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Research Article

Risk Factors Associated with Tunneled Hemodialysis Catheter Use at the Start of Dialysis in Patients Referred for Early Arteriovenous Fistula Placement

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ABSTRACT

Objectives: We reviewed a consecutive series of patients who had arteriovenous fistula (AVF) placement in advance of starting hemodialysis and sought to determine what factors were associated with failure of the AVF to be ready for use which required patients to start dialysis with a tunneled dialysis catheter (TDC)?

Methods: We analyzed all patients who had an AVF placed at our institution from 2013-2018 using data from the Vascular Quality Initiative database and retrospective chart review. The primary study group included patients who had an AVF placed in advance of needing hemodialysis. Patients were categorized as "Success": AVF placement with hemodialysis initiated using the AVF or "Failure": AVF placement with hemodialysis initiated using a TDC.

Results: Of the 46 patients reviewed 26 (56.5%) were classified as "Failure." Pre-operative factors associated with failure included: uremia (5% of success group, vs. 26.9% of failure group; p=0.031), uremic males (37.5% of uremic male patients failed vs. 0% of uremic females p=0.007), history of coronary artery disease among males (success, 8.33% vs. fail, 50%, p=0.04), and history of percutaneous coronary intervention among males (fail male, 25% vs. fail female, 0%; p=0.030).

Conclusion: In our series of patients referred for AVF placement prior to starting dialysis we noted an unexpectedly high rate of hemodialysis initiation with a TDC. This study suggests that patient related factors such as uremia and a history of coronary artery disease or intervention may be associated with failure of the AVF to be ready for hemodialysis. Further work building from findings in this study may help with patient selection decisions to minimize the need to initiate hemodialysis with a TDC.

Keywords: Arteriovenous fistula; Hemodialysis; Dialysis access; Risk factors

INTRODUCTION

As the population ages, chronic kidney disease will become more prominent as a source of morbidity and mortality. Approximately 4.9 million adults have Chronic Kidney Disease (CKD) and it ranks as the 9th leading cause of death accounting for 15.5 deaths per 100,000 persons [1]. In the near future more than 500,000 people in the United States will depend on dialysis as the life sustaining treatment for their kidney failure [1,2]. By acting as the link between the patient and the dialysis machine, vascular access plays a critical role in the life of every dialysis patient.

Vascular access can take various forms including a tunneled catheter (TDC), an arteriovenous graft (AVG) using prosthetic material, or an arteriovenous fistula (AVF) created with autogenous superficial veins [3]. Clinical experience and outcome studies show that autogenous AVFremain the safest and most durable type of vascular access [2]. Although prosthetic AVGcan provide effective hemodialysis, they are more vulnerable to infection and dysfunction [2]. TDCs represent the least desirable form of vascular access as patients relying on catheters have higher rates of hospitalization, more episodes of sepsis, less effective dialysis, and shorter survival [2]. These findings prompted the "Fistula First" initiative to increase the use of autogenous AVFs in hopes of reducing hemodialysis related morbidity and mortality [4,5].

According to Fistula First guidelines, patients should be referred for AVF placement 6-12 months in advance of needing to start

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hemodialysis [4,5]. A surgically created autogenous AVF would theoretically have ample time to "mature" before the patient needed hemodialysis [3]. Maturation of an AVF refers to the time required for the vein to enlarge enough for safe needle cannulation and the initiation of hemodialysis. Achieving maturity requires at least 6-8 weeks and may take as long as 6-12 months according to real world data [3]. This delay from surgical creation to functionality is the main drawback of AVFs. If the AVF is not ready when the patient needs dialysis, the patient usually relies on a TDC for dialysis until the AVF matures or a new access is placed [6]. Prolonged catheter times in these patients can result in infection, sepsis, hospitalization, ineffective dialysis, and central venous stenosis [6].

One of the unintended consequences of "Fistula First" has been an increase in the number of patients using a TDC for dialysis while they wait for AVF maturation [4,5]. This group of patients includes those with slow maturing or non-functional AVFs who use a catheter until they have a functional access. Although it is not currently possible, predicting which patients will require hemodialysis before their AVF is ready to use would be valuable information. Reliably identifying this subgroup of patients could influence the decision to place an AVG instead of waiting for an AVF to mature. In general, AVGs can be used within 2 weeks of placement which usually obviates the need for TDC placement.

This study retrospectively analyzed all patients who have had an AVF placed at SUNY Upstate University Hospital from January 2012-October 2018. All patients were referred for vascular access before they required hemodialysis and all patients had an AVF placed. Patient's were then analyzed according to whether they initiated dialysis with a functional AVF or required a TDC before their AVF was ready to use. We searched for variables which consistently identify patients at increased risk for requiring a TDC to initiate dialysis. Identifying this subgroup of patients could help establish a new treatment algorithm in which high risk patients for AVF failure are treated with an AVG. This change in treatment strategy could decrease the number of patients requiring a catheter for dialysis and potentially reduce some of the morbidity, hospital admissions, and health care costs associated with hemodialysis.

MATERIALS AND METHODS

Patient records

Our study analyzed all patients who have had an AVF a placed at Upstate University Hospital during January 2013-October 2018. All vascular access cases performed at Upstate University Hospital have been enrolled in the Vascular Quality Initiative (VQI), a national database using clinical based variables entered by a dedicated vascular nurse. The study dealt with de-identified health data collected retrospectively. Consent was not obtained, and the study was considered exempt from IRB approval.

Study design

The primary study group included patients that presented for AVF assessment not already on dialysis. Patients were then assigned into one of two main groups: 1) Patients who had an AVF placed and started dialysis by using the fistula ("Success"); 2) Patients who had an AVF placed and initiated dialysis with a TDC ("Fail"). At out institution, criteria that were used to determine if a patient's AVF was ready for access included: physical exam and clinical judgement, ultrasound duplex on an as needed basis and it is worth noting that there was no mandatory 6-weekswait period. All patients that required a dialysis catheter had a tunneled catheter (TDC) and no patients had non-tunneled catheters which are reserved for acute, inpatient dialysis.

Statistical methods

Univariate statistical analyses using t-tests for continuous measures and comparison of means, as well as Fisher's exact tests for categorical variables was used to analyze the clinical and demographic measures. P-values <0.05 were considered statistically significant.

RESULTS

General and demographics

A total of 46 records were used for analysis during the defined study period (13 records excluded due to incomplete records or loss to follow-up). The AVF fail rate, defined as the proportion of cases initiating dialysis with a TDC, was found to be 56.5% (26/46). The average age for AVF fail cases did not differ from the AVF success cases (54.6 ± 12.4 years vs. 56.9 ± 12.3 years; p=0.39). When examined by categorized age groups of ≥ 65 and ≥ 70, age was still a non-factor (p=0.89 and p=0.29). Similarly, gender was not a significant factor as the proportion of male: female AVF success and fail cases did not differ (success of 12:8 vs. fail of 8:18; Fisher's exact p=0.07) (Table 1). A breakdown of the demographics for ethnicity and male vs. female for each demographic group is provided (Table 2). Higher rates of AVF success was not associated with white vs. Black or African American (p=0.60), Native Hawaiian or other Pacific Islander (p=0.23), or "Unknown/other" (p=0.77); American Indian or Alaska Native (n=3) did however have a 100% success rate vs. 39.4% (n=33) for white/Caucasian (p=0.046) (Table 3). No significant relationship was found between success vs. failure for smoking status (Fisher's exact p=0.10), BMI of overweight/obese (p=0.64), primary insurer (commercial p=0.80; Medicaid p=0.81; Medicare p=0.99) or American Society of Anesthesiologists (ASA) physical status of ≥ 4 (p=0.41) (Table 4).

Table 1: General characteristics of study cases, characteristics of cases used in the study separated by AVF success vs. failure.

	AVF success	AVF fail	p-value
Count (n, %)	20 (43.5%)	26 (56.5%)	0.39
Average Age (years)	54.6 ± 12.4	56.9 ± 12.3	
Male (n)	12	8	
Female (n)	8	18	0.07

Table 2: Ethnicity breakdown, ethnicity information of study participants.

Race/ Ethnicity	Male (n)	Female (n)	Net
White	14	19	33
Black or African American	3	4	7
Native Hawaiian and other Pacific Islander	0	1	1
American Indian or Alaska Native	2	1	3
Unknown/Other	1	1	2

Vein mapping and AVF types

Overall, there were 20 distal radial-cephalic (43.5%), 16 brachial-cephalic (34.8%), 5 forearm basilic (10.8%), and 5 upper arm basilic (10.8%) AVF fistulas. There was no statistical difference observed for success rates among the different types of AVF (data not reported). Additionally, preoperative vein mapping (performed on 45/46 cases, 97.8%) did not show an association between vein diameter and success or failure to mature as an aggregate of cases nor when stratified by each AVF type (data not reported). Data was not stratified to compare AVF type and co-morbidities/clinical data with rates of success as the type of AVF was not a primary or secondary focus of this study.

Clinical and laboratory factors

In our study we identified that pre-operative uremia was an independent risk factor associated with increased AVF failure (success, 5% vs. fail, 30.7%; p=0.031). Uremia was identified in the patient's chart as reported by their primary nephrologist. In particular, males with uremia had higher rates of failure than did females (AVF fail male, 37.5% vs. AVF fail female, 0%; p=0.007). Additionally, history of Coronary Artery Disease (CAD) among males (success, 8.33% vs. fail, 50%, p=0.04) and history of Percutaneous Coronary Intervention (PCI) among males (AVF fail male, 25% vs. AVF fail female, 0%; p=0.030) were associated with higher rates of AVF failure (Table 5).

With respect to pre-operative clinical factors, no significant relationship was found between success vs. failure rates for: hypertension (HTN) (p=0.069), insulin dependent diabetes (p=0.39), peripheral arterial disease (PAD) (p=0.36), chronic obstructive pulmonary disease (COPD) (p=0.43), and congestive heart failure (CHF) (p=0.25). Additionally, with respect to pre-operative laboratory factors, no significant relationship was found between success vs. failure rates for elevated red blood cell distribution width (>14.5%) (p=0.27), platelet count (low, p=0.79; high, p=0.093), white blood cell count (p=0.71), male low hematocrit (p=0.24), and female low hematocrit (p=0.16) (Table 6).

Importantly, it was observed that the time from referral for access creation to the surgical date was not statistically different between the successful (average=17.1 weeks) and failed (average=21.4 weeks) cases (two-sample t-test, p=0.49; data not reported). In addition, time (weeks) to AVF maturity was not greater for AVF fail cases (success=30.0 weeks vs. fail=22.4 weeks, p=0.44). With cases that experienced primary AVF failure, the time (weeks) until dialysis initiated was significantly shorter than for the successful cases. This was calculated as the number of week's difference between initiating dialysis and the original AVF surgery date. The average

Table 3: Ethnicity and AVF Success, AVF success rate by ethnicity group compared to Caucasian/white.

AVF Success	Percent (%)	P-value
White	39.4	Ref
Black or African American	28.6	0.6
Native Hawaiian and Other Pacific Islander	100	0.23
American Indian or Alaska Native	100	0.046
Unknown/Other	50	0.77

Table 4: Basic clinical factors and rates of AVF success vs. failure. Non-laboratory clinical parameters such as age, smoking status, primary insurer, and obesity were assessed with respect to rates of AVF success vs. failure.
† Performed using Fisher-exact 2 × 2 analysis.

	AVF Success (%)	AVF Fail (%)	p-value
Age ≥ 65	25	26.9	0.89
Male	25	37.5	0.56
Female	25	22.2	0.88
p-value	1	0.43	
Age ≥ 70	5	15.4	0.28
Male	8.33	12.5	0.77
Female	0	16.7	0.23
p-value	0.41	0.79	
Smoking status			
Never (n)	3	10	ref
Prior/Current (n)	17	16	0.10†
Primary insurer			
Commercial	50	53.8	0.8
Medicaid	35	38.5	0.81
Medicare	15	3.79	0.99
Overweight/Obese	75	80.77	0.64

Table 5: Laboratory data and rates of AVF success vs. failure. Clinical laboratory data was assessed to determine any associations with AVF failure. Uremia was defined as presence of uremic symptoms first noted by the patient's primary nephrologist. Categories were assessed as a whole and by sex.

	AVF Success (%)	AVF Fail (%)	p-value
Uremia	5	30.7	0.031
Male	8.33	37.5	0.12
Female	0	0	1
p-value	0.41	0.007	
Thrombocytopenia	10	7.69	0.79
Male	16.7	0	0.24
Female	0	0	1
p-value	0.24	1	
Thrombocytosis	0	7.69	0.093
Male	0	0	0.24
Female	12.5	12.5	1
p-value	0.24	0.34	
Elevated white blood cell count	15	19.23	0.71
Male	8.33	37.5	0.12
Female	25	11.1	0.37
p-value	0.32	0.12	
Low Hematocrit	-	-	-
Male	83.3	100	0.24
Female	62.5	77.8	0.16
p-value	0.3	0.43	
Red blood cell distribution width (>4.5)	30	46.2	0.27
Male	33.3	75	0.075
Female	25	33.3	0.68
p-value	0.7	0.06	

Table 6: Comorbidities and rates of AVF success vs. failure. Significant co-morbidities including hypertension, peripheral arterial disease, insulin-dependent diabetes mellitus, coronary artery disease, COPD, percutaneous coronary intervention and congestive heart failure were assessed to determine an association with AVF failure. Categories were assessed as a whole and by sex.

	AVF Success (%)	AVF Fail (%)	p-value
Hypertension	100	84.6	0.069
Male	100	87.5	0.22
Female	100	83.33	0.14
p-value	1	0.79	
Peripheral arterial disease	15	23.08	0.36
Male	16.7	12.5	0.8
Female	12.5	27.8	0.4
p-value	0.8	0.4	
Insulin dependent diabetes	45	57.7	0.39
Male	58.3	50	0.72
Female	25	61.1	0.1
p-value	0.15	0.6	
Coronary artery disease	15	26.9	0.5
Male	8.33	50	0.04
Female	25	16.7	0.63
p-value	0.32	0.083	
Chronic obstructive pulmonary Disease	20	11.5	0.43
Male			
Female	8.33	0	0.41
p-value	37.5	16.7	0.23
	0.12	0.23	
Percutaneous coronary intervention	5	7.69	0.72
Male			
Female	0	25	0.075
P	12.5	0	0.13
	0.22	0.03	
Congestive heart failure	10	23.1	0.25
Male	16.7	0	0.23
Female	0	33.33	0.068
P	0.23	0.068	

length of follow-up was 64.3 weeks in the AVF success cases versus 24.3 weeks for the AVF fail cases. This difference was significantly shorter for the AVF fail cases (t(33)=-2.33, p=0.026) (Table 7).

Clinical relevance

Over the entire study period, on follow up, 70% of AVF success cases were receiving dialysis *via* the original AVF vs. 38.5% of the AVF fail cases (p=0.036) (Table 8). Similarly, 0% of AVF success cases were using a TDC on follow-up, while 30.8% of AVF fail cases were (p=0.013). When restricted to cases before 1/1/2017 (to allow for adequate time to assess case records), a similar pattern was observed where AVF fail cases were using TDCs at a higher rate (23.1% vs. 0%; p=0.037), however follow-up AVF use was actually not significantly different between success and fail cases (60% vs. 30.8%, p=0.078). Additionally, there was no difference in the average number of AVF interventions between the two groups (success=1.85 vs. fail=2.00; p=0.78). Similarly, there were no differences in the proportions of cases who had AVF interventions (0, 1, 2, 3, or >4) or times between the two groups (Supplemental Table 1). Moreover, on most recent status, there was a higher mortality rate for the AVF fail cases versus AVF success (34.6% vs. 10%) however this was not statistically significant (χ^2, [1, N=46]=3.76, p=0.086) (Supplemental Table 2). These results may be limited due to power.

In order to determine the outcome of long-term dialysis access for the "AVF Fail" cases alone, we compared the proportions of types of access between initial access and last known access. In order to stratify the cases, categories of access use included: original (primary) AVF, TDC, and non-AVF (which included TDC, primary failure, HD not initiated, and death). On last known HD access, there was no difference in the use of primary-AVF vs. TDC (fisher's exact; p=0.069), TDC vs. non-TDC (fisher's exact; p=0.051), and primary-AVF vs. non-AVF (fisher's exact; p=0.17). There was however a decrease in non-AVF use (predominantly from decreased TDC use) from initial access to primary outcome, along with a higher proportion of cases that used an AVF (either the primary or a secondary AVF) vs. non-AVF use (Fisher's exact, p=0.027) (Supplemental Table 3).

Table 7: Hemodialysis access on Follow-up. Last known hemodialysis access type was recorded to determine the patient's status on follow-up. This was categorized according to AVF vs. TDC.

	Follow-up access *via* AVF (%)	Follow-up access *via* TDC (%)	Time (weeks) to AVF mature	Time (weeks) until initiating hemodialysis
AVF Success (n=20)	70	0	30	64.3
AVF Fail (n=26)	38.5	30.8	22.4	24.3
p-value	0.036	0.013	0.44	0.026

Table 8: Hemodialysis Access on Follow-up before 1/1/2017. Cases were restricted to only include those from prior to 1/1/2017 to allow for adequate time to assess case records for last known hemodialysis. This was categorized according to AVF vs. TDC.

	Follow-up access *via* AVF (%)	Follow-up access *via* TDC (%)
AVF Success (n=17)	60	0
AVF Fail (n=20)	30.8	23.1
p-value	0.078	0.037

DISCUSSION

Patients with CKD and End-Stage Renal Disease (ESRD) have significant health problems with a heterogenous array of co-morbidities and risk factors. Identifying who among this patient population may beat the highest risk for AVF failure, and for what exact reasons, proves to be challenging and no consistent predictors have emerged despite multiple investigations. Demographic, clinical, and hemodynamic risks are among the most commonly studied factors which may explain why one patient may experience AVF FTM while another does not. We report a real-world failure rate of 56.5% for AVF creation (defined as the proportion of cases initiating dialysis with a TDC) for patient's anticipating-dialysis over the course of 2013-late 2018. This rate is in agreement with existing literature [7]. Moreover, our study provides some insight into which patients may be more likely initiate dialysis with a TDC before AVF usage.

Age as an independent risk factor for AVF FTM has been inconsistently reported in the literature, and in our study, we found no association among AVF FTM and older age [8-11]. Such inconsistency is not surprising since age is difficult to isolate as a risk fact because it is associated with reduced kidney function and cardiovascular co-morbidities. Similarly, sex of the patient has many conflicting reports; some suggesting female sex is associated with increased risk for AVF FTM [12-15]. Others, like our study, did not find an association between sex and AVF FTM [10,16,17].

Pre-operative history of CAD was associated with higher rates of AVF failure (vs. success) for men specifically. Additionally, history of PCI was higher within the AVF fail group for men vs. women. It is understood that normal cardiovascular function is a critical component of maintaining a functioning dialysis access circuit. Furthermore, AVF creation increases cardiac workload [18]. Previous studies have described a phenomenon of "AVF toxicity" which draws a connection between AVF creation and increased cardiovascular mortality and shortening lifespans [19]. Ahn et al. reported that pre-existing coronary artery bypass grafting (CABG) in HD patients with an AVF experienced higher rates of ipsi lateral coronary steal related to reduce left-ventricular ejection fraction [20]. Other forms of cardiac toxicity cited with AVF creation included diastolic dysfunction, CHF, cardiomyopathy among others. Additionally, blood pressure, both hypertension and hypotension, have shown inconsistent findings in the literature with respect to AVF FTM [9,11,15,21]. We did not find any association with the most immediate office-based, pre-operative blood pressure reading, both systolic and diastolic, and rates of AVF success or failure. Together, these previous studies and our data suggest that pre-operative history of CAD might affect AVF failure, likely associated with hyperdynamic changes and toxic effects on the cardiovascular system. Although not uniformly reported, this is perhaps particularly prevalent in males as seen with our study.

Another significant finding from our study was that pre-dialysis uremia (as reported in a progress note by the patient's nephrologist) was associated with higher rates of failure overall and was also specifically significant for male patients. The presence of uremic symptoms (e.g. platelet dysfunction/bleeding, pericarditis, nausea/anorexia, encephalopathy, etc.) is among a myriad of reasons that a patient with ESRD may need to initiate HD. Since the symptoms of uremia are often vague and complex, other standards are used to determine the appropriate time to begin HD. According to the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative, other clinical indications such as acid-base physiology, electrolytes, and refractory volume/blood pressure control are commonly used indicators, in conjunction estimated glomerular filtration rate measurements [22].

The topic of uremia and AVF failure is not commonly reported however has been reviewed in a few studies. A cell-proliferation assay study found that uremia was associated with early AVF failure, irrespective of surgical creation site. The authors suggested that uremia up regulates vascular smooth muscle pro-mitogenic mechanisms, thus contributing to higher failure rates [23]. Similarly, a study using human venous segments from CKD patients suggested that intimal hyperplasia and inflammation are associated with AVF failure [24]. Brahmbhatt et al. detail the various mechanisms of inflammation, uremia, and intimal hyperplasia that are associated with proposed AVF failure [25]. Among these mechanisms, processes that increase nitric oxide and increase active metalloproteinases at the time of AVF creation may be important inflammatory biomarkers for FTM [26]. It is worth noting however, that a study by Duque et al. found that blood urea nitrogen, creatinine, and GFR were not associated with AVF FTM in pre-dialysis [27]. Thus, it is reasonable to postulate that uremia, which leads to systemic inflammation and intimal hyperplasia, may contribute to early AVF failure and warrants future investigation. It is also possible that the presence of uremia symptoms is a marker for patients who are closer to initiating dialysis because of their more advanced disease.

Low hemoglobin, platelet count, and protein levels are among other laboratory variables reported in the literature that were either not significant in our study or were not assessed. We did not find an association between low hematocrit AVF FTM unlike a study by Yap and colleagues [13]. It should be noted that we used hematocrit to assess anemia and not hemoglobin. Additionally, Wen et al. suggest that not only anemia, but also thrombocytosis is associated with AVF FTM, where we found no association with the latter (in addition to thrombocytopenia) [8]. Hypoproteinemia, and specifically hypoalbuminemia, were both reported to be independent risk factors associated with AVF FTM, however were not assessed in our study [28,29]. These factors may warrant future investigation.

Finally, over the entire study period, a subgroup analysis found that significantly more AVF fail cases were still using TDCs. Although it was not statistically significant, there was roughly a 3.5 times increased risk of mortality with primary AVF failure in our study. Morbidity and mortality were not primary endpoints of this study however, this small analysis agrees with the known risks of TDC use [5]. Additionally, in cases that experienced AVF FTM we discovered that time from original creation date to initiating HD with a TDC was roughly 2.5 times shorter as compared to cases that successfully initiated HD with an AVF. However, the time to AVF maturity was not significantly different between these groups. This potentially suggests that the pre-operative risk factors, such as those described in our study, were associated with a higher likelihood of failure. Interestingly, we found that when compared to initial HD access, patients who experienced initial AVF failure increasingly used a primary or a secondary AVF for HD over the follow-up period while their use of non-AVF access (mainly TDCs, as well as kidney

transplant or death) decreased. This finding may suggest that long-term HwD access *via* AVF is possible for a portion of those that initially fail to start HD with their original AVF.

Study limitations

A retrospective case-series study based on chart review has inherent sources of potential error including missing/incomplete data, variability in encounter note quality and sufficiency, and sample size/power limitations. We attempted to mitigate these factors by performing a systematic mining of each chart in an organized and reproducible way, with clear definitions and guidelines. With respect to sample size, we had to exclude 13 cases due to grossly missing data or immediate loss to follow-up. We acknowledge that this is a limitation to the study, which can create selection bias in a retrospective analysis. Next, we acknowledge that the clinical definition of uremia in this study is subjective based on the patient's Nephrologist's documentation. This however should not be considered a significant limitation as signs and symptoms of uremia were clearly argued for or against in each case upon chart review of attending Nephrologist clinical documentation.

We chose not to do any subgroup analyses of AVF type and clinical risk factors associated with AVF failure as this was not a primary focus of the study. Future work might choose to perform such analyses however the study purpose and design would need to center around this question. Also, additional significant pre-operative risk factors may exist that were never accounted for during the study design and data collection stages. Future studies should account for not only these variables but also take into consideration what other labs, imaging, or even physical exam data has not been extensively studied in the literature.

CONCLUSION

In our series of patients referred for AVF placement prior to starting dialysis we noted ahigh rate of hemodialysis initiation with a TDC. Factors associated with failure of the AVF to be ready for hemodialysis were uremic status as reported by a nephrologist for men and patients with a history of CAD or PCI. We did not find any significant association between AVF FTM and age, sex, diabetes, PAD, and smoking status. Identifying patients at high risk for AVF failure could help decrease the rate of TDC use. This study provides some insight into patients at risk for AVF failure which may help in the decision to place an AVF or AVG and may be useful as a hypothesis generator in studies with larger sources of clinical data.

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CONFLICTS OF INTEREST

There are no potential or perceived conflicts of interest involved with this study.

Presentation information

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