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CLINICAL STUDY

An Experience of Arteriovenous Fistulas Created for Hemodialysis in the Largest Health Center in Eastern Turkey

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Abstract

Background: The aim of the study was to evaluated the primary and secondary (after reoperation) patency rates and some effect factors in fistula patency for hemodialysis patients. *Material and methods*: Over a 10-year period, 1529 arteriovenous fistulas (AVFs) were fashioned in 1003 (611 males, 392 females; median age range 7–72) patients using the native vascular tissue and prosthetic graft material. We also evaluated the effects of various factors in fistula patency and primary and secondary patency rates in AVF patients. *Results*: The primary patencies of fistulas in this series were 72%, 64%, 51%, 41%, and 26%, and secondary patencies were 79%, 70%, 56%, 46%, and 33% at 6 months, 1, 2, 4, and 6 years, respectively. There was no statistically significant difference between the primary and secondary patencies ($p = 0.082$) in the 6-year follow-up. Factors affecting the patency of fistulas were diabetes mellitus ($p < 0.005$), hypertension ($p < 0.005$), and smoking habits ($p < 0.005$). *Conclusion*: Even if shown to be not statistically significant, successful surgical revision after fistula occlusion improves secondary patency with potential benefits in terms of patient morbidity. Besides, the AVF patency was shortened in chronic renal-insufficiency patients with diabetes mellitus, hypertension, and smoking habits.

Keywords: chronic renal failure, arteriovenous fistulas, hemodialysis access, fistula patency, synthetic grafts

INTRODUCTION

As the population of patients requiring chronic hemodialysis has increased, the number of patients needing multiple repairs due to failed blood access has increased. The durability of arteriovenous fistula (AVF) creation has been evaluated through patency rate. A large proportion of patients with end-stage renal disease (ESRD) are not suitable candidates for kidney transplantation therapy.[1] In general, AVF is the appropriate dialysis access for hemodialysis patients. Depending on the facts of poor longevity of prosthetic fistula grafts, a native AVF is the most suggestible procedure.[2,3]

The ground-breaking article by Brescia and Cimino in 1966 revolutionized the creation of the vascular access, and the "Cimino fistula" was soon used in almost all dialysis patients.[4] It still represents the best form of vascular access for chronic hemodialysis. Many factors influence the patency of AVF in patients with chronic hemodialysis.[5]

With an analysis of these retrospective data, we review our experience of using surgical intervention to restore or maintain the function of fistulas constructed using autogenous vein and prosthetic graft. In addition to primary and secondary rates, this study aimed to evaluate whether some factors had any prognostic relation to the patency of the vascular access in 1003 chronic renal-insufficiency patients.

MATERIALS AND METHODS

A retrospective case note review was performed on all patients identified from the hospital vascular access database as having undergone construction of a native vein and graft AVF. Initial preoperative evaluation of the cases includes blood tests (complete blood count, electrolytes, renal and liver functions, blood-type definition, coagulation profile, serology for hepatitis, and HIV), electrocardiography, chest X-ray, extremity Doppler ultrasound for arteriovenous systems, and magnetic

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resonance imaging vascular angiography investigations with indications.

In our study, we scanned the data of 1003 patients with 1529 AVF operations for permanent vascular access with native vascularities and synthetic polyurethane grafts. The male:female ratio was 611:392. The first 1003 initial procedures associated with primary patency and the 526 reoperative procedures associated with secondary patency were performed for fistula. There were 110 pediatric patients (defined as age $\leq$ 16 years). Diabetes mellitus and hypertension were the most frequently adding pathologies. The preoperative data are summarized in Table 1. The causes for hemodialysis are given in Table 2. A total of 27 patients were admitted to the hospital because of trauma and 13 patients because of renal failure due to medications including antibiotics and radiological agents. None of our patients had kidney transplantation prior to our study.

AVFs were created generally under local anesthesia (lidocaine 1% with a combination of bupivacaine 0.25% solution) by seven of the senior staff surgeons of cardiovascular surgery. Procedural sedation was administered, when necessary to maintain patient concordance, with intravenous midazolam injections. The nondominant upper extremity, usually the left, was preferentially used. Lower extremity fistulas of adult patients were performed with spinal anesthesia. All pediatric patients received a general anesthesia for their operations. Hemodialysis through the new blood access was begun no sooner than 3 weeks after creation of the AVF. Generally, AVFs should be performed from distal to proximal, using the patients' own otogenic veins

Table 1. Preoperative parameters in fistula patients.

Variable	Male	Female	Total
Number of operations	831	698	1529
Number of patients	611	392	1003
Adults	498	395	893
Smoking	539	175	714
HT	413	227	640
DM	203	166	369
CAD	87	67	154
Pediatrics	36	74	110
CVE	71	36	107
CABG	51	23	74
PABG	31	8	39

Note: HT, hypertension; DM, diabetes mellitus; CAD, coronary artery disease; CABG, coronary artery bypass grafting; PABG, peripheral artery bypass grafting; CVE, cerebrovascular event.

Table 2. Causes for hemodialysis.

Causes	Male	Female	Total
Diabetic nephropathy	203	166	369
Glomerulonephritis	154	70	224
Chronic pyelonephritis	107	100	207
Polycystic kidney disease	83	80	163
Others	30	10	40

Table 3. Types of fistulas.

Localization	Primary fistula	Reoperation fistula
Total	1003	526
Radial–cephalic AVF	572	312
Brachial–cephalic AVF	234	101
Brachial–basilic AVF	75	45
VSM loop to SFA AVF	46	28
Brachial–axillary AVG	44	23
SFA to femoral vein AVG	17	9
Brachial–cephalic AVG	15	8

Note: AVF, arteriovenous fistula; AVG, arteriovenous graft; VSM, vena saphena magna; SFA, superficial femoral artery.

for hemodialysis. Besides, the majority of the AVFs were performed in radial–cephalic wrist or more proximally. In this study, the surgical access types are described in Table 3 according to primary and reoperative surgical procedure.

We generally used end-to-side anastomosis technique. Anastomosis was constructed with a continuous 6/0 or 7/0 prolene suture. Antibiotherapy and antiaggregant treatment were not used routinely during the postoperative term. Special care was taken to ensure the formation of a smooth hemicircle for the divided vein; the wound was then closed in a single layer and the hand was kept elevated, coupled with active finger exercises for 24–48 h. The patients prospectively underwent follow-up for 4.8 $\pm$ 1.2 years (mean 4.9 years). If the patient underwent kidney transplantation or died during the follow-up period, the follow-up ended on the day of transplantation or the day of death.

The operations were performed at multiple localizations on the upper extremities in 941 patients and lower extremities in 62 patients. Nondominant upper extremity was the first choice for operation. The order of preference is summarized as follows:

- √ Nondominant upper extremity: radial–cephalic native AVF
- √ Nondominant upper extremity: brachial–cephalic native AVF
- √ Nondominant upper extremity: brachial–basilic native AVF
- √ Dominant upper extremity: radial–cephalic native AVF
- √ Dominant upper extremity: brachial–cephalic native AVF
- √ Dominant upper extremity: brachial–basilic native AVF
- √ Arteriovenous grafts (AVGs) for nondominant upper extremity
- √ AVGs for dominant upper extremity
- √ Lower extremity great saphenous vein loop to superficial femoral artery (SFA)
- √ Lower extremity SFA to femoral vein AVGs

Upper and lower extremities AVFs and AVGs are shown in Table 2.

Primary patency after first operation refers to fistulas functioning after dialysis up to the time of first failure or intervention. The secondary patency associated with reoperations is defined as multiple operations (second, third, etc.) performed following the initial procedure.

Primary Operations

A total of 1003 primary operations took place. These operations included native AVFs and in some cases AVGs where necessary. Native AVFs of upper extremity included radial–cephalic fistula, and brachial–cephalic fistula, and brachial–basilar fistula operations. AVGs as an initial operation were localized at the brachial artery to axillary vein and brachial artery to proximal cephalic vein. Initial fistulas at the lower extremity consisted of great saphenous vein loops to SFA and polytetrafluoroethylene (PTFE) grafts between SFA and femoral vein. Reasons to choose the lower extremity for an initial fistula are summarized as follows:

- √ Proximally venous stenosis due to previous multiple hemodialysis catheters
- √ Posttraumatic bilaterally bone fractures
- √ Extremity amputations due to vasculopathies such as Buerger's disease
- √ Pediatric patients with smaller arm vessels
- √ Patients' disagreement for upper extremity for personal reasons
- √ Multiple intravenous medications with multiple thrombophlebitis
- √ Unsatisfactory calibers and/or flow patterns of native arm vessels

Reoperations

Secondary reoperations are defined as multiple operations performed following initial procedure. For each reoperation, we examined the existing fistula (native or graft) with thrombectomy and possibilities to reanastomosis at the same localization among patients with an early fistula dysfunction. It is clearly understandable not to examine an existing native fistula which was created within months and after a long period of dysfunction. Indications for secondary reoperations in an order of frequency were loss of thrill with dysfunction and thrombosis, stenosis or partial dysfunction, infection, hemorrhage, pseudoaneurysms, ischemia and steal syndrome, seroma, venous hypertension, and hand edema. The indications for second and further reoperations are depicted in Table 4.

The patients prospectively underwent follow-up for 6 years and retrospectively to the day of fistula creation. Patients who underwent kidney transplantation or died during the follow-up period were followed up until the day of transplantation or the day of death.

Statistical Analysis

Student's *t*-test was used to compare age, and chi-square test and Fisher's exact test were used to compare sex, diabetes mellitus, peripheral arterial disease, and smoking habits associated with patency. The statistically significant probability level was set at 0.05. The 6 years follow-up of fistulas was analyzed with the Kaplan–Meier survival analysis and log-rank test. Cox regression analysis was used to determine whether the factors had effectiveness on patency rates. Data related to age were presented as arithmetic average ± standard deviation; categorical variables as count and percent; and the results of the Cox regression analyses as odds ratio (OR) and 95% confidence interval (CI).

Table 4. Indications for second and further reoperations.

Indications for reoperations	Second	Further reoperations
Total	394	132
Hemorrhage	108	36
Thrombosis	81	35
Infection	60	5
Stenosis or partial dysfunction	50	30
Pseudoaneurysm	46	4
Ischemia/steal syndrome	20	10
Venous hypertension	13	3
Hand edema	8	6
Seroma	8	3

RESULTS

The analysis included 1003 patients including 611 (60.9%) men and 392 (39.1%) women with median age of 52 (range 7–72). The mean ages were 62 ± 11.2 and 57 ± 12.5 for the primary patency and secondary patency patients, respectively, and there was no statistical significance ($t = 0.68$, df: ±520, $p = 0.681$). The glomerular filtration rates (GFRs) were less than 60 mL/min/1.73 m^2 in all patients.

The primary patencies of fistulas in this series were 72%, 64%, 51%, 41%, and 26% at 6 months, 1, 2, 4, and 6 years, respectively. A further 526 revision procedures were performed on fistulas to maintain fistula function, and secondary patencies after surgical revision were 79%, 70%, 56%, 46%, and 33% at 6 months, 1, 2, 4, and 6 years, respectively. There was no statistically significant difference between the primary and secondary patencies ($p = 0.082$) in the 6-year follow-up (Figure 1, Table 5).

Glomerulonephritis (22.3%) and chronic pyelonephritis were determined to be the most frequent causes of hemodialysis (36.7%) (Table 1). Comparisons of primary patency and reoperative secondary patency fistulas with regard to some variables are presented in Table 6.

The patency rates were not influenced by sex ($p = 0.711$), age ($p = 0.613$), and peripheral arterial disease ($p = 0.973$). Diabetes mellitus was found in 369 patients and in 211 reoperative patients, which affected the fistula patency. AVF patency was significantly

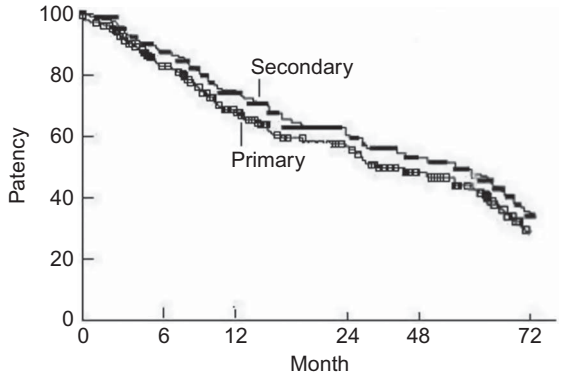

Figure 1. Kaplan–Meier survival curves for fistula primary and secondary patency rates in 6-year follow-up.

Table 5. Life tables demonstrating primary and secondary patencies of fistulas constructed.

Time (months)	Primary patency (%)	Secondary (after reoperative) patency (%)	*p*-Value
0	100	100	
6	72	79	
12	64	70	
24	51	56	
48	41	46	
72	26	33	0.082

Table 6. Comparisons of primary patency and secondary (after reoperation) patency fistulas with regard to some variables.

Variable	Primary fistula patency patients	Secondary (after reoperation) patency patients
Number of patients	1003	354
Number of operations	1003	526
Male/female	611/392	204/150
Mean age (years)	62 ± 11.2	57 ± 12.5
Adults	893	321
Smoking	714	301
HT	640	344
DM	369	211
Pediatrics	110	33
CVE	107	44
CABG	74	53
PABG	39	24

Note: DM, diabetes mellitus; HT, hypertension; CABG, coronary artery bypass grafting; PABG, peripheral artery bypass grafting; CVE, cerebrovascular event.

induced in diabetic patients. Hypertension was detected in 640 primary fistula patients and in 344 reoperative fistula patients. In these patients, the patency of AVFs was worse than in other patients. Smoking habits were found in 714 primary fistula patients and in 301 reoperative fistula patients. In these patients, AVF patency was significantly reduced. The factors that affect nonpatency in the 6-year follow-up were evaluated using Cox regression analysis. According to the analysis, the existence of diabetes mellitus (OR: 0.379, 95% CI: 0.215–0.668), smoking habits (OR: 0.502, 95% CI: 0.392–0.645), and hypertension (OR: 2.914, 95% CI: 1.926–4.409) was found to be the effective factors in patency (Table 7).

Table 7. The results of Cox regression analysis on the factors effective on patency (p-value < 0.05: statistically significant).

	OR	95% CI	*p*-Value
Sex			
Female	1		
Male	1.010	0.988–1.025	0.711
Age	1.013	0.992–1.014	0.613
Smoke history			
(−)	1		
(+)	0.502	0.392–0.645	**<0.05**
Diabetes mellitus			
(−)	1		
(+)	0.379	0.215–0.668	**<0.05**
Hypertension			
(−)	1		
(+)	2.914	1.926–4.409	**<0.05**
Peripheral arterial disease			
(−)			
(+)	0.999	0.750–1.331	0.973

DISCUSSION

ESRD is a common worldwide disease with high prevalence in every region. ESRD is defined as a GFR less than 60 mL/min/1.73 m^2 for 3 or more months. Pathophysiology consists of irreversible nephron loss and sclerosis of renal parenchyma.[1,6] ESRD follows five steps:

- Stage 1: GFR more than 90 mL/min/1.73 m^2 with mild kidney damage
- Stage 2: GFR 60–89 mL/min/1.73 m^2 defining a mild GFR decrease
- Stage 3: GFR 30–59 mL/min/1.73 m^2 defining a moderate GFR decrease
- Stage 4: GFR 15–29 mL/min/1.73 m^2 defining a severe GFR decrease
- Stage 5: GFR less than 15 mL/min /1.73 m^2 defining a chronic renal failure (CRF) with dialysis indication

In our patients, GFRs were less than 60 mL/min/1.73 m^2, which hemodialysis necessitates. Mortality and morbidity rates are particularly high in this disease. ESRD treatment strategies accumulate mainly in two groups besides medications: dialysis and renal transplantation (RTx). In Turkey, RTx is rarely an option for ESRD patients due to small numbers of RTx centers and the lack of compatible donors. Therefore, CRF patients are almost candidates for AVF operations in the long term. Dialysis catheters are a bridging technique before AVF or RTx. Dialysis is performed in two strategies: hemodialysis and peritoneal dialysis. Indications for a hemodialysis access occur in 150–200 cases

per million population. These hemodialysis techniques improve the quality of life of patients with ESRD and prolong the overall survival. Following a hemodialysis catheter, patients usually present with a need for AVF. These patients have a hospitalization rate of at least 2 per year. The 5-year survival rate for this group differs between 35% and 45%. The most frequent reason for these deaths is cardiovascular events as in morbidity. Cardiovascular mortality is 10–20 times higher in ESRD patients compared with the normal society.[7] In our study, the patients were hospitalized several times due to fistula thrombi, hematoma, fistula occlusion, and/or aneurysm. Besides, approximately 22% of our patients had cardiovascular disease. Our study was continued until the death of the patient or RTx.

An AVF is a connection between an artery and a vein. AVF is performed mainly in two ways: native AVF and with grafts consisting of PTFE synthetic graft, Dacron, polyurethane, or bovine vessels as in hemodialysis access AVGs. In our group of patients, AVFs of upper extremity took place in three localizations: radial artery to cephalic vein, brachial artery to cephalic vein, and brachial artery to basilic vein with an end-to-side anastomosis. Native AVFs of lower extremity were characterized by a loop of vena saphena magna to SFA with an end-to-side anastomosis. AVGs took place in two ways of the upper extremity: with a graft between brachial artery and proximal cephalic vein, and between brachial artery and axillary vein. AVGs of lower extremity were replaced between SFA and femoral vein.

Creation of an AVF is an interdisciplinary task. In several countries, the task of coordination is delegated to a fistula manager who integrates the activities of the nephrologist, the ultrasonographer, the surgeon, or the interventional radiologist.[8] The creation of fistulas should be delegated to a restricted number of dedicated surgeons, because good results are only achieved by surgeons with considerable expertise. All the AVFs in this study were created by senior surgeons.

Our results did not show that AVF survival depended on either age or gender, which is consistent with some[9] and opposite to other reports.[10,11] Besides, contrary to identical studies,[12] in our results, the patency of AVF was affected by smoking habits, which is consistent with some studies.[10,13] In this study, current or previous smoking was associated with a low patency rate (OR: 0.502, 95% CI: 0.392–0.645) for subsequent access events.

Our results did not show that AVF survival depended on peripheral arterial disease. In these patients, peripheral arterial disease with thickened or even calcified arteries might have impaired fistula maturation. In this study, peripheral arterial disease was not associated with low patency rates (OR: 0.999, 95% CI: 0.750–1.331). The patients with our peripheral arterial disease (39 patients) had operation due to various arterial occlusions in previous years. In all patients, lower and upper extremity arterial pulses were available.

Except for diabetic patients, we preferred a radial–cephalic fistula as a first choice. For male or female diabetic patients, our first choice was brachial–cephalic fistula because of the poor patency rates of more distal fistulas. The major artery diameter of the brachial artery seems to ensure a sufficient arterial inflow for fistula patency and maturation even in the case of a restricted distensibility and compliance of the arterial wall in these patients. Gibson et al.[14] described an increased risk of revision in diabetic patients, a finding in line with our own observation. Diabetes mellitus may influence the formation of intimal hyperplasia at the anastomosis or venous valve. This had an effect on the fistula patency.[15] In both primary and secondary patencies, AVF patency was significantly reduced in diabetic patients.

In our study, hypertension was effected by fistula patency. The patency of AVFs was worse with hypertension patients as in identical studies.[16–18] After the fistula creation, vessel calcifications are detected in diabetics and hypertensive patients.[17,18] In this study, almost one-third of all patients suffered from diabetes and half of the patients from arterial hypertension which were distinguished as independent risk factors associated with a decreased patency rate. During vascular access creation, these comorbidities were commonly accompanied by arteriosclerosis and thickening of the arterial wall.[15,16]

AVF is generally used thrice a week for hemodialysis. All patients in this study group received lower doses of aspirin (100–150 mg/day) besides their nephroprotective medications. Warfarin was not used even for AVGs. Warfarin was replaced with a single enoxaparin daily for the first 2 months of graft administration. Andrassy et al.[19] compared two groups of patients treated with aspirin and placebo on the effects of early AVF thrombosis, defined as the thrombosis within first 30 days. Early thrombosis incidence in aspirin group was 4% compared to 24% in placebo group. Our opinion is parallel to this study's results.

Almost one-fourth of dialysis patients are admitted to hospitals on complaints of AVF or AVG dysfunctions including stenosis, thrombosis, and/or infections. In fact, only 15% or less of these AVF operations remain functional in a patient's entire dialysis period. The mean of this functional time is 3 years for native AVFs and 2 years for AVGs. Following a "renewal," secondary patencies reported are as 5–7 years for forearms, 3–5 years for upper arms, and 2–3 years for AVGs.[19–21] The secondary (reoperative patency) fistulas survived longer than primary fistulas. But, there was no statistically significant difference between primary and secondary patency rates in our study ($p = 0.082$) (Table 4). Our study results are consistent with some studies.[22,23] Endpoints for AVFs and AVGs most commonly include thrombosis, anastomosis stenosis, seroma, infection, steal syndrome, hemorrhage, venous hypertension of extremity, and aneurysms.[20,21] Dysfunction limits are accepted as 700 mL/min for AVGs and 500 mL/min for native AVFs. Lower flow rates are accepted as

fistula dysfunction requiring further surgical investigation. Radiological interventions such as percutaneous angiographies with embolectomy/thrombolysis, stent implantations, or balloon angioplasty were not admitted for any of our patients.

CONCLUSION

The comparison of end results obtained from the analysis of parameters observed in the 1003 patients showed that peripheral arterial disease, age, and sex are not the factors with a significant effect on patency during hemodialysis procedures, whereas diabetes mellitus, smoking habits, and hypertension were the factors with a significant negative effect on AVF patency.

In addition, these results demonstrate that surgical reoperation is a treatment option in the management of the failing fistula. Although there was no significant difference between the primary and secondary patencies, the secondary patency was higher than the primary patency in our study.

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