Endovascular Arteriovenous Dialysis Fistula Intervention: Outcomes and Factors Contributing to Fistula Failure

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Rationale & Objective: Primary patency is variable with arteriovenous fistulas, and many patients require angiographic procedures to obtain patency. Accordingly, we determined postintervention patency rates and contributing factors for fistula failure following intervention to establish secondary patency in non–dialysis-dependent patients with advanced chronic kidney disease following creation of an arteriovenous fistula.

Study Design: Observational study from a single referral center.

Setting & Participants: 210 non–dialysis-dependent patients with advanced chronic kidney disease who underwent upper-extremity fistula creation for anticipated dialysis between October 1995 and January 2015 and who required subsequent endovascular therapy to establish or maintain patency were reviewed.

Exposure: Endovascular therapy for dialysis arteriovenous fistula primary patency failure.

Outcomes: Postintervention patency duration following endovascular therapy.

Analytical Approach: Descriptive study with outcomes determined using Cox proportional hazards models.

Results: Multiple fistula configurations were reviewed: 138 (65.7%) brachiocephalic, 39 (18.6%) radiocephalic, 30 (14.3%) brachiobasilic, 2 (1.0%) ulnocephalic, and 1 (0.5%) radiobasilic. There were 261 initial stenoses treated. Postintervention primary patency is defined as the time from the index intervention to repeat intervention for stenosis. Postintervention primary-assisted patency is the time from the index intervention to thrombectomy for fistula thrombosis or change in modality. Postintervention secondary patency is the time from the index intervention to fistula abandonment. Median postintervention primary patency, postintervention primary-assisted patency, and secondary patency were 2.7, 3.2, and 3.6 years, respectively. The overall 1-year primary, primary-assisted, and secondary patency rates in this cohort were 53.0%, 87.7%, and 83.5%, respectively. Compared with radiocephalic fistulas, brachiocephalic fistulas had higher risk for postintervention primary patency loss (HR, 1.90; 95% CI, 1.13-3.20; P = 0.02).

Limitations: Dialysis fistula revascularization techniques varied.

Conclusions: The radiocephalic fistula configuration had the best postintervention primary patency in this cohort. Postintervention primary-assisted patency and secondary patency were not significantly different among different fistula configurations.

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Kidney Med. 2(3):326-331. Published online April 21, 2020.

doi: 10.1016/j.xkme.2020.02.004

In 2015, approximately 124,000 new cases of end-stage kidney disease were reported and nearly 500,000 patients were receiving dialysis treatment in the United States.[1] In the current practice environment, the Fistula First initiative emphasizes the creation of arteriovenous fistulas over grafts or catheter placement.[2,3] However, 20% to 50% of the fistulas created never mature to support dialysis.[4,5] Furthermore, 27% of fistulas fail and are abandoned within 18 months of creation.[6,7] These outcomes have significant economic consequences and constitute ~8% of total Medicare end-stage kidney disease spending.[8]

Fistulas are often constructed when patients are in the non–dialysis-dependent stage of kidney disease in anticipation for future dialysis. When these fistulas fail to mature, patients are often referred for endovascular management to evaluate and treat lesions that can inhibit fistula maturation, such as dilating stenoses, with angioplasty.[9] Approximately 50% of fistulas require interventions before successful arteriovenous fistula use.[10] In some cases, multiple endovascular procedures are required to aid in the maturation of the fistulas.[11] At present, there are limited data for factors contributing to postintervention patency in fistulas constructed in non–dialysis-dependent patients, and given the high incidence of endovascular procedures on immature fistulas, more investigation is warranted.[12,13] The purpose of this study was to determine the predictors of recurrent lesions in fistulas constructed in the non–dialysis-dependent population and evaluate the outcomes after endovascular therapy.

METHODS

Study Population and Design

Electronic medical records were reviewed and 407 non–dialysis-dependent patients with fistulas constructed between October 1995 and February 2015 were identified. Patients were excluded if they had incomplete medical or imaging data. The final cohort consisted of 210 patients, all

Table 1. Baseline Patient Characteristics by Fistula Configuration

Characteristic	Brachiocephalic (n = 138)	Brachiobasilic (n = 30)	Radiocephalic (n = 42)
Female sex	50 (36.2%)	12 (40.0%)	13 (31.0%)
Age, y	74.1 [59.2-78.8]	75.8 [68.0-78.1]	70.1 [58.8-75.5]
CKD stage			
4	23 (16.7%)	5 (16.7%)	7 (16.7%)
5	115 (83.3%)	25 (83.3%)	35 (83.3%)
Adequate fistula maturation for use	129 (92.8%)	22 (73.3%)	40 (95.2%)
Time from fistula creation to use, d	141.0 [58.0-360.0]	73.5 [45.0-170.0]	106.0 [51.0-463.0]
Catheter use while awaiting fistula maturation	33 (23.9%)	12 (40.0%)	11 (26.2%)
Tobacco smoker	7 (5.1%)	0 (0%)	2 (4.8%)
Diabetes mellitus	75 (54.3%)	18 (60.0%)	26 (61.9%)
Coronary artery disease	51 (37.0%)	10 (33.3%)	20 (47.6%)
Hyperlipidemia	87 (63.0%)	13 (43.3%)	24 (57.1%)
Hypertension	128 (92.8%)	28 (93.3%)	41 (97.6%)
Peripheral arterial disease	13 (9.4%)	4 (13.3%)	5 (11.9%)
Medications at time of fistula construction			
Aspirin	83 (60.1%)	25 (83.3%)	25 (59.5%)
Clopidogrel	6 (4.3%)	5 (16.7%)	2 (4.8%)
Warfarin	16 (11.6%)	5 (16.7%)	3 (7.1%)
Calcium channel blocker	122 (88.4%)	13 (43.3%)	26 (61.9%)
β-Blocker	9 (6.5%)	25 (83.3%)	19 (45.2%)
Statins	74 (54.3%)	5 (16.7%)	14 (33.3%)

Note: Data for categorical variables expressed as number (percent); data for continuous variables expressed as median [interquartile range].
Abbreviation: CKD, chronic kidney disease.

of whom had the fistula constructed before the initiation of maintenance hemodialysis.

Patient demographics are summarized in Table 1. There were 135 (64.3%) men and 75 (35.7%) women. All patients in this study had either stage 4 or 5 chronic kidney disease (CKD). There were 175 (83.3%) patients with stage 4 CKD and 35 (16.7%) patients with stage 5 CKD. Of the 210 fistulas, there were 138 (65.7%) brachiocephalic fistulas, 39 (18.6%) radiocephalic fistulas, 30 (14.3%) brachiobasilic fistulas, 2 (1.0%) ulnocephalic fistulas, and 1 (0.5%) radiobasilic fistula. Given anatomic similarities, the ulnocephalic and radiobasilic configurations were analyzed with radiocephalic fistulas.

Institutional review board approval was obtained (IRB # 17-008191) and informed consent was waived for this retrospective single-institution study evaluating postintervention patency rates of fistulas constructed in non–dialysis-dependent patients.

Definitions

Fistulas were divided into 4 anatomical regions based on prior definitions: juxta-anastomotic segment (JAS; artery ≤ 2 cm from the anastomosis, anastomosis, and vein ≤ 2 cm central to the anastomosis), outflow vein (vein central to cannulation zone but peripheral to cephalic arch or central vein), cephalic arch, and central vein. The central veins included any vein central to the axillary vein (eg, subclavian vein, brachiocephalic vein, or superior vena cava).[13-16]

Definitions of postintervention patency duration have been previously described.[17,18] Postintervention primary patency is defined as the time from the index intervention to repeat intervention for stenosis. Postintervention primary-assisted patency is the time from the index intervention to thrombectomy for fistula thrombosis or change in modality. Postintervention secondary patency is the time from the index intervention to fistula abandonment.

CKD stages were determined based on the Kidney Disease: Improving Global Outcomes CKD Work Group classification: stage 1, glomerular filtration rate (GFR) ≥ 90 mL/min/1.73 m^2; stage 2, GFR of 60 to 89 mL/min/1.73 m^2; stage 3A, GFR of 45 to 59 mL/min/1.73 m^2; stage 3B, GFR of 30 to 44 mL/min/1.73 m^2; stage 4, GFR of 15 to 29 mL/min/1.73 m^2; and stage 5, GFR < 15 mL/min/1.73 m^2.[19]

Procedure

Patients were referred to Interventional Radiology for diagnostic fistulography by the Department of Nephrology if they had sonographic evidence of fistula stenosis or thrombosis, abnormal upper-extremity physical examination results including arm pain and swelling, were unable to achieve fistula maturation to sustain adequate dialysis (blood flow < 500 mL/min), or cannulation difficulties at the initiation of dialysis. Procedures were performed by 9 different interventionalists with 3 to 17 years of experience (median, 10 years). Patients were referred for surgical intervention if the fistula failed satisfactory percutaneous therapy. Fistulas were accessed in the outflow vein. The

Table 2. Postinterventional Patency Rates Based on Fistula Configuration

Fistula Configuration	Risk for Patency Loss HR (95% CI)	*P*
Primary Patency		
Radiocephalic	1.0 (reference)	
Brachiobasilic	1.43 (0.71-2.88)	0.31
Brachiocephalic	1.90 (1.13-3.20)	0.02
Primary-Assisted Patency		
Radiocephalic	1.0 (reference)	
Brachiobasilic	1.87 (0.65-5.38)	0.25
Brachiocephalic	1.39 (0.58-3.34)	0.46
Secondary Patency		
Radiocephalic	1.0 (reference)	
Brachiobasilic	1.16 (0.48-2.80)	0.74
Brachiocephalic	1.22 (0.64-2.35)	0.55

Abbreviations: CI, confidence interval; HR, hazard ratio.

direction of access was based on the lesion location. Fistulas were evaluated fluoroscopically with iodinated contrast. Stenoses with at least 50% visual luminal narrowing were treated with plain-balloon angioplasty to the end point of ≤30% stenosis by fluoroscopic assessment. Pressure measures were not routinely performed. Noncovered stents were not used. Covered stents were used only in cases of fistula rupture. Target lesion revascularization, defined as reintervention of recurrent stenosis at the same location, was performed on recurrent hemodynamically significant lesions as needed.

Statistical Analysis

All analyses were completed using SAS, version 9.4 (SAS Institute). Descriptive statistics of patient characteristics are reported as mean (standard deviation) for continuous variables. Non-normally distributed data was described as median (25th-75th percentile). A Cox proportional hazard model was used to assess the association between patency and patient characteristics, fistula configuration, and comorbid conditions. The alpha level was set at 0.05 for statistical significance.

RESULTS

All patients in this study received hemodialysis. Patients with brachiobasilic fistulas had the shortest maturation time with a median of 73.5 (interquartile range [IQR], 45.0-170.0) days from the time of construction to first use. In comparison, brachiocephalic fistulas had a median time of 141.0 (IQR, 58.0-360.0) days and radiocephalic fistulas had a median time of 106.0 (IQR, 51.0-463.0) days. Ultimately, 19 (9.0%) fistulas never matured adequately for dialysis: 2 of 42 (4.8%) radiocephalic fistulas, 10 of 135 (7.4%) brachiocephalic fistulas, and 7 of 30 (23.3%) brachiobasilic fistulas.

Median postintervention primary patency was 2.7 years, median postintervention primary-assisted patency was 3.2 years, and median postintervention secondary patency was 3.6 years. Overall 1-year primary, primary-assisted, and secondary patency rates in this cohort were 53.0%, 87.7%, and 83.5%, respectively. There were 261 stenoses treated among the 210 fistulas, establishing the baseline for postintervention patency. This included 107 (41.0%) stenoses in the JAS, 86 (33.0%) in the outflow vein, 55 (21.1%) in the cephalic arch, and 13 (5.0%) in the central veins. From the time of the first intervention to the end of follow-up, 156 new or recurrent flow-limiting lesions were identified, which included 60 (38.5%) JAS lesions, 57 (36.5%) outflow vein lesions, 29 (18.6%) cephalic arch lesions, and 10 (6.4%) central vein lesions. Of the 210 fistulas initially treated for stenosis, 46 (21.9%) developed thrombosis and 74 (35.2%) fistulas were eventually abandoned. Fistula patency is summarized in Table 2.

Compared with the radiocephalic configuration, brachiocephalic fistulas had significantly higher risk for postintervention primary patency loss (hazard ratio [HR], 1.90; 95% confidence interval [CI], 1.13-3.20; P = 0.02), but not postintervention primary-assisted and postintervention secondary patency (P = 0.46 and P = 0.55, respectively). The cumulative probability of significant recurrent stenosis at 1 year is summarized in Table 3.

Several comorbid conditions were evaluated as potential contributors to patency loss, including diabetes mellitus, coronary artery disease, peripheral artery disease, hyperlipidemia, and hypertension. None of these were significant factors affecting postintervention primary, primary-assisted, or secondary patency. Tobacco smoking increased the risk for loss of postintervention primary patency (HR, 2.22; 95% CI, 1.12-4.40; P = 0.02), but postintervention primary-assisted and secondary patency loss were not significantly affected (P = 0.98 and P = 0.25, respectively).

Medications were reviewed, which included β-blockers, calcium channel blockers, aspirin, clopidogrel, warfarin, and statins. None of these medications were associated with lower rates of patency loss. Aspirin was associated with increased risk for loss of postintervention primary patency (HR, 1.52; 95% CI, 1.04-2.21; P = 0.03), though no association with postintervention primary-assisted or secondary patency loss was found (P = 0.99 and P = 0.64, respectively). A total of 133 (63%) patients were taking aspirin at the time of fistula construction.

DISCUSSION

This study evaluated postintervention patency in the largest cohort of dialysis fistulas constructed in the non–dialysis-dependent population. Among the radiocephalic, brachiocephalic, and brachiobasilic fistulas, the radiocephalic fistula demonstrated the best postintervention primary patency. Of the 4 different fistula locations examined, the most common site for primary stenosis was the JAS

Table 3. Target Lesion Revascularization Rate Based by Fistula Configuration

	1-y Cumulative Probability of Recurrent Stenosis by Lesion Location (95% confidence interval)			
Fistula Configuration	**Juxta-anastomosis**	**Outflow Vein**	**Cephalic Arch**	**Central Vein**
Radiocephalic	23.8% (13.0%-43.6%)	12.5% (2.0%-78.2%)	0%	0%
Brachiobasilic	23.5% (10.0%-55.4%)	32.5% (15.8%-67.0%)	0%	50.0% (12.5%-100.0%)
Brachiocephalic	40.7% (29.5%-56.2%)	33.9% (23.9%-48.0%)	36.5% (25.5%-52.3%)	45.5% (23.8%-86.8%)

segment. Recurrent stenosis at 1 year of treatment occurred most frequently at the cephalic arch, whereas central venous stenoses were the least likely to reoccur after angioplasty. The rate of restenosis was not influenced by any of the comorbid conditions reviewed. However, smoking increased the risk for postintervention primary patency loss.

The construction of radiocephalic and other fistulas in the forearm can be challenging due to small vessel size. As a result, forearm fistulas may have lower maturation rates compared with arm fistulas.[13,20,21] However, if the vessel diameter is adequate, the data in the current study demonstrate that these fistulas may be at least as durable as those created in the upper arm. Furthermore, fistulas in the wrist have the benefit of enabling the creation of upper-arm fistulas after failure of the forearm fistula, whereas it is usually impossible to create fistulas in the opposite order.[22]

A retrospective study investigating endovascular therapy in 153 immature fistulas by Han et al[23] demonstrated that the radiocephalic fistula configuration was not associated with better primary ($P = 0.819$) or secondary patency rates ($P = 0.465$). However, a subsequent retrospective study by Lee et al[12] demonstrated better primary patency among 42 immature radiocephalic fistulas compared with 12 immature brachiocephalic fistulas ($P = 0.003$). In a study of mature fistulas, Rajan et al[24] reported that among 94 radiocephalic and 57 brachiocephalic fistulas, radiocephalic fistulas had significantly better 3-, 6-, and 12-month primary patency ($P = 0.004$), but not secondary patency ($P = 0.45$).

The 1-year postintervention primary patency rate in this study was 53%. This finding is similar to mature fistulas that develop recurrent stenosis after endovascular therapy.[25,26] Dialysis fistula stenoses most often occur at or adjacent to the anastomosis, which was further confirmed in this study.[27,28] The location of stenosis recurrence varied by fistula configuration. The juxta-anastomosis was the most common location of recurrence for radiocephalic fistulas. However, recurrent central venous stenosis was the most prevalent site of recurrence among both brachiobasilic and brachiocephalic fistulas. Previously reported primary patency for treated central venous stenoses in patients with dialysis fistulas was 46% at 9 months.[29] The lower patency rate for central venous stenosis at 1 year may be due to higher elastic recoil of central venous lesions.[30]

However, treatment of primary stenoses involving the cephalic arch had the worst postintervention primary patency with a 1-year probability of recurrent stenosis of 34.6%. Previously reported primary patency of cephalic arch stenosis treated using plain balloon angioplasty was 11%.[31] In contrast, central venous stenoses recurred the least often at a rate of 7.7% at 1 year after intervention in the present study.

Tobacco smoking was associated with poorer postintervention primary patency outcomes. Smoking is an established risk factor for primary failure in dialysis fistulas, though data for the effect of tobacco use and postintervention patency are limited.[32,33] The incidence of primary fistula failure may be 4.3 times greater among patients with a history of smoking. Other previously reported risk factors for arteriovenous fistula patency loss, including age, sex, and diabetes, were not found to have a significant impact on postintervention patency rates.[32,34,35]

Aspirin use at the time of intervention was associated with an increased risk for loss of postintervention primary patency, but not postintervention primary-assisted or secondary patency. Consistent aspirin use has been shown to be associated with a 37% reduction in fistula failure, but no data are available for postintervention primary patency.[36] A meta-analysis by Tanner and da Silva[37] failed to demonstrate any beneficial effect from aspirin as an adjuvant therapy. The current study is the first to show that aspirin may have a deleterious effect on fistula patency postintervention. This finding may reflect the fact that recurrent fistula failure is typically a result of venous intimal hyperplasia rather than in situ thrombosis.[38] Furthermore, aspirin use can be a marker for cardiovascular disease and may signify a more comorbid population.

This study was limited by its retrospective design, resulting in variations in angioplasty technique, medical treatment, and follow-up. Angioplasty technique including balloon pressure and duration of dilation was not measured and is a major limitation. The interval between fistula construction and initiation of dialysis, whether through the fistula or a catheter, was variable. Radiocephalic fistulas in this study demonstrated better primary patency than other configurations. This may be explained by this group of patients having healthier veins or potentially less peripheral arterial disease. Vessel quality was not evaluated and may be a confounding variable for these findings.

In conclusion, among non–dialysis-dependent patients who undergo initial endovascular therapy to maintain

fistula patency, the radiocephalic configuration was found to have the best postintervention primary patency compared with other configurations. Although the majority of hemodynamically significant lesions occurred at the anastomosis, lesions in the noncannulation zone of the outflow vein had the highest rates of target lesion revascularization and may require more aggressive treatment.

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Support: Dr Misra has funding from National Institutes of Health grant DK107870 from the National Heart, Lung, and Blood Institute (HL 098967). Funders had no role in the study design, decision to submit for publication, or other input into this study.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Prior Presentation: This manuscript was presented in abstract form at the Society for Interventional Radiology Annual Scientific Meeting; March 23-28, 2019; Austin, TX.

Peer Review: Received July 28, 2019. Evaluated by 1 external peer reviewer, with direct editorial input from the Statistical Editor, an Associate Editor, and the Editor-in-Chief. Accepted in revised form February 11, 2020.

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