Initial Vascular Access Type in Patients with a Failed Renal Transplant

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Abstract

Background and objectives Permanent hemodialysis vascular access is crucial for RRT in ESRD patients and patients with failed renal transplants, because central venous catheters are associated with greater risk of infection and mortality than arteriovenous fistulae or arteriovenous grafts. The objective of this study was to determine the types of vascular access used by patients initiating hemodialysis after a failed renal transplant.

Design, setting, participants, & measurements Data from the US Renal Data System database on 16,728 patients with a failed renal transplant and 509,643 patients with native kidney failure who initiated dialysis between January 1, 2006, and September 30, 2011 were examined.

Results At initiation of dialysis, of patients with a failed transplant, 27.7% (n=4636) used an arteriovenous fistula, 6.9% (n=1146) used an arteriovenous graft, and 65.4% (n=10,946) used a central venous catheter. Conversely, 80.8% (n=411,997) of patients with native kidney failure initiated dialysis with a central venous catheter ($P<0.001$). Among patients with a failed transplant, predictors of central venous catheter use included women (adjusted odds ratio, 1.75; 95% confidence interval, 1.63 to 1.87), lack of referral to a nephrologist (odds ratio, 2.00; 95% confidence interval, 1.72 to 2.33), diabetes (odds ratio, 1.14; 95% confidence interval, 1.06 to 1.22), peripheral vascular disease (odds ratio, 1.31; 95% confidence interval, 1.16 to 1.48), and being institutionalized (odds ratio, 1.53; 95% confidence interval, 1.23 to 1.89). Factors associated with lower odds of central venous catheter use included older age (odds ratio, 0.85 per 10 years; 95% confidence interval, 0.83 to 0.87), public insurance (odds ratio, 0.74; 95% confidence interval, 0.68 to 0.80), and current employment (odds ratio, 0.87; 95% confidence interval, 0.80 to 0.95).

Conclusions Central venous catheters are used in nearly two thirds of failed renal transplant patients. These patients are usually followed closely by transplant physicians before developing ESRD after a failed transplant, but the relatively low prevalence of arteriovenous fistulae/arteriovenous grafts in this group at initiation of dialysis needs to be investigated more thoroughly.

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Introduction

Despite national initiatives and programs to increase the use of arteriovenous (AV) fistulae (AVFs) among hemodialysis patients in the United States, vascular access procedures and their complications remain a major cause of morbidity and mortality for this population (1–4). It is well known that AVFs are superior to AV grafts (AVGs) and that both are superior to central venous catheters (CVCs). Based on this vascular access hierarchy, the National Kidney Foundation (NKF) Kidney Disease Outcome Quality Initiative (KDOQI) guidelines have recommended greater than 50% incident use of AVFs at initiation of dialysis and at least 40% prevalence (5). Indeed, the Centers for Medicare and Medicaid Services (CMS) breakthrough initiative Fistula First has been even more aggressive in its campaign, pushing for 66% AVF prevalence and in agreement with the NKF, less than 10% catheter prevalence by 90 days (6). In addition, the CMS ESRD Quality

Incentive Program implemented specific clinical performance measures for vascular access starting in payment year 2014, which include metrics for AVF rates and catheters in place >90 days, with significant consequences in the form of payment reductions to dialysis facilities if these metrics are not up to standard (7). Despite these efforts, more than 80% of CKD patients initiate dialysis with a CVC (8).

Multiple studies have shown that late referral to nephrologists before dialysis initiation is associated with poor outcomes in terms of survival and hospitalization. We showed in a meta-analysis that there was an almost 2-fold increased risk of death and a significantly longer duration of hospital stay in patients referred late to nephrologists (9). There has been compelling data showing that, perhaps, the higher mortality and hospitalization rates in the first 1 year of dialysis are associated with late nephrology referral and initial vascular access use (10–15).

Based on the US Renal Data System (USRDS), 17,671 kidney transplants were performed in the United States in 2011. The overall graft failure rate among adult transplant recipients was 6.2 per 100 patient-years in 2011, whereas the rate of failure requiring dialysis or retransplantation was 3.1 (10). Although long-term allograft survival has improved throughout the years, there are approximately 5000 patients with graft loss returning to dialysis each year. In these patients, there is a >3-fold higher adjusted risk of death compared with patients with a functioning allograft (16,17). The leading causes of death in these patients are cardiovascular complications and infections. Given that these patients are being cared for by nephrologists after transplantation, it would be expected that they have a higher prevalence of AVF/AVG at the time of hemodialysis initiation than those patients with native kidney failure. We showed in a preliminary report from our center that 41% of failed transplant patients were still dialyzing with a CVC at 3 months and that only 16% were using an AVF (K. Gupta, M.R. Chan, H.N. Young, A. Djamali, and A.S. Yevzlin, unpublished data).

The purpose of this study was to investigate whether current vascular access guidelines are being adhered in patients initiating dialysis after a failed transplant. We postulated that, given the close nephrologic care provided to transplant recipients, there should be a substantially higher prevalence of permanent AV access use and a significantly lower prevalence of CVC use at initiation of dialysis.

Materials and Methods

We analyzed data from the USRDS on all adult (age≥18 years) incident ESRD patients initiating hemodialysis from January 1, 2006, to September 30, 2011. Relevant data were derived from CMS Form 2728 and included demographics, insurance status (public insurance refers to Medicare/Medicaid), employment status, comorbidities, height and weight, initial dialysis modality, timing of nephrology referral, type of vascular access used, and whether a maturing AVF or AVG was present. Initial vascular access type was categorized as AVF, AVG, or catheter. Timing of nephrology referral was reported as never or 0–6, 6–12, or >12 months. Race was categorized as black or not black. Additional variables collected from the USRDS included current smoking status and institutionalization.

Baseline characteristics were compared across transplant failures and transplant-naïve patients with chi-squared and t tests as appropriate. Multivariate logistic regression models were developed to assess the independent associations between covariates and AVF/AVG use and AVF/AVG creation among patients with a failed transplant. These models adjusted for age, race, sex, peripheral vascular disease, cardiovascular disease, hypertension, insurance status, employment history, and timing of nephrology referral. For all statistical tests, α-levels were set a priori at 0.05 (two sided). The statistical analyses were performed using Stata MP 12.1 (www.stata.com).

Results

We examined data on 16,728 patients with a failed renal transplant and 509,643 patients with native kidney failure

(Table 1). Patients initiating hemodialysis after a failed transplant were much younger than those patients with native kidney failure. They were also less likely to be women, had lower body mass index, and generally, had fewer comorbidities. Whereas 93.5% of those patients with a failed transplant had been under the care of a nephrologist, fewer than two thirds (63.7%) of transplant-naïve patients had been under the care of a nephrologist (P<0.001). Only 50% had seen a nephrologist more than 6 months before initiating hemodialysis.

At the initiation of dialysis, 27.7% (n=4636) of patients with a failed transplant used an AVF, 6.9% (n=1146) of patients used an AVG, and 65.4% (n=10,946) of patients used a CVC. Conversely, 80.8% (n=411,997) of patients with native kidney failure initiated dialysis with a CVC (P<0.001) (Figure 1). An additional 14.0% of patients with a failed transplant had AV access created but not in use compared with an additional 18.8% of patients with native kidney failure (P<0.001).

Although only approximately 6.5% of patients with a failed transplant were reported as not having seen a nephrologist before initiation of hemodialysis, lack of referral was strongly associated with use of a CVC (P<0.001). This association remained after adjustment for other characteristics (adjusted odds ratio [OR], 2.00; 95% confidence interval [95% CI], 1.72 to 2.33) (Table 2). Other predictors of CVC use included women, institutionalization, diabetes, and peripheral vascular disease. Factors associated with lower odds of CVC use included public insurance, current employment, older age, and black race.

Among those patients with a failed transplant, predictors of AV access (AVF or AVG) in use at the time of dialysis initiation were the inverse of the predictors of CVC use and included older age, black race, public insurance, and currently employed. Factors associated with lower odds of AVF use included women, diabetes, peripheral vascular disease, being institutionalized, and lack of referral to a nephrologist.

Lack of referral to a nephrologist also was strongly inversely associated with having AV access (AVF or AVG) in place at the time of dialysis initiation (OR, 0.51; 95% CI, 0.44 to 0.58) (Table 3). The predictors of AV access placement were generally similar to the predictors for AV access use. Older age was more strongly associated with AV access placement (OR, 1.12 per 10 years; 95% CI, 1.10 to 1.15) than AV access use (OR, 1.02; 95% CI, 1.01 to 1.02). The presence of peripheral vascular disease and diabetes remained inversely associated with AV access placement, but the associations were less strong than for AV access use.

Discussion

In the present study, we show that, despite vascular access guidelines recommending AVF first and catheter last, most patients with failed transplants still initiate dialysis with a CVC. Although the proportion of patients using an AVF was higher among patients with a failed transplant, nearly two thirds of such patients started hemodialysis with a CVC. Although few patients with a failed transplant were not seen by a nephrologist before initiating hemodialysis, it remained a strong predictor of CVC use. Younger age, women, not black race, diabetes, institutionalization, and unemployment

Table 1. Selected patient demographics of study group

Characteristics	Native Kidney Failure (n=509,643)	Failed Transplant (n=16,728)	P Value
Mean age, yr (SD)	62.8 (15.7)	36.3 (14.9)	<0.001
Sex, % women	43.3	39.6	<0.001
Race, %			<0.01
White	66.1	66.9	
Black	28.5	28.2	
Other	5.4	4.9	
Mean BMI, kg/m^2	29.1 (7.8)	27.0 (7.0)	<0.001
Comorbidities, %			
PVD	14.7	9.5	<0.001
Diabetes	54.3	39.5	<0.001
Hypertension	85.7	87.6	<0.001
Coronary heart disease	34.6	23.0	<0.001
Congestive heart failure	33.6	18.7	<0.001
Other variables, %			
Institutionalized	7.9	2.8	<0.001
Current smoker	6.6	4.8	<0.001
Employed	10.6	23.9	<0.001
Nephrology referral			
None	36.3	6.5	
<6 mo	13.6	13.1	<0.001
6–12 mo	23.1	11.6	
>12 mo	26.9	68.8	
Access type used, %			
Arteriovenous fistula	15.5	27.7	<0.001
Arteriovenous graft	3.6	6.9	
Central venous catheter	80.8	65.4	
Access type in place, %			
Arteriovenous fistula	32.5	40.0	<0.001
Arteriovenous graft	5.4	8.6	
Neither	62.1	51.4	

Summary statistics represent percentages unless otherwise stated. BMI, body mass index; PVD, peripheral vascular disease.
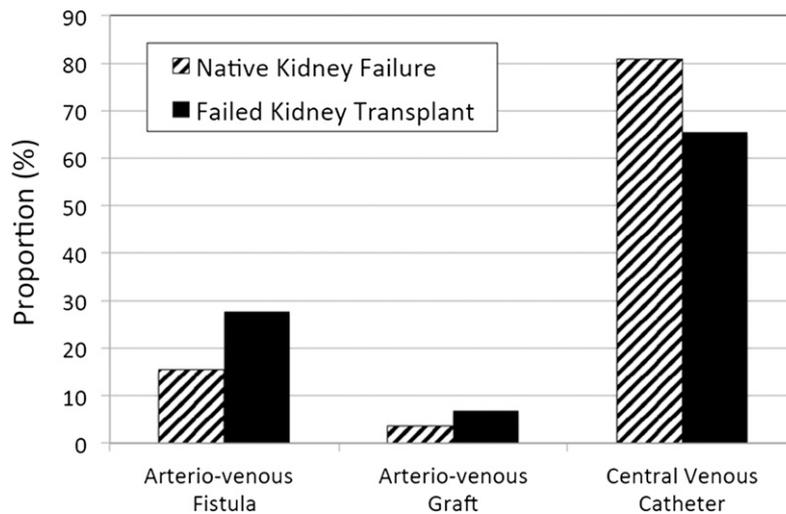
Figure 1. | The proportion of vascular access use between native kidney failure and failed kidneys transplants. Types of vascular access in use at initiation of hemodialysis among patients with native kidney failure and failed transplant recipients.

also were significantly associated with use of a CVC at initiation of hemodialysis after graft failure.

It is well known that death after graft loss is exceedingly high compared with death in age-matched incident dialysis patients, patients with a functioning transplant, and patients on the waiting list (17–19). Moreover, the risk of sepsis 3–6 months after transplant failure is 3-fold higher than among age-matched dialysis patients with no

Table 2. Association of independent variables on central venous catheter used at initiation of dialysis in failed renal transplant recipients

Variable	Odds Ratio	95% Confidence Interval	P Value
Age (per 10 yr)	0.85	0.83 to 0.87	<0.001
Women	1.75	1.63 to 1.87	<0.001
Black race	0.77	0.72 to 0.83	<0.001
PVD	1.31	1.16 to 1.48	<0.001
Diabetes	1.14	1.06 to 1.22	0.001
Hypertension	0.95	0.86 to 1.05	0.31
Congestive heart failure	1.01	0.93 to 1.11	0.79
Coronary heart disease	1.03	0.95 to 1.12	0.49
Institutionalized	1.53	1.23 to 1.89	<0.001
Current smoker	0.93	0.80 to 1.08	0.33
Public insurance	0.74	0.68 to 0.80	<0.001
Employed	0.87	0.80 to 0.95	0.002
Nephrology referral[a]			
None	2.00	1.72 to 2.33	<0.001
<6 mo	1.04	0.94 to 1.15	0.42
6–12 mo	1.02	0.92 to 1.13	0.72
>12 mo	1.00	Reference	Reference

PVD, peripheral vascular disease.
[a]Compared with referral 12 months before initiation of dialysis.

Table 3. Association of independent variables on arteriovenous access in place at initiation of dialysis in failed renal transplant recipients

Variable	Odds Ratio	95% Confidence Interval	P Value
Age (per 10 y)	1.12	1.10 to 1.15	<0.001
Women	0.61	0.57 to 0.65	<0.001
Black race	1.17	1.09 to 1.26	<0.001
PVD	0.87	0.78 to 0.98	0.02
Diabetes	0.92	0.86 to 0.99	0.02
Hypertension	1.07	0.97 to 1.17	0.18
Congestive heart failure	1.06	0.97 to 1.15	0.21
Coronary heart disease	0.96	0.88 to 1.04	0.32
Institutionalized	0.61	0.50 to 0.75	<0.001
Current smoker	1.13	0.98 to 1.31	0.09
Public insurance	1.28	1.18 to 1.38	<0.001
Employed	1.05	0.97 to 1.14	0.27
Nephrology referral[a]			
None	0.51	0.44 to 0.58	<0.001
<6 mo	1.01	0.92 to 1.10	0.91
6–12 mo	1.03	0.93 to 1.13	0.61
>12 mo	1.00	Reference	Reference

PVD, peripheral vascular disease.
[a]Compared with referral 12 months before initiation of dialysis.

transplant. There likely are many variables affecting these observations, including immunologic and nonimmunologic factors, such as inflammation, malnutrition, dialysis vintage, fragmented care, and initiation of dialysis with a CVC. Perl *et al.* (20) recently showed in the Dialysis Outcomes and Practice Patterns Study that, compared with transplant-naïve patients on the waiting list, transplant failure patients on dialysis had higher all-cause mortality (adjusted hazard ratio, 1.32; 95% CI, 1.05 to 1.66) and especially, higher infection-related mortality (adjusted

hazard ratio, 2.45; 95% CI, 1.36 to 4.41). Perl *et al.* (20) showed that, compared with transplant-naïve patients, patients with transplant failure were also less likely to use a permanent AV access, particularly within the first 3 months of initiating dialysis. This infection risk is quite concerning, especially because many patients after allograft failure remain on immunosuppression, including prednisone, calcineurin inhibitors, and/or antiproliferatives. Many studies propose that the CKD staging classification as recommended by KDOQI and Kidney Disease

Improving Global Outcomes (KDIGO) and the guidelines for mild, moderate, and severe dysfunction in GFR should also be applied to kidney transplant recipients in the same way as nontransplanted patients (19,21–25). Included in these guidelines are the recommendations to place permanent vascular access in stage 4 CKD.

Why is there a reticence in initiating the vascular access workup in patients with failing transplant allografts? There may be a number of reasons, some of which are psychological, such as a patient not wanting to give up on the kidney or even a false sense of security from the physician who believes that there are immunologic factors to treat to prolong residual graft function. Some surgeons may feel that placing an AV access may damage the transplanted kidney by diminishing renal blood flow. One large bias to waiting to place an AV access may be the consideration for retransplantation. Often, transplant nephrologists as well as patients could hope that a pre-emptive transplant may happen; even if they start on dialysis, the hope is that the CVC will not be in for very long until retransplantation happens. Patients and their physicians may want to avoid a more invasive surgery to create an AV access and opt for a tunneled CVC. Another factor that may explain why transplant nephrologists may wait longer to initiate access workup is that CKD with transplant patients have a slower creatinine clearance decline compared with their native CKD counterparts (26). Nevertheless, we believe that delaying the workup for an AV access in these patients with failing transplants is comparable to not addressing their anemia, mineral bone disorders, hypertension, or quality of life issues.

Dawoud et al. (27) recently showed in a single center study of 96 failing kidney transplants compared with 218 failing native kidneys that predialysis vascular access surgery was less common in the transplant group (25% versus 60%; hazard ratio, 0.42; 95% CI, 0.29 to 0.60; $P<0.001$). We also showed in an earlier single center study that, at 3 months after initiating dialysis, 41.4% had a CVC compared with 15.7% had an AVF (K. Gupta, M.R. Chan, H.N. Young, A. Djamali, and A.S. Yevzlin, unpublished data). These data were from the 1990s and before the KDOQI and Fistula First guidelines on vascular access.

To our knowledge, this study is the first study to use data collected on a nationally representative United States transplant population to focus on the type of access. Of the incident hemodialysis patients with failed renal transplants, a surprisingly 65% of patients initiated dialysis with a CVC. Although 93% of these patients had been seen by a nephrologist within the previous 6 months before dialysis, the prevalence of AVF use was low, and the prevalence of CVC use was high. We expect that nephrologists and transplant nephrologists are well aware of the CKD classification system by KDOQI and KDIGO and therefore, would follow guidelines to make vascular access a priority in the care of their patients. Patients who had a higher associated risk of starting with a CVC included women, institutionalized patients, patients with diabetes and peripheral vascular disease, and patients not referred to a nephrologist. Women, diabetes, and peripheral vascular disease are traditional risk factors associated with poor maturation rates of AVF; however, lack of referral to a nephrologist and care for institutionalized

patients are broader system-wide issues that need to be addressed (28–32). Interestingly, those same risk factors were associated with a lower likelihood of having a permanent AV access in place and used at the time of initiation of dialysis.

Data from the USRDS show that percentages of AVF use have increased; however, a concurrent increase in CVC use was also evident (33). There have been a number of theories for this finding. AVF access primary failure may play a significant role. Whether it is because of poor candidacy evaluation, surgical techniques, or inadequate surveillance and referral for intervention, these recent trends are being investigated. According to the CMS, during the 5-year period between 1998 and 2003, catheter use increased from 19% to 27% (34). Lee et al. (35) concur that each 1% increase in fistula prevalence is associated with a 1% increase in catheter prevalence. Most likely, this finding is the result of primary fistula failure.

Interestingly, a significantly higher proportion of failed transplant recipients had an AVF in place at the time of hemodialysis initiation than the proportion using an AVF (40% versus 28%). This finding suggests that the AVF in place was either immature or in place while the patient still had an actively working transplant. It also suggests that many patients may have needed to initiate dialysis with a CVC with a nonmatured AVF in place. We know that up to 10%–24% of radiocephalic AVFs thrombose or fail to mature according to multiple reports (36–39). In the largest randomized study to date on early fistula failure, the Dialysis Access Consortium showed an alarming 49.9% suitability failure of AVF at the time of initiation of dialysis (40). This result speaks loudly to the poor access selection and workup of predialysis patients in the United States. Lok and colleagues (41–43) have derived a risk score for access selection, taking into account traditional factors that have been associated with failure to mature and incorporating them into a simple-to-use algorithm for vascular access creation. We believe that this scoring method can also be used in failed renal transplant patients and ideally, will decrease the use of catheters and increase the use of AVF at initiation of dialysis. Perhaps, if the right patients are chosen for AVF placement, the goal of 50% AVF initiation can be attainable as per Fistula First (6).

The limitations of our study include its observational nature and secondary analysis of existing USRDS data, which make the analysis subject to unmeasured confounding factors. We tried to mitigate this effect by including in our analyses several comorbid conditions previously associated with vascular access outcomes. Some patients were excluded because of missing data. Also, it was not possible to extrapolate from the CMS 2728 form whether failed transplant patients had a previously functioning AVF in place. These data could influence how we interpret the importance of prehemodialysis access planning in these patients. However, in sum, the findings remain generalizable given the large United States cohort included in this analysis.

In summary, CVCs are used in nearly two thirds of failed renal transplant patients at the initiation of hemodialysis. Only 40% of patients had an AVF in place. This group of patients usually is being followed closely by transplant physicians before graft failure, but the relatively low prevalence of AVF/AVG in this group at the initiation of

dialysis needs to be investigated more thoroughly. Our results emphasize the need for earlier recognition and acceptance of a failing renal transplant and the need for earlier referral for access placement as outlined by KDOQI. Perhaps the guidelines established by KDOQI and the Fistula First Breakthrough Initiative need to be re-examined for their applicability to failed renal transplant recipients.

Acknowledgments

Disclosures
None.

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