Clinical Outcomes of Vascular Accesses in Hemodialysis Patients

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ABSTRACT **Background:** Reliable vascular access is a fundamental tool for providing effective hemodialysis. Vascular access dysfunction is associated with increased morbidity and mortality among hemodialysis patients. Current vascular access guidelines strongly recommend creating an arteriovenous fistula (AVF) as the first option; however, a substantial proportion of new AVFs may not be usable.

Objectives: To assess possible predictors of primary and secondary failure of vascular access.

Methods: This retrospective cohort study included all vascular access sites created at Meir Medical Center from 2006 through 2012. Vascular access site, primary and secondary failure rates, and relevant demographic and clinical data were recorded during 60 months of follow-up.

Results: A total of 612 vascular accesses were created and followed for a median of 32 ± 29.4 months. Of these, 490 (80%) were suitable for initiating hemodialysis. Vascular access site was the most important predictor of primary failure but did not predict secondary failure. Co-morbidities such as diabetes mellitus and congestive heart failure, as well as the use of antiplatelet agents did not predict primary or secondary failure. Preoperative vascular mapping using Doppler ultrasonography was performed in 36.4% of cases and was not associated with lower rates of primary or secondary failure.

Conclusions: Vascular access site is an important predictor of primary failure. We did not find a benefit of pre-operative vessel mapping or chronic antiplatelet therapy in terms of decreasing primary and secondary failure rates. Physicians should carefully consider the characteristics of the patient and blood vessels before creating vascular access in patients requiring chronic hemodialysis.

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The population of patients with end-stage kidney disease is growing, with over 1.5 million people worldwide receiving hemodialysis. Reliable permanent vascular access is a fundamental tool for providing adequate and effective hemodialysis. It optimizes vascular patency and decreases the frequency of infectious events, hospitalizations and mortality [1-4].

A large proportion of patients initiate hemodialysis with a central venous catheter and when available, they switch to permanent vascular access (VA). Both arteriovenous fistula (AVF) and arteriovenous graft (AVG) are strongly recommended [1]. AVFs are considered to be the preferred method for VA because they exhibit greater functional longevity, are less prone to infection, and are associated with decreased mortality and lower costs.

However, 28% to 53% of created VA do not mature and subsequently are never useable for hemodialysis [5]. Several large studies have reported a high failure rate of primary AVF (AVF non-maturation), especially among elderly patients. The advantage of the AVF first program as a policy for all patients who are candidates for hemodialysis is not necessarily appropriate due to patient preferences, poor life expectancy, or co-morbidities such as severe pulmonary hypertension, heart failure, or severe peripheral vascular disease [6,7]. High primary failure rates remain a major obstacle to decreasing the proportion of dialyzed patients with unusable VA.

Percutaneous transluminal angioplasty has become routine for managing VA dysfunction and could improve the rate of useable VA. One study achieved successful percutaneous transluminal angioplasty for VA dysfunction in 87% of 75 non-maturing AVF (assisted maturation), allowing more than 50% of these VA to be functional after 3 years [8]. Up to 25% of functional AVF fail 2 years after they are created. Interventional procedures are commonly undertaken to salvage failing AVFs due to high complication rates and low success rates once a stenosis has caused AVF thrombosis (secondary failure) [9].

In this study, we assessed possible predictors of primary and secondary VA failure among patients undergoing chronic hemodialysis to improve the criteria for choosing patients for VA creation.

PATIENTS AND METHODS

This retrospective cohort study included all VA created from 1 January 2006 through 31 December 2012 at Meir Medical Center. Patients 18 years of age or older were referred by a nephrologist to the Vascular Surgery Clinic in which all patients undergo basic evaluation of vascular history and physical examination. Based on clinical evaluation of the vascular surgeon, select patients undergo vascular mapping of vessels in both arms. Vessels are mapped using Doppler ultrasonography, which measures flow velocity as well as the inner diameters of arteries and veins. Vascular surgeons create the VA.

Demographic and clinical data from the electronic medical records were recorded for each patient when the VA was created.

STUDY OUTCOMES

The primary endpoints were primary and secondary failure of the VA. Primary failure was defined as permanent failure of VA before it was suitable for hemodialysis. This result included non-maturation of the VA, thrombosis, and failure of first and subsequent cannulations, which led to the inability to initiate hemodialysis through the VA. Secondary failure was defined as permanent failure of the VA after it met dialysis suitability criteria but was subsequently abandoned.

Dialysis suitability criteria were defined as VA that was used for hemodialysis and enabled blood flow rates of at least 300 ml/min, *via* two-needle cannulation consistently, for at least 1 month, within 6 months of its creation.

Secondary endpoints were postoperative complications. Complications related to creating VA included arterial steal syndrome and postoperative infections.

ETHICS CONSIDERATIONS

The study was approved by the local institutional ethics committee in keeping with the principles of the Declaration of Helsinki. In accordance with Ministry of Health regulations, the institutional ethics committee did not require written informed consent because data were collected anonymously from the electronic medical records without active patient participation.

STATISTICAL ANALYSIS

Data are expressed as mean ± standard deviation (SD) for continuous variables and as numbers and percentage for non-metric parameters. Metric data were checked for normality with Shapiro–Wilk test. As some of the variables were not normally distributed, *t*-test and Mann–Whitney nonparametric test were used to compare the two groups for the different variables. Chi-squared or Fisher's exact test was used to compare categorical parameters. A P-value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 21 (SPSS, IBM Corp, Armonk, NY, USA).

RESULTS

From 1 January 2006 through 31 December 2012, 612 VAs were created. Table 1 summarizes the demographic and clinical characteristics of the study population. The mean age was 67.0 ± 13 years. Diabetic kidney disease was the most frequent etiology of end-stage kidney disease followed by hypertensive kidney disease. The most common VA was brachiocephalic AVF (46.4% of the VA) followed by brachiobasilic AVG (25.3%). Patients with radiocephalic AVF were younger than those who received brachiocephalic AVF (63.0 ± 15.5 years vs. 68.5 ± 12.5 years, respectively; $P = 0.001$).

Among the 612 VA created, 490 (80%) were suitable for starting hemodialysis, 61 (9.9%) of which required an angiographic or surgical procedure before successful first use (assisted maturation).

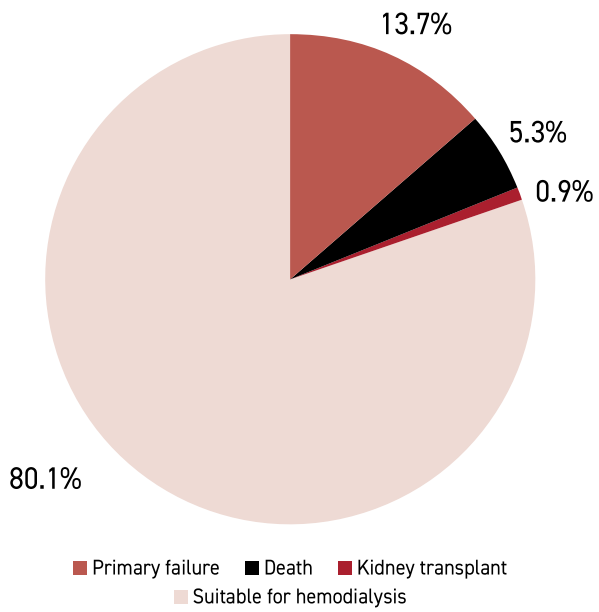
The median time from VA creation to end of follow-up was 31.5 months (range 1–60 months). A total of 38 VAs were not used, either due to patient death (n=32) or kidney transplantation (n=6). At the end of follow-up, 53.6% of the VAs were suitable for dialysis [Figure 1].

Table 1. Baseline characteristics of the study population (N=612)

Baseline characteristics	Value
Age (years, mean ± standard deviation)	67 ± 13
Sex (male/female)	378/234
Etiology of renal disease	
Diabetes mellitus	324 (52.9%)
Hypertension	107 (17.5%)
Glomerulonephritis	44 (7.2%)
Autosomal dominant polycystic kidneys	27 (4.4%)
Miscellaneous	110 (18%)
Co-morbidities	
Diabetes mellitus	379 (62%)
Congestive heart failure	237 (38.7%)
Antiplatelet agent	400 (65.3%)
Vascular mapping	223 (36.4%)
Vascular access site	
Brachiocephalic AVF	284 (46.4%)
Radiocephalic AVF	86 (14%)
Brachiobasilic AVG	155 (25.3%)
Other	87 (14.3%)

The data are presented as absolute numbers and percentages unless otherwise mentioned. AVF = arteriovenous fistula, AVG = arteriovenous graft

Figure 1. Clinical outcome of all included VA (median follow-up 31.5 months; range 1–60 months). A total of 612 VA was included; 80.1% (490/612) of VA were suitable for hemodialysis, 13.7% (84/612) had primary failure, 5.3% (32/612) were not used due to patient death, and 0.9% (6/612) were not used due to kidney transplant before use



PRIMARY FAILURE

Primary failure occurred in 84 of 612 (13.7%) of the VA. Patient age, sex, co-morbidities such as diabetes mellitus and congestive heart failure, preoperative vascular mapping, and the use of antiplatelet therapy did not affect the primary failure rate [Table 2]. Multivariate analysis of demographic and clinical data showed that the most important predictor of primary failure was VA site. Table 2 details the odds ratio of primary failure, using radiocephalic AVF as the reference group. Primary failure occurred more frequently with radiocephalic AVF as compared to non-radiocephalic AVF (30.2% vs. 11.0 %, $P < 0.001$).

There was a trend toward lower incidence of primary failure between AVG vs. AVF (9.7% vs. 15.3%), odds ratio (OR) for primary failure in AVG 0.59 with 95% confidence interval (95%CI) 0.34–1.04, $P = 0.067$.

SECONDARY FAILURE

Secondary failure occurred in 170 of 528 VAs that were suitable for hemodialysis at a mean of 21.1 ± 15 months from creation.

Secondary failure occurred more frequently in younger patients (64.7 ± 12.8 vs. 67.6 ± 13.8 years, $P = 0.019$). There was no significant difference in the prevalence of co-morbidities and the use of antiplatelet therapy in patients who developed secondary failure, compared to patent VA. Thrombosis occurred more frequently with radiocephalic AVF than with non-radiocephalic AVF (31.3% vs. 24.5%, respectively) and with brachiobasilic AVG vs. non-brachiobasilic AVG (33.5% vs.22.7%, respectively; $P < 0.005$). Survival rates of AVG vs. AVF, based on time from creation until secondary failure and usage were similar ($P = 0.382$).

Overall, secondary failure occurred more often with AVG vs. AVF (34.7% vs. 24.8%). OR for secondary failure with AVG was 1.6 with 95%CI 1.1–2.4, $P = 0.013$.

Secondary failure was more frequent in VA that required assisted maturation (intervention before use) and in those that needed first angiographic intervention prematurely. The number of interventions did not differ between the groups [Table 3].

POSTOPERATIVE COMPLICATIONS

Postoperative complications leading to VA closure included steal syndrome (4.5%), and infections (3.6%). VA closure due to infection was more frequent in non-brachiocephalic AVF compared to brachiocephalic (8.4% vs. 0.7%, $P < 0.001$) and in non-diabetic patients compared to those with diabetes (10.3% vs. 4.2%, $P < 0.005$). The incidence of infections that led to surgical VA closure was higher among patients with AVG compared to AVF (8.9% vs. 1.4%, $P = 0.01$).

VA stenosis is a well-known complication that often develops before the first use. Among 612 patients, 282 (46%) underwent angiographic procedures to improve patency during the study period, of which 61 (9.9%) were performed before first use. Angiographic procedures occurred less often in patients with brachiocephalic AVF than with non-brachiocephalic AVF (43.3% vs.48.5%, $P < 0.05$).

VASCULAR MAPPING

Preoperative vascular mapping was performed in 223 cases (36.4%) and did not significantly affect the rate of primary or secondary failure or the need for angiographic intervention.

DISCUSSION

We reported the outcomes of 612 consecutive vascular accesses in a single center cohort of patients on chronic hemodialysis, in Israel. AVF and AVG are preferred for VA due to fewer complications and lower mortality rates, as compared with central venous catheters [1]. Yet both AVF and AVG are not free of complications. Primary failure occurred in 13.7% of all VA created,

Table 2. Predictors of primary failure (permanent failure of vascular access before hemodialysis suitability) and comparison of clinical and demographic data between patients with primary failure or patent vascular access (n=612)

Variable	Patent vascular access (N=528)	Primary failure (n=84)	Odds ratio (95% confidence interval)	*P* value
Age (years, mean ± standard deviation)	66.68 ± 13.52	67.54 ± 13.27		0.91
Female, %	37.1%	45.2%		0.155
Mapping before operation	195 (36.9%)	28 (33.3%)		0.524
Serial number of accesses, first vascular access	334 (63.3%)	51 (60.7%)		0.816
Diabetes mellitus	330 (62.5%)	49 (58.3%)		0.465
Congestive heart failure	205 (38.8%)	32 (38.1%)		0.898
Chronic use of antiplatelet agents	345 (65.3%)	55 (65.5%)		0.981
Previous peritoneal dialysis	51 (9.7%)	8 (9.5%)		0.923
Braciocephalic arteriovenous fistula*			0.35 (0.123–0.996)	0.049
Brachiobasilic arteriovenous fistula*			0.226 (0.133–0.531)	0.000
Arteriovenous graft*			0.220 (0.048–1.007)	0.051

*Reference: radiocephalic AVF
AVF = arteriovenous fistula

Table 3. Clinical and demographic data of 528 patients with vascular access that resulted in secondary failure*

Variable	Patent vascular access (N=358)	Secondary failure (n=170)	Odds ratio (95% confidence interval)	*P* value
Age (years, mean ± standard deviation)	67.6 ±13.7	64.7 ± 12.8		0.019
Male, n (%)	225 (62.8%)	107 (62.9%)	1.00 (0.69–1.5)	0.984
Mapping before operation	125 (34.9%)	70 (41.2%)	0.76 (0.52–1.11)	0.164
Diabetes mellitus	225 (62.8%)	105 (61.8%)	1.05 (0.71–1.52)	0.810
Congestive heart failure	142 (39.7%)	63 (37.1%)	0.896 (0.6–1.3)	0.566
Chronic use of antiplatelet agents	239 (66.8%)	106 (62.4%)	0.825 (0.56–1.2)	0.320
Need intervention before use	32 (8.9%)	29 (17.1%)	0.48 (0.28–0.81)	0.006
Time to first intervention (months ± standard deviation)	14.4 ± 15.9	10.9 ± 11.8		0.042
Number of interventions	2.8 ± 2.6	2.6 ± 2.6		0.428

*Patients with vascular access defined as primary failure (n=84) were excluded from this analysis

an acceptable rate compared to other studies, which range from 28% to 53% [2,5].

The most important predictor of primary failure in our cohort was VA site. Radiocephalic AVF was the most prone to primary failure, and other than location, we did not find factors, such as chronic antiplatelet treatment or co-morbidities, which predicted VA patency. The high rate of primary failure in radiocephalic AVF is well-recognized and could be due to an imbalance between neointimal hyperplasia and impaired arterial vasodilation following fistula creation [10]. This finding should encourage physicians to carefully consider the radial artery diameter, its ability to dilate, and other patient and blood vessel characteristics before creating radiocephalic AVF in patients requiring chronic hemodialysis [5,9].

In our cohort, the mean age of patients who received radiocephalic AVF (63 years) was younger than those who received brachiocephalic AVF (68 years, $P = 0.001$), which may explain the significant difference in age between patients with secondary failure VA and those who remained patent.

VA that required earlier angiographic intervention or assisted maturation was more likely to be defined as secondary failure during follow-up. This observation may be explained by the limited success of percutaneous interventions before and after the VA were used for hemodialysis. Percutaneous interventions may salvage some of the VA and help their maturation, but their success is limited [5,10]. In a recent prospective randomized trial that enrolled 330 patients with dysfunctional AVF, Lookstein et al. showed that at the 6-month

follow-up, drug-coated balloon angioplasty was superior to standard angioplasty for treating VA stenosis [11]. These results could potentially provide a more successful method to improve the duration of VA in hemodialysis patients [11].

We did not find significant differences in primary and secondary failure rates in VA that were created with or without vessel mapping. The lack of clear benefit of mapping before VA creation was also demonstrated in a meta-analysis [12], although other studies reported a benefit [13,14]. This result can be explained by differences in local experience and the exact information derived from the vessel mapping. For example, during the study period, routine mapping in our institution did not evaluate radial artery flow and vessel diameter and focused only on venous vasculature. Another explanation is a possible selection bias, in that patients referred for vessel mapping were more likely to have problematic, impalpable veins on physical examination or other risk factors compared to patients who did not undergo mapping. Recently, Farrington et al. [15] showed that using a combination of preoperative arterial diameter, systolic blood pressure, and left ventricular ejection fraction could improve the rate of successful AVF maturation.

Similar to other studies, we did not observe any benefits from chronic antiplatelet therapy on VA patency [16,17]. Chronic antiplatelet therapy did not affect the rates of primary or secondary failure in our study, which is the same finding as in other cohorts [16,17].

We observed a relatively low rate of complications necessitating VA closure (4.5% steal syndrome and 3.6% infections). The incidence of these complications is similar to those described in other studies, which ranged from 1% to 20% and depended on the prevalence of known risk factors such as VA site, peripheral arterial disease, and diabetes. In our cohort, significantly more patients with diabetes underwent AVG than radiocephalic AVF, which probably explains the infection rate after VA surgery.

LIMITATIONS

This study was a single center, retrospective study. Since mapping was not performed on all patients, a clear conclusion regarding its benefits cannot be reached based on this study alone. We did not have important data concerning dialysis vintage, the presence of peripheral arterial disease, central venous stenosis, and central venous catheter duration, which might affect the success rate and patency of VA. The study included mainly an older population with a mean age of 67 years. Therefore, the results cannot be generalized to younger patients.

STRENGTHS

This study has several strengths, including a relatively long-term follow-up of a large cohort representative of a population on chronic hemodialysis. In addition, the high quality of the electronic data at the individual patient level allowed us to determine the exact site and outcome of each VA.

The current study provides important clinical implications to the field of vascular access. With the population requiring hemodialysis growing and the need for reliable VA increasing, information to improve success rates is needed. VA has an important impact on patient survival, morbidity, and hospitalization. Until now, except for percutaneous angiography, to the best of our knowledge, no intervention has been found to increase VA success rates. We found that the VA site is an important predictor of its patency. We did not find benefits from pre-operative vessel mapping or chronic antiplatelet therapy in terms of decreasing primary and secondary failure rates. Our findings support the need for careful, multi-disciplinary evaluation of each patient before creating VA.

CONCLUSIONS

Our cohort included 612 VA with acceptable primary and secondary failure rates (13.7% and 32.2%, respectively). VA site is an important predictor of VA patency.

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Capsule

Parental inflammatory bowel disease and autism in children

Evidence linking parental inflammatory bowel disease (IBD) with autism in children is inconclusive. **Sadik** and co-authors conducted four complementary studies to investigate associations between parental IBD and autism in children, and elucidated their underlying etiology. Conducting a nationwide population-based cohort study using Swedish registers, the authors found evidence of associations between parental diagnoses of IBD and autism in children. Polygenic risk score analyses of the Avon Longitudinal Study of Parents and Children suggested associations between maternal genetic liability to IBD and autistic traits in children. Two-sample Mendelian randomization analyses provided evidence of a potential causal effect of genetic liability to IBD, especially ulcerative colitis, on autism. Linkage disequilibrium score regression did not indicate a genetic correlation between IBD and autism. Triangulating evidence from these four complementary approaches, they found evidence of a potential causal link between parental, particularly maternal, IBD and autism in children. Perinatal immune dysregulation, micronutrient malabsorption and anemia may be implicated.

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Capsule

Omicron infection enhances Delta antibody immunity in vaccinated persons

The extent to which Omicron infection, with or without previous vaccination, elicits protection against the previously dominant Delta (B.1.617.2) variant is unclear. **Khan** et al. measured the neutralization capacity against variants of severe acute respiratory syndrome coronavirus 2 in 39 individuals in South Africa infected with the Omicron sublineage BA.1 starting at a median of 6 (interquartile range 3–9) days post symptom onset and continuing until last follow-up sample available, a median of 23 (interquartile range 19–27) days post symptoms to allow BA.1-elicited neutralizing immunity time to develop. Fifteen participants were vaccinated with Pfizer's BNT162b2 or Johnson & Johnson's Ad26.CoV2.S and had BA.1 breakthrough infections, and 24 were unvaccinated. BA.1 neutralization increased from a geometric mean 50% focus reduction neutralization test titer of 42 at enrolment to 575 at the last follow-up time point (13.6-fold) in vaccinated participants and from 46 to 272 (6.0-fold) in unvaccinated participants. Delta virus neutralization also increased, from 192 to 1,091 (5.7-fold) in vaccinated participants and from 28 to 91 (3.0-fold) in unvaccinated participants. At the last time point, unvaccinated individuals infected with BA.1 had low absolute levels of neutralization for the non-BA.1 viruses and 2.2-fold lower BA.1 neutralization, 12.0-fold lower Delta neutralization, 9.6-fold lower Beta variant neutralization, 17.9-fold lower ancestral virus neutralization and 4.8-fold lower Omicron sublineage BA.2 neutralization relative to vaccinated individuals infected with BA.1. These results indicate that hybrid immunity formed by vaccination and Omicron BA.1 infection should be protective against Delta and other variants. By contrast, infection with Omicron BA.1 alone offers limited cross-protection despite moderate enhancement.

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