102)	24 week (*n*=100)	Baseline (*n*=82)	24 h (*n*=73)	12 week (*n*=72)	24 week (*n*=69)
Age	≥65 years	41	40	38	37	5	2	2	2
Diabetes	Present	52	48	47	46	35	30	29	28
Hemodialysis	≥ 2 weeks	49	48	46	44	26	23	22	20
Anastomosis	End-side	66	59	58	56	42	37	36	35
	Side-side	49	48	44	44	40	36	36	34
Type of AVF	RC	102	97	93	93	45	37	36	33
	BC	13	10	9	7	37	36	36	36
Arterial IMT	≥0.26 mm	75	70	69	67	29	24	23	22
Arterial Plaque	Present	53	48	43	43	23	18	18	16
Loupe Magnification	Not Used	29	27	27	27	19	13	13	13
Thrill >60 min	Present	108	107	102	100	72	73	72	69
AVF Diameter	≤5 mm	26	20	16	14	28	19	18	15

AVF=Arteriovenous fistula, RC=Radiocephalic, BC=Brachiocephalic, IMT=Intima–media thickness

RCAVFs had equal success rate (86% vs. 85.7%, *P* = NS). The selection of suture material for anastomosis was based on the size and wall thickness of the artery and vein. The majority (*n* = 159, 80.7%) of the patients underwent surgery with 6–0 polypropylene suture, whereas 7–0 suture was used in 27 (13.7%) cases. 5.1% (*n* = 10) cases required 8–0 polypropylene suture because of thin veins. One patient required 5–0 polypropylene suture because of the thick artery and presence of thick plaque in it. Despite the use of different sizes of suture material for AVF creation, there was no significant impact on the success of AVF (*P* = 0.53). The success rate was numerically higher in patients with 8–0 suture (because of thin arteries and veins) but was statistically insignificant (*P* = 0.4).

Correlation of gender, age, and diabetes with clinical characteristics and intraoperative variables on AVF success

AVF success rates were correlated with different factors, correlating gender with pre- and intra-operative variables [Table 2], age with pre- and intra-operative variables [Table 3], diabetes with pre- and intra-operative variables [Table 4] on AVF success. Of the total patients, 35.6% of the males were aged ≥65 years as compared with 6.1% females (*P* = 0.03), whereas 45.2% males were diabetics compared with nondiabetics (54.8%) on analysis of preoperative variables among gender groups at baseline. A total of 26.1% of males had previously failed AVF compared with 7.3% females (*P* = 0.02), but the incidence was equal among age groups. Of the 61.9% dialysis naive patients (no HD or <2 weeks of HD), the gender distribution [Table 2] and diabetes status [Table 4] was almost equal, whereas the difference was significant in age groups (77.9%, <65 years vs 21.1%, ≥65 years, *P* = 0.001). The majority of the patients underwent E-S AVF creation, whereas males dominated S-S AVF. All BCAVF were end vein-to-side artery anastomosis, whereas among RCAVF, 60.5% were S-S anastomosis and 39.4% were end vein-to-side artery anastomosis. Majority had RCAVF (74.6%) with males dominating it (69.4% vs 30.6% females), whereas females dominated BCAVF (74% vs 26% males). Loupe magnification was used in 75.6% cases with near equal gender distribution. [Table 2]. Presence of intraoperative thrill at 60 min and 24h duration was seen in 91.4% cases (males-93.2%, females-89%, *P* = NS), the number reduced over the follow-up period of 6 months with functional AVF in 85.8% patients. There was no increased risk of primary AVF failure among either gender with age <65 years, the presence of diabetes, first AVF creation, uncontrolled hypertension, or while being on HD ≥2 weeks duration.

Multivariate analysis was done for the presumed high-risk groups with various factors as well as for low-risk groups. There was a statistically significant risk of developing primary AVF failure in female gender in the presence of age ≥65 years (OR = 10.05, 95%CI = 1.49–67.77, *P* = 0.018) and in those undergoing second AVF creation (OR = 6.6, 95%CI = 1.17–37.34, *P* = 0.03; RR = 7.5, 95% CI = 1.57–35.6, *P* = 0.01) [Table 2].

Similarly, females were at a higher risk of primary AVF failure if they underwent AVF creation without Loupe magnification than those with magnification (OR = 3.6, 95%CI = 1.06–12.83, *P* = 0.03; RR = 4.57, 95% CI = 1.02–20.6, *P* = 0.046) or if arterial plaque was present (OR = 3.86, 95%CI = 1.13–13.16, *P* = 0.03). However, thickened arterial IMT(≥0.26 mm) was not an independent risk factor for primary AVF failure in either gender (RR = 0.61, 95% CI = 0.23–1.55, *P* = 0.31) or those with higher age groups (RR = 0.78, 95% CI = 0.19–3.08, *P* = 0.72) or in diabetics (RR = 1.5, 95% CI = 0.57–4.3, *P* = 0.37) [Table 5]. Contrary to the convention, we were surprised to see increased risk for primary AVF failure among diabetics who underwent AVF creation with use of Loupe magnification (RR = 27.7, 95% CI = 1.69–453.6, *P* = 0.019) and males with BCAVF creation (RR = 17.07,

Table 3: Influence of age with pre- and intraoperative variables on AVF success

Variable ↓	Functional AVF →	Age <65 years				Age ≥65 years			
	Subgroup↓	Baseline (*n*=151)	24 h (*n*=138)	12 week (*n*=135)	24 week (*n*=130)	Baseline (*n*=46)	24 h (*n*=42)	12 week (*n*=39)	24 week (*n*=39)
Gender	Male	74	66	65	63	41	41	37	37
Diabetes	Present	70	64	64	61	17	15	13	13
Nonfunctional AVF	Present	20	18	17	15	16	16	16	16
Hemodialysis	≥2 weeks	56	52	50	47	19	19	17	17
Anastomosis	End-Side	85	78	77	74	23	20	20	20
	Side-Side	66	60	58	56	23	22	19	19
Type of AVF	RC	128	119	117	112	19	17	14	14
	BC	23	19	18	18	27	25	25	25
Arterial IMT	≥0.26 mm	75	65	64	64	29	25	25	25
Arterial Plaque	Present	41	38	36	33	34	32	31	31
Loupe Magnification	Not Used	35	32	32	30	13	10	10	10
Thrill >60 min	Present	142	138	135	130	38	39	39	39
AVF Diameter	≤5 mm	37	26	24	19	17	14	10	10

AVF=Arteriovenous fistula, RC=Radiocephalic, BC=Brachiocephalic, IMT=Intima–media thickness

Table 4: Influence of diabetes with pre and intraoperative variables on AVF success

Variable ↓	Functional AVF →	Diabetics				Nondiabetics			
	Subgroup↓	Baseline (*n*=87)	24 h (*n*=80)	12 week (*n*=77)	24 week (*n*=74)	Baseline (*n*=110)	24 h (*n*=100)	12 week (*n*=97)	24 week (*n*=95)
Gender	Female	35	31	29	28	47	42	42	41
Age	≥ 65 years	17	16	13	13	29	29	28	26
Nonfunctional AVF	Present	21	20	18	18	15	13	13	13
Hemodialysis	≥ 2 weeks	32	28	27	26	43	41	40	38
Anastomosis	End-Side	44	39	37	37	64	57	56	56
	Side-Side	43	41	40	37	46	43	41	39
Type of AVF	RC	50	45	42	42	97	87	86	84
	BC	37	35	35	32	13	14	11	11
Arterial IMT	≥0.26 mm	37	31	31	30	67	59	59	59
Arterial Plaque	Present	40	34	33	33	35	34	31	31
Loupe Magnification	Not Used	18	16	13	10	30	30	30	30
Thrill >60 min	Present	79	80	77	74	101	100	97	95
AVF Diameter	≤5 mm	33	26	22	21	21	11	10	8

AVF=Arteriovenous fistula, IMT=Intima–media thickness

95% CI = 2.26–128.79, P = 0.0059, Table 2). We used Loupe magnification in 75.6% patients and the gender wise distribution being 57.7% males and 42.3% females, age wise distribution being 77.9% in <65 years and 22.1% in ≥65 years, and in 79.3% of diabetic patients.

AVF diameter ≤5 mm was an important independent risk factor for primary failure of AVF, the RR being statistically significant in females (RR = 51.2, 95%CI = 3.15–830.9, P = 0.005), in males (RR = 13.6, 95% CI = 4.1–44.8, P = 0.001), in those with age <65 years (RR = 18.4, 95% CI = 5.7–59.2, P = 0.001), with age ≥65 years (RR = 56.2, 95%CI = 3.58–883.9, P = 0.004), with presence of diabetes (RR = 19.36, 95%CI = 2.67–144.8, P = 0.002) and absence of diabetes (RR = 27.5, 95% CI = 6.72–112.9, P < 0.0001) [Table 6]. One elderly female had no thrill after surgery but within 24 h, she developed thrill and had successful AVF. Taking in account the preoperative venous diameters, the primary unassisted patency rates were 100% with venous diameters >3 mm in both RCAVF and BCAVF (P < 0.0001). On further analysis, the odds of poor primary unassisted patency rates were more at a venous diameter cut-off of <2.5 mm for RCAVF (OR = 43.1, 95%CI = 5.57–331.7, P = 0.0003) and BCAVF (OR = 111.8, 95% CI = 4.94–2528.4, P = 0.002).

The two factors that were strongly related to the outcome of the AVF were the presence of thrill on the fistula site after release of clamps and presence of palpable thrill across the AVF at 24 h (P < 0.0001–0.0005) in all subgroups [Table 5].

Discussion

Due to better survival and the increasing average age of the general population, the median age at onset of end-stage renal disease has been progressively increasing over the

Table 5: OR calculated in presumed high-risk categories with pre- and intraoperative variables

Risk group	Variable	OR	95% CI LL	95% CI UL	*P*
Females	Vs Males	1.25	0.56	2.80	0.57
	Age ≥65 Years vs <65 Years	10.05	1.49	67.77	0.018
	Diabetes vs Nodiabetes	1.71	0.52	5.62	0.38
	HTN: ≥ 3 Drugs vs ≤2 Drugs	1.81	0.55	5.98	0.33
	Second AVF Creation vs First AVF	6.6	1.17	37.34	0.031
	Arterial Plaque Present	3.86	1.13	13.16	0.028
	Without Loupe Magnification	3.6	1.06	12.83	0.03
	Intraoperative Thrill Present	345.0	28.59	4162.92	<0.0001
	Thrill at 24 h vs No Thrill	345.0	28.59	4162.92	<0.0001
Age ≥65 years	Males vs <65 Year	0.62	0.18	2.08	0.43
	Females vs <65 Year	10.05	1.49	67.77	0.018
	Diabetes vs Nodiabetes	2.66	0.51	13.72	0.24
	HTN: ≥ 3 vs ≤2 Drugs	3.46	0.18	67.52	0.41
	Second AVF Creation vs First AVF	0.09	0.01	1.78	0.11
	Arterial Plaque Present	0.19	0.03	1.04	0.06
	Without Loupe Magnification	2.17	0.41	11.44	0.36
	Intraoperative Thrill Present	342.33	12.54	9341.5	0.0005
	Thrill at 24 h vs No thrill	342.33	12.54	9341.5	0.0005
Diabetes	Males vs Nondiabetic Males	1.04	0.37	2.92	0.93
	Females vs Nondiabetic Females	1.71	0.52	5.62	0.38
	Age≥65 Years vs <65 Years	2.08	0.55	7.81	0.27
	HTN: ≥ 3 Drugs vs ≤2 drugs	0.19	0.03	0.97	0.04
	Second AVF creation vs First AVF	0.93	0.23	3.76	0.92
	Arterial Plaque Present	1.44	0.44	4.73	0.53
	Without Loupe Magnification	10.2	2.78	37.61	0.0005
	Intraoperative Thrill Present	103.6	10.5	1015.5	0.0001
	Thrill at 24 h vs No Thrill	103.6	10.5	1015.5	0.0001

OR=Odds ratio, CI=Confidence interval, LL=Lower limit, UL=Upper limit, vs=versus, HTN=Hypertension control, AVF=Arteriovenous fistula

Table 6: RR in presumed high-risk categories with pre and intraoperative variables

Risk Group	Variable	OR	95% CI LL	95% CI UL	*P*
Females	RCAVF vs BCAVF	9.86	1.34	72.46	0.02
	E-S vs S-S Anastomosis	1.11	0.41	3.02	0.83
	IMT: ≥ 0.26 mm vs ≤0.25 mm	1.86	0.78	4.79	0.19
	AVF Diameter: ≤5 mm vs ≥5.1 mm	51.2	3.15	830.9	0.005
	HD Duration: ≥2 Week vs <2 Week	1.84	0.68	4.95	0.22
Age ≥65 years	RCAVF vs BCAVF	3.55	0.77	16.42	0.09
	E-S vs S-S Anastomosis	0.75	0.19	2.98	0.68
	IMT: ≥ 0.26 mm vs≤0.25 mm	0.78	0.19	3.08	0.72
	AVF Diameter: ≤5 mm vs. ≥5.1 mm	56.2	3.58	883.9	0.004
	HD Duration: ≥2 Week vs <2 Week	0.56	0.12	2.63	0.41
Diabetes	RCAVF vs BCAVF	1.18	0.42	3.32	0.74
	E-S vs S-S Anastomosis	1.14	0.42	3.11	0.79
	IMT: ≥ 0.26 mm vs≤0.25 mm	1.57	0.57	4.36	0.32
	AVF Diameter: ≤5 mm vs. ≥5.1 mm	19.36	2.67	144.8	0.002
	HD Duration: ≥2 Week vs <2 Week	2.43	0.74	7.98	0.14

RR=Relative risk, CI=Confidence interval, LL=Lower limit, UL=Upper limit, vs=versus, RCAVF=Radiocephalic arteriovenous fistula, BCAVF=Brachiocephalic arteriovenous fistula; E-S=End-to-side, S-S=Side-to-side, IMT=Intima–media thickness, AVF=Arteriovenous fistula, HD=Hemodialysis

last few decades. More than 20% of people have diabetes as a cause of CKD and average age is 54.5 years.[6] Even though the National Kidney Foundation/Disease Outcome Quality Initiative (NKF/DOQI) Vascular Access Clinical Practice Guidelines 2006 advises that at least 50% of all the new patients with CKD anticipated to receive hemodialysis in the next 1 year should undergo a vascular access procedure, our rates were only 61.9%. The rest

of the 38.1% patients were already on hemodialysis for >2 weeks, and AVF creation prior to initiation of MHD failed in them because of the lack of patient education for advanced stages of CKD, practice of alternative medicine in India, and admission of patients in critical condition because of advanced azotemia-related complications.[15] Early identification of such patients and diligent protection of distal forearm veins for future AVF creation was practiced by all concerned with the care of patients with CKD at our center. However, when a patient required early hemodialysis at the time of referral, central venous catheter insertion was done to carry out hemodialysis until a mature AVF could be used. These devices suffer from several complicating factors like infection, thrombosis, central venous stenosis, and damage to proximal and larger veins.[16] Patients who received dialysis across a functional AVF had lower complication rates and longer duration of event-free patency than patients with catheter access and arteriovenous grafts (AVGs).[17] Thus, the construction of a native AVF on arm or forearm is considered a good practice over prosthetic grafts and central venous catheters.

The procedure of choice for the freshly detected patient with CKD with a creatinine clearance of less than 15 ml/min/1.73m^2 or serum creatinine level that had attained a plateau at 4 mg/dl or more, was the creation of the RCAVF, as initially described by Brescia *et al.* in 1966.[4] RCAVF is still considered to be the gold standard for vascular access for HD and it accounted for 74.6% of our operative procedures whereas high radio-cephalic (mid-forearm) and BCAVF were done for patients (25.3%) with previously failed ipsilateral RCAVF or where patent adequate size vessels at wrist level were not available for anastomosis in the other arm. Vascular mapping and selection of appropriate sites of AVF were important prior to the creation of AVF. AVFs were created using patent veins which showed antegrade flow.[18] Guidelines suggest role of preoperative duplex USG for vascular mapping preoperatively to assess arterial diameter, flow, venous diameter and evaluation of central veins in case of ipsilateral central venous catheter.[19] In our study, duplex USG was used for preoperative assessment of peripheral vessel diameters and flow but assessment of ipsilateral central veins in patients with prior central venous catheters was not done, hence outcomes of AVF with ipsilateral central venous catheter was not assessed. Ideally, assessment of peripheral vessels and central veins should be done prior to AVF creation, as it improves primary unassisted patency rates of AVFs.[20]

The primary failure of AVF has been defined as failure of vascular access without any intervention after creation of the AVF.[7] However, the NKF/DOQI workgroup did not recommend the use of primary failure as an index of quality because it would discourage attempts at AVF construction in patients with complex vascular anatomy.[15] Some authors have also defined primary AVF failure as thrombosis or failure to mature till 06 weeks of fistula creation.[21] Our study highlighted that there was increased risk of primary AVF failure in female gender in the presence of elderly age (age ≥65 years), undergoing 2nd AVF creation, without use of Loupe magnification, presence of arterial plaque, RCAVF and AVF size ≤5 mm. Similarly, other studies have cited female gender[5-7,9,12-14] and advanced age (>65 years)[5,8,10,11,13,14] as non-modifiable predisposing factors for primary failure of AVF. Lok *et al.* have shown contrary results in their study.[22] Our study also showed that elderly females with RCAVF creation and males with BCAVF had increased risk of primary failure.

We also assessed the influence of diabetes and severe hypertension (requiring ≥3 antihypertensives) on AVF patency. Many studies concluded increased primary AVF failure incidence in patients with diabetes[6,7-12,22] and with a higher incidence of conversion to AV grafts in this subgroup.[23] There was no increased risk of primary AVF failure among higher age groups (age ≥65 years) with either presence of diabetes or uncontrolled hypertension or 2nd AVF creation or hemodialysis duration or thickened arterial IMT or presence of plaque or absence of Loupe magnification, except in BCAVF. Similarly, there was no increased incidence of primary AVF failure in diabetics with increased age or 2nd AVF creation or hemodialysis vintage or presence of thickened IMT or arterial plaques, or location of AVF, except in those where loupe magnification was used and those with uncontrolled hypertension. This fact was also highlighted by a meta-analysis by Rooijens *et al.* who stated that diabetes and female gender did not play any significant role in primary failure of autogenous RCAVF.[21] Our study did not show any relation of AVF failure rates with poorly controlled hypertension although Culp *et al.* had postulated that intradialytic hypotension contributed to the higher incidence of primary AVF failure in patients with poorly controlled preoperative hypertension.[24] Though low serum albumin was a marker for inflammation and associated with early AVF failure,[25] our low albumin cohort was not associated with increased risk of primary AVF failure (RR = 0.69, 95% CI = 0.23–1.65, P = 0.28).

We could not establish any role of IMT in primary AVF failure in our cohort, as has been reported earlier.[26] But, vessel diameter played a significant role in fistula success.[5,27] The most significant factors associated with the success of AVF in our study were venous diameter (≥3 mm), side to side fistula configuration, fistula diameter (≥5.1mm), use of loupe magnification, and presence of thrill across the fistula after release of clamps and at 24 h. However, there was no incidence of venous hypertension or steal phenomenon among patients with S-S AVFs. Our study reinforced the fact that intraoperative factors played a prominent role in the outcome of the AVF in addition to certain preoperative non-modifiable risk factors. The presence of atheromatous plaques in the arterial intima

at the time of arteriotomy and anastomosis had no effect on the outcome of the fistula except in female gender. We did not find any study in literature to support or refute this finding. In our study, E-S AVF fared slightly poorer and may be attributed to the borderline venous size, and more distantly located vein in those undergoing the end to side AVF. S-S AVF had comparatively better patency than E-S version, as it was done only when the artery and vein could be mobilized close together.

The reported incidence of primary failure in the medical literature varies from 9% to 40%[28,29] and our results with 8.6% and 11.7% as AVF failure at the time of surgery and 12 weeks respectively were comparable. The AVF patency rates were 85.8% at 24 weeks. Sultan *et al.* observed that primary functional patency at 4 years (P = <0.0001) as well as freedom from major adverse clinical events at 5 years (P < 0.005) was better with proximal AVF as compared with distal AVF.[30] This was outside the scope of our study because of the shorter follow-up period. Though statistically not significant, proximal AVF had favorable results. The failed AVFs salvaged with interventions were not part of this study, hence not included in analysis.

Conclusion

Female gender, in presence of elderly age (age ≥ 65 years), second AVF creation, arterial plaques, smaller AVF size (<5 mm), absence of Loupe magnification, and diabetics with ≥3 antihypertensives were prime factors for primary AVF failure. The presence of immediate thrill and a fistula size of ≥5.1 mm were the key indicators for sustained AVF success. Elderly patients with RCAVF and males with BCAVF had poorer outcomes. The presence of diabetes, arterial IMT, and HD duration were essentially noncontributory for primary failure of AVF.

Compliance with ethical standards

Ethical approval (study involved human participants): All procedures performed in this study involved human participants and were in accordance with the ethical standards of the institution as well as the national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Hospital Ethics Committee clearance was taken prior to this study. The authors took mandatory informed consent from the patients prior to doing AVF surgery for the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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