# Association of Proteinuria with Central Venous Catheter Use at Initial Hemodialysis

Ken J Park, MD; Eric S Johnson, PHD; Ning Smith, PHD; David M Mosen, PHD; Micah L Thorp DO, MPH

Perm J 2018;22:16-194

E-pub: 12/06/2017

https://doi.org/10.7812/TPP/16-194

## ABSTRACT

**Context:** Central venous catheter (CVC) use is associated with increased mortality and complications in hemodialysis recipients. Although prevalent CVC use has decreased, incident use remains high.

**Objective:** To examine characteristics associated with CVC use at initial dialysis, specifically looking at proteinuria as a predictor of interest.

**Design:** Retrospective cohort of 918 hemodialysis recipients from Kaiser Permanente Northwest who started hemodialysis from January 1, 2004, to January 1, 2014.

**Main Outcome Measures:** Multivariable logistic regression was used to examine an association of proteinuria with the primary outcome of CVC use.

**Results:** More than one-third (36%) of patients in our cohort started hemodialysis with an arteriovenous fistula, and 64% started with a CVC. Proteinuria was associated with starting hemodialysis with a CVC (likelihood ratio test, $p < 0.001$) after adjustment for age, peripheral vascular disease, congestive heart failure, diabetes, sex, race, and length of predialysis care. However, on pairwise comparison, only patients with midgrade proteinuria (0.5-3.5 g) had lower odds of starting hemodialysis with a CVC (odds ratio = 0.39, 95% confidence interval = 0.24-0.65).

**Conclusion:** Proteinuria was associated with use of CVC at initial hemodialysis. However, a graded association did not exist, and only patients with midgrade proteinuria had significantly lower odds of CVC use. Our findings suggest that proteinuria is an explanatory finding for CVC use but may not have pragmatic value for decision making. Patients with lower levels of proteinuria may have a higher risk of starting dialysis with a CVC.

## INTRODUCTION

Patients with end-stage renal disease (ESRD) have a mortality rate that is higher than that for cancer, heart disease, heart failure, or diabetes.[1] The 1-year mortality rate for patients with ESRD is estimated to be 17%.[1] One major reason for higher mortality rates in ESRD is the high rate of central venous catheter (CVC) use. Several studies have shown that patients who dialyze with a CVC have a 50% to 70% increased risk of dying compared with patients who dialyze with an arteriovenous fistula (AVF).[2-6] For this reason, several national initiatives have targeted increasing AVF use. The Fistula First campaign[7] was started in 2003 to increase AVF placement and to decrease use of CVCs to improve morbidity and mortality. Fistula First has been credited with a reduction in prevalent CVC use from 27.7% in 2007 to 16.3% in 2014.[1] However, despite reduction in prevalent CVC use, its use remains high at initial hemodialysis. This remains a concern because patients starting hemodialysis with CVCs have been shown to have a higher mortality and higher risk of sepsis.[5,8] One of the goals in Healthy People 2020,[9] a national initiative involving the US Department of Health and Human Services, is to increase use of AVF or presence of a maturing AVF at the start of hemodialysis to a target of 34.5%. Despite meeting Healthy People 2020 targets, more than 80% of patients with ESRD dialyze with CVCs at initial treatment.[1] Even with optimal predialysis care under the supervision of a nephrologist, about 50% of patients start dialysis with a CVC.[10] This statistic suggests that this is an area requiring further improvement.

Several factors have been found to be associated with CVC use at initial hemodialysis treatment, including elderly age,[11] black race,[4] female sex,[12,13] diabetes,[14] peripheral vascular disease,[14] late referrals to a nephrologist,[15] and cardiac disease.[4] Reasons for higher CVC use include rates of primary AVF failures (defined as an AVF that is never usable) of between 20% and 50%[16] and delayed AVF placement.[11] Elderly age, peripheral vascular disease, and coronary artery disease have been associated with primary AVF failures.[17,18] Older age, black race, female sex, and shorter pre-ESRD nephrology care have been associated with delayed AVF placement.[19]

Proteinuria has been shown to be associated with mortality and progression of chronic kidney disease (CKD).[20] In addition, after AVF placement, patients with proteinuria had a higher likelihood of AVF use[21] or initiation of hemodialysis.[22] However, to the best of our knowledge, the association of proteinuria with CVC use at initial hemodialysis has not been examined. The aim of this study was to look at factors associated with CVC use at time of dialysis initiation specifically looking at proteinuria as a primary variable of interest. Our hypothesis was that higher grades of proteinuria were associated with higher rates of CVC use at initial hemodialysis. Proteinuria may be helpful in identifying patients who may benefit from earlier referral for AVF placement or closer monitoring for failure of an AVF to mature after placement, to decrease the rate of CVC use at initial hemodialysis.

## METHODS

### Study Population

We created a retrospective cohort from the Kaiser Permanente Northwest (KPNW) dialysis registry, a large integrated health care system with approximately 500,000 members in Oregon and

**Ken J Park, MD,** is a Nephrologist at the Salem Medical Center in OR. E-mail: ken.j.park@kp.org. **Eric S Johnson, PHD,** is a Research Investigator at the Center for Health Research in Portland, OR. E-mail: eric.s.johnson@kpchr.org. **Ning Smith, PHD,** is a Research Investigator at the Center for Health Research in Portland, OR. E-mapil: ning.x.smith@kpchr.org. **David M Mosen, PHD,** is an Affiliate Investigator at the Center for Health Research in Portland, OR. E-mail: david.m.mosen@kpchr.org. **Micah L Thorp, DO, MPH,** is the Chief of Nephrology for Kaiser Permanente Northwest in Portland, OR. E-mail: micah.l.thorp@kp.org.

Washington. Eligible patients were adults aged 18 years or older who started hemodialysis from January 1, 2004, to January 1, 2014. Patients were excluded if they recovered renal function, started dialysis with an arteriovenous graft, had a peritoneal dialysis catheter present, had less than 6 months of continuous membership at KPNW, or had transferred to KPNW with a previous diagnosis of ESRD. Variables were obtained through review of electronic health records and databases that included outpatient laboratory values. This study was reviewed and approved by the institutional review board of KPNW and conducted in accordance with the ethical standards laid down in the Declaration of Helsinki.

## Primary Outcome

Our primary outcome was the use of CVC at initial hemodialysis. This was obtained through chart review of vascular surgery notes in the electronic health record. Use of CVCs was defined as patients in which a CVC was used at first hemodialysis regardless of whether an AVF was present. Patients who started hemodialysis with an AVF but required placement of a CVC within 30 days were also included in this category. We chose to classify these patients in the CVC group on the basis of prior studies using successful cannulation of an AVF during a 30-day time frame to define successful use of an AVF.[17]

## Predictors

Proteinuria was divided into 4 categories by the highest level of spot urine protein/creatinine ratio, urine albumin/creatinine ratio, or urinalysis noted according to KDIGO (Kidney Disease: Improving Global Outcomes) staging.[23] *Absent* (no proteinuria present) was defined as less than 0.2 g of protein per gram of creatinine, a urine albumin/creatinine ratio below 30 mg/g, or 0 on urinalysis; *low grade,* 0.2 to 0.5 g of protein per gram of creatinine, urine albumin/creatinine ratio of 30 to 300 mg/g, or 1+ on urinalysis; *midgrade,* 0.5 to 3.5 g of protein per gram of creatinine, urine albumin/creatinine ratio of 301 to 2200 mg/g, or 2+ or greater on urinalysis; and *high grade,* above 3.5 g of protein per gram of creatinine or urine albumin/creatinine ratio greater than 2200 mg/g.[23]

Other variables studied included presence of congestive heart failure, diabetes, peripheral vascular disease, history of acute kidney injury in the prior 2 years, sex, race, age at start of hemodialysis, length of predialysis care in months, and number of hospitalizations in the 2-year period before the start of hemodialysis. When race was missing or unknown (about 22% of the cohort), patients were labeled as white because this was the most common race among our members. Age was divided into categories of younger than 50 years, 50 to 70 years, and older than 70 years. Among patients who had an AVF present at the time of initial dialysis, variables recorded

**Table 1. Baseline characteristics of patients with central venous catheter with arteriovenous fistula vs arteriovenous fistula at initial dialysis**

| Variable | CVC with immature AVF (n = 152) | AVF (n = 329) | p value[a] |
|---|---|---|---|
| Sex (men), % | 50 | 62 | 0.03 |
| Mean age, y | 65.8 | 64.1 | 0.19 |
| PVD, % | 28.9 | 21.5 | 0.10 |
| CHF, % | 49 | 37.9 | 0.02 |
| Diabetes, % | 72.3 | 67.2 | 0.30 |
| History of AKI, % | 36.2 | 45 | 0.10 |
| Hospitalizations, median no. | 5.7 | 4.6 | 0.01 |
| Proteinuria grade, %[b] | | | |
| Absent | 13.1 | 7.5 | 0.10 |
| Low grade | 9.2 | 10.3 | 0.83 |
| Midgrade | 33.5 | 52.2 | < 0.001 |
| High grade | 44.1 | 29.8 | 0.006 |
| Race, % | | | |
| Asian | 3.3 | 5.1 | 0.49 |
| Black | 7.8 | 8.8 | 0.87 |
| White | 87.5 | 83.3 | 0.29 |
| Native American | 1.3 | 2.7 | 0.52 |
| Length of predialysis care, % | | | |
| None | — | — | — |
| 0-6 mo | 17.1 | 4.2 | < 0.001 |
| 6-12 mo | 11.8 | 8.5 | 0.43 |
| 12-24 mo | 15.8 | 14.3 | 0.77 |
| > 24 mo | 55.2 | 72.9 | < 0.001 |
| AVF, % | | | |
| Radiocephalic location | 13.8 | 15.5 | 0.73 |
| Brachiocephalic location | 69.1 | 76.6 | 0.15 |
| Brachiobasilic location | 15.8 | 7.0 | 0.01 |
| Early start | 38 | 41 | 0.32 |
| Access revised | 23 | 24 | 0.84 |
| Timing of AVF placement, % | | | |
| 0-3 mo | 55.6 | 17 | < 0.001 |
| 3-6 mo | 13.1 | 19.8 | 0.15 |
| 6-9 mo | 4.6 | 15.5 | 0.002 |
| 9-12 mo | 5.3 | 8.2 | 0.33 |
| 12-24 mo | 12.5 | 16.4 | 0.33 |
| > 24 mo | 9.8 | 23.1 | 0.002 |

[a] Unadjusted comparisons between AVF vs CVC with immature AVF group.

[b] Low grade was defined as urine protein/creatinine ratio 0.2 to 0.5, urine albumin/creatinine ratio of 30 to 300 mg/g, or 1+ on urinalysis; midgrade as urine protein/creatinine ratio of 0.5 to 3.5, urine albumin/creatinine ratio > 300 to 2200 mg/g, or 2+ or greater on urinalysis; and high grade as urine protein/creatinine ratio > 3.5 or urine albumin/creatinine ratio > 2200 mg/g.

AKI = acute kidney injury; AVF = arteriovenous fistula; CHF = congestive heart failure; CVC = central venous catheter; PVD = peripheral vascular disease.

included location of the AVF, whether the AVF was revised before dialysis (defined as requiring additional surgical or interventional procedures), and timing of AVF placement before initial dialysis. Location of the AVF was divided into radiocephalic, brachiocephalic, or brachiobasilic. Time of the AVF placement before the start of dialysis was divided into categories: 0 to 3 months, 3.1 to 6 months, 6.1 to 9 months, 9.1 to 12 months, 12.1 to 24 months, and greater than 24 months.

Estimated glomerular filtration rate (eGFR) was calculated using the CKD-Epidemiology Collaboration equation[24] after 2010 and by the Modification of Diet in Renal Disease equation[24] in 2010 and earlier. Last outpatient eGFR available within 31 days of dialysis initiation was recorded (available in 63.6% of the cohort). Patients were classified as "early start" of dialysis if the last recorded outpatient eGFR was greater than 10 mL/min. The eGFR at the time of AVF placement was available in 38% of patients with AVFs placed.

**Table 2. Baseline characteristics of study cohort by access type at initial dialysis**

| Variable | Entire sample (N = 918) | CVC (n = 589) | AVF (n = 329) | p value[a] |
|---|---|---|---|---|
| Sex (men), % | 59 | 57 | 62 | 0.10 |
| Mean age, y | 63.8 | 63.6 | 64.1 | 0.60 |
| PVD, % | 25.6 | 28 | 21.5 | 0.04 |
| CHF, % | 42.8 | 45 | 37.9 | 0.03 |
| Diabetes, % | 66.2 | 66 | 67.2 | 0.70 |
| History of AKI, % | 42.2 | 40 | 45 | 0.25 |
| Hospitalizations, median no. | 4.0 | 6.1 | 4.6 | < 0.001 |
| Proteinuria grade, %[b] | | | | |
| Absent | 11.5 | 13.7 | 7.5 | 0.009 |
| Low grade | 11.5 | 12.2 | 10.3 | 0.45 |
| Midgrade | 40.4 | 33.7 | 52.2 | < 0.001 |
| High grade | 36.5 | 40.2 | 29.8 | 0.004 |
| Race, % | | | | |
| Asian | 5.0 | 4.9 | 5.1 | 0.89 |
| Black | 8.1 | 7.6 | 8.8 | 0.63 |
| White | 84.3 | 84.9 | 83.3 | 0.52 |
| Native American | 2.6 | 2.5 | 2.7 | 0.86 |
| Length of predialysis care, % | | | | |
| None | 9.5 | 14.9 | NA | < 0.001 |
| 0-6 mo | 12.4 | 17 | 4.2 | < 0.001 |
| 6-12 mo | 8.8 | 9 | 8.5 | 0.89 |
| 12-24 mo | 13.3 | 12.7 | 14.3 | 0.72 |
| > 24 mo | 55.9 | 46.3 | 72.9 | < 0.001 |
| AVF, % | | | | |
| Radiocephalic location | NA | NA | 15.5 | NA |
| Brachiocephalic location | NA | NA | 76.6 | NA |
| Brachiobasilic location | NA | NA | 7.0 | NA |
| Early dialysis start | 37.3 | 35 | 41 | 0.13 |
| Access revised | NA | NA | 24 | NA |
| Timing of AVF placement, % | | | | |
| 0-3 mo | NA | NA | 17 | NA |
| 3-6 mo | NA | NA | 19.8 | NA |
| 6-9 mo | NA | NA | 15.5 | NA |
| 9-12 mo | NA | NA | 8.2 | NA |
| 12-24 mo | NA | NA | 16.4 | NA |
| > 24 mo | NA | NA | 23.1 | NA |

[a] Unadjusted comparisons between AVF vs CVC.

[b] Low grade was defined as urine protein/creatinine ratio of 0.2 to 0.5, urine albumin/creatinine ratio of 30 to 300 mg/g, or 1+ on urinalysis; midgrade as urine protein/creatinine ratio of 0.5 to 3.5, urine albumin/creatinine ratio > 300 to 2200 mg/g, or 2+ or greater on urinalysis; and high grade as urine protein/creatinine ratio > 3.5 or urine albumin/creatinine ratio > 2200 mg/g.

AKI = acute kidney injury; AVF = arteriovenous fistula; CHF = congestive heart failure; CVC = central venous catheter; NA = not applicable; PVD = peripheral vascular disease.

### Statistical Analysis

Patients were divided into 2 groups on the basis of access used at first hemodialysis: AVF and CVC. Baseline characteristics were compared between AVF vs CVC using the $\chi^2$ test for categorical variables and the *t*-test for continuous variables. A logistic regression model was used to determine which variables were associated with the outcome for CVC. Odds ratio (OR) with 95% Wald confidence intervals (CIs) were calculated. For categorical variables with multiple categories (including proteinuria grade, race, age, and time of AVF placement), the likelihood ratio test was calculated using logistic regression. If the overall test was statistically significant ($p < 0.05$), then pairwise differences for categories were calculated. The multivariable logistic regression model was repeated after removing nonsignificant variables using backward stepwise selection. Statistical significance was defined as $p < 0.05$. All calculations were done using R Version 3.1.0 (The R Foundation, Free Software Foundation, Boston, MA) and SAS Version 9.2 (SAS Institute Inc, Cary, NC).

Patients who started hemodialysis with CVC were further divided into subgroups by whether or not they had an immature AVF present. Baseline characteristics were compared between patients starting hemodialysis with AVF vs CVC with AVF present (Table 1). Logistic regression models were used to determine which variables were associated with the outcome of CVC with AVF present.

## RESULTS

Our final dialysis cohort consisted of 918 patients, of which 35.9% started dialysis with an AVF and 64.1% started with a CVC. Of the 64% that started with a CVC, 25% had an immature AVF present (Table 2). The average age at initial hemodialysis was 63.8 years, with a range of 18 to 94 years, and 40.2% of the cohort was older than age 70 years. The average

last outpatient eGFR before the start of hemodialysis was 12.9 mL/min, with an interquartile range of 9 to 15 mL/min (data missing in 36% of the sample). In patients who had an AVF placed before hemodialysis, 29% had an AVF placed less than 3 months beforehand. Only 9.5% of patients were not seen by a nephrologist, whereas most patients (69.3%) had greater than 1 year of follow-up with a nephrologist before hemodialysis.

Measurement of proteinuria was present in the health records of the entire cohort. Most patients (77%) had overt proteinuria (> 0.5 g); 36% had high-grade proteinuria, (> 3.5 g) whereas 40.4% had midgrade proteinuria (0.5 to 3.5 g). Patients with high-grade proteinuria were more likely to be younger, have diabetes, and be less likely to have predialysis nephrology care of greater than 2 years compared with patients with midgrade proteinuria (Table 3). Patients with low-grade or absent proteinuria were more likely to be older, have congestive heart failure, be white, have no predialysis care, and start hemodialysis at a higher eGFR, and were less likely to have diabetes. Compared with patients with low-grade or absent proteinuria and those with midgrade proteinuria, patients with high-grade proteinuria were more likely to have their AVF placed later, at less than 90 days, and at a lower eGFR.

Proteinuria grade was associated with CVC use vs AVF use at initial hemodialysis in univariate analysis using the global likelihood ratio test ($p < 0.001$; Table 4, Model 1). However, on pairwise comparison, only patients with midgrade proteinuria remained with a statistically significant association and had the lowest odds of 0.36 for starting hemodialysis with a CVC (95% CI = 0.21-0.58) compared with patients with absent proteinuria. Patients with low-grade and high-grade proteinuria had higher odds of starting with a CVC compared with patients with midgrade proteinuria (low grade: OR = 0.65, 95% CI = 0.35-1.10; high grade: OR = 0.75, 95% CI = 0.44-1.22), but the difference was not statistically significant.

After adjustment with logistic regression with all variables (Table 4, Model 2) and removal of nonsignificant variables (Table 4, Model 3), proteinuria grade was still associated with CVC use (likelihood ratio test, $p < 0.001$). However, this association was statistically significant only in patients with midgrade proteinuria, who had the lowest odds of starting hemodialysis with a CVC (OR = 0.39, 95% CI = 0.24-0.65). Proteinuria grade was also associated with presence of an AVF in patients starting hemodialysis with a CVC in multivariate analysis compared with patients starting dialysis with AVF. Patients with midgrade proteinuria had the lowest odds of starting hemodialysis with a CVC with an AVF present (Table 5).

**Table 3. Unadjusted comparisons in baseline characteristics between patients divided by proteinuria grade**

| Variable | Proteinuria grade | | |
|---|---|---|---|
| | < 0.5 g (n = 212) | 0.5-3.5 g (n = 371) | > 3.5 g (n = 335) |
| Sex (men), % | 58 | 60.4 | 57.6 |
| PVD, % | 22.2 | 28.8 | 24.2 |
| CHF, % | 56[a] | 41 | 36 |
| Diabetes, % | 50.1[a] | 64.4 | 78.2[a] |
| History of AKI, % | 44.3 | 45.8 | 36.4[a] |
| eGFR at start of dialysis, median mL/min | 15.4[a] | 12.9 | 11.7 |
| Early dialysis start, % | 42 | 38.5 | 33.1 |
| Time of AVF placement, median d | 214 | 277 | 130[a] |
| eGFR at AVF placement, median mL/min | 19[a] | 16 | 15 |
| AVF placed < 90 d before first dialysis, % | 21.5 | 22.8 | 41.6[a] |
| Access type, % | | | |
| CVC | 56.1[a] | 39.9 | 50.7[a] |
| AVF | 27.8[a] | 46.4 | 29.3[a] |
| CVC with immature AVF | 16 | 13.7 | 20 |
| Age groups (y), % | | | |
| < 50 | 8 | 13.7 | 24.2[a] |
| 50-70 | 35.3[a] | 49.3 | 54.9 |
| > 70 | 56.6[a] | 36.9 | 20.9[a] |
| Race, % | | | |
| Asian | 2.4 | 4.9 | 6.8 |
| Black | 4.7 | 9.2 | 9.3 |
| White | 92[a] | 83.8 | 80 |
| Length of predialysis care, % | | | |
| None | 18.9[a] | 7.5 | 6 |
| 0-6 mo | 10.4 | 10.8 | 15.5 |
| 6-12 mo | 7.5 | 6.2 | 12.5[a] |
| 12-24 mo | 9.4 | 12.7 | 16.4 |
| > 24 mo | 53.8 | 62.8 | 49.6[a] |

[a] Denotes group with significant p value with 0.5 to 3.5 g of proteinuria as comparator group.
AKI = acute kidney injury; AVF = arteriovenous fistula; CHF = congestive heart failure; CVC = central venous catheter; eGFR = estimated glomerular filtration rate; PVD = peripheral vascular disease.

## DISCUSSION

Our findings demonstrate that midgrade proteinuria is associated with lower CVC use at initial hemodialysis. Our results did not support our hypothesis that higher levels of proteinuria were associated with higher rates of CVC use. Surprisingly, we found that patients with midgrade proteinuria had the lowest odds (ie, best outcome) of starting dialysis with CVC compared with other levels of proteinuria, including absent and low-grade proteinuria. When we looked at differences in patient characteristics between proteinuria grades, we found that patients with high-grade proteinuria had the shortest time from AVF placement until starting hemodialysis, the lowest eGFR at the time of AVF placement, and the highest percentage of an AVF placed 90 days or less before starting dialysis, compared with other grades of proteinuria. This suggests that one reason for higher rates of CVC use in the high proteinuria group was delay in referral

for AVF placement. This group may benefit from earlier referral for access placements or closer monitoring by a nephrologist.

Interestingly, patients with absent or low-grade proteinuria were also more likely to start dialysis with a CVC compared with patients with midgrade proteinuria. We found these patients were more likely to have a diagnosis of congestive heart failure, were more likely to have a higher eGFR before starting dialysis, and were less likely to have been followed-up by a nephrologist before dialysis. We theorize that this group included patients in whom acute kidney injury occurred or patients who had previously stable CKD but experienced acute kidney injury and did not recover. In addition, this group included a higher number of elderly patients. Elderly patients present a challenge to the nephrologist for dialysis preparation because of the competing risk of death,[25] lower incidence of proteinuria than in younger patients with CKD,[26] and slower rate of CKD progression,[25] which will often result in later referral for AVF placement.[11]

Another important finding in our study was that even with optimal nephrology care before dialysis, CVC use remains high. This finding was illustrated in our cohort of whom approximately 60% of patients starting hemodialysis with CVCs had seen a nephrologist for at least 12 months. This has been shown in other studies to be partly because of late AVF placement.[11,27] In our cohort, almost 30% of AVFs were placed less than 90 days before the start of dialysis, and longer predialysis care was not associated with decreased rates of immature AVF use at initial dialysis. A major challenge comes from predicting which patients will progress to ESRD and when to place an AVF. Placing an AVF too early will result in patients undergoing unnecessary procedures who may die before progressing to ESRD or requiring more interventions to maintain patency,[28] whereas placing an AVF too late will result in higher CVC use. Several conflicting guidelines have been published regarding the optimal timing for AVF placement. The National Kidney Foundation Kidney Disease Outcome Quality Initiative[29] recommends placement of an AVF at least 6 months before initiation of hemodialysis. However, the Canadian Society of Nephrology suggests referral for AVF placement at an eGFR of 15 mL/min to 20 mL/min,[30] and the European Renal Best Practice guidelines recommends referral when the eGFR is below 30 mL/min.[31] Hod et al[32] examined the timing of AVF placement in elderly patients from the United States Renal Data System and suggests that the optimal timing is 6 to 9 months before dialysis. With the current recommended threshold of 20 mL/min for eGFR, about 40% of patients in our cohort would have had their AVF placed less than 6 months before starting hemodialysis.

Several prediction models have been recently published predicting risk of progression to ESRD in patients with CKD.[33,34] In addition, two recent studies found that higher levels of proteinuria predicted which patients would go on to start hemodialysis after AVF placement.[21,22] These models and studies suggest that factors other than eGFR, such as proteinuria, age, and diabetes status, may help in individualizing

**Table 4. Logistic regression model for central venous catheter vs arteriovenous fistula at initial dialysis**

| | Model 1[a] | | | Model 2[b] | | | Model 3[c] | | |
|---|---|---|---|---|---|---|---|---|---|
| Variable | OR | 95% CI | p value | OR | 95% CI | p value | OR | 95% CI | p value |
| Sex (men, reference) | 1.27 | 0.96-1.68 | 0.09 | 1.23 | 0.91-1.66 | 0.18 | — | — | — |
| CHF | 1.36 | 1.04-1.80 | 0.03 | 1.20 | 0.86-1.66 | 0.28 | — | — | — |
| Diabetes | 0.94 | 0.70-1.25 | 0.65 | 0.75 | 0.54-1.04 | 0.08 | — | — | — |
| History of AKI | 0.85 | 0.64-1.11 | 0.22 | 1.07 | 0.79-1.44 | 0.68 | — | — | — |
| PVD | 1.40 | 1.02-1.93 | 0.04 | 1.38 | 0.96-1.98 | 0.08 | — | — | — |
| Hospitalizations | 1.07 | 1.04-1.10 | < 0.001 | 1.07 | 1.04-1.11 | < 0.001 | 1.07 | 1.04-1.11 | < 0.001 |
| Length of predialysis care (mo) | 0.98 | 0.98-0.99 | < 0.001 | 0.99 | 0.98-0.99 | < 0.001 | 0.99 | 0.98-0.99 | < 0.001 |
| Proteinuria[d] | — | — | < 0.001 | — | — | < 0.001 | — | — | < 0.001 |
| Absent (reference) | — | — | — | — | — | — | — | — | — |
| Low grade | 0.65 | 0.35-1.19 | 0.17 | 0.78 | 0.42-1.48 | 0.45 | 0.72 | 0.39-1.34 | 0.30 |
| Midgrade | 0.36 | 0.21-0.58 | < 0.001 | 0.44 | 0.26-0.75 | 0.002 | 0.39 | 0.24-0.65 | < 0.001 |
| High grade | 0.75 | 0.44-1.22 | 0.26 | 0.94 | 0.54-1.64 | 0.84 | 0.76 | 0.45-1.28 | 0.30 |
| Age groups, y[d] | — | — | 0.06 | — | — | 0.11 | — | — | — |
| < 50 | 1.16 | 0.76-1.77 | 0.50 | 1.10 | 0.68-1.79 | 0.70 | — | — | — |
| 50-70 | 0.76 | 0.57-1.03 | 0.08 | 0.76 | 0.54-1.06 | 0.10 | — | — | — |
| > 70 (reference) | — | — | — | — | — | — | — | — | — |
| Race[d] | — | — | 0.78 | — | — | 0.52 | — | — | — |
| White (reference) | — | — | — | — | — | — | — | — | — |
| Native American | 0.91 | 0.40-2.20 | 0.83 | 0.66 | 0.27-1.66 | 0.35 | — | — | — |
| Asian | 0.93 | 0.51-1.76 | 0.83 | 0.81 | 0.42-1.62 | 0.55 | — | — | — |
| Black | 0.85 | 0.52-1.40 | 0.52 | 0.96 | 0.56-1.65 | 0.89 | — | — | — |

[a] Model 1: Univariate logistic regression.
[b] Model 2: Multivariate logistic regression with all variables.
[c] Model 3: Multivariate logistic regression after removal of nonsignificant variables.
[d] Likelihood ratio test between model with categorical variable and model without.
AKI = acute kidney injury; CHF = congestive heart failure; CI = confidence interval; OR = odds ratio; PVD = peripheral vascular disease.

which patients should be prepared for dialysis and possibly determining the timing of AVF placement. However, our study suggests that these models, in which patients who are younger and have higher levels of proteinuria are more likely to have higher risk scores, may miss older patients with lower levels of proteinuria who progress to ESRD and may be more likely to start with a CVC. An important future study would look at performance of these models in predicting which of these patients are at risk of progression to ESRD.

Our study had some limitations. The observational study design shows association rather than causation. Factors in other studies, including obesity, cerebrovascular disease, smoking, and malignancy were not included in our analysis, which may have altered our findings regarding proteinuria because of confounding. Outcome of access used at dialysis was based on a review of vascular surgery notes, which may have been incomplete or documented incorrectly. The applicability of this study to the general population may be limited because patients were members of an integrated health care system, which may result in different practice patterns because of more integrated delivery. Patients were predominantly white, so applicability to other racial groups will be limited. We chose to divide proteinuria as a categorical rather than continuous variable because of the variability of proteinuria in our dataset. Glomerular filtration data were missing for more than one-third of our dataset, which could have altered those findings. In patients with an eGFR available, about 60% started hemodialysis at an eGFR above 10 mL/min. The IDEAL (Initiating Dialysis Early and Late) trial showed no improved outcomes with initiation of dialysis at a higher eGFR.[35] It is possible that these associations may be different in a more contemporary cohort of patients starting dialysis at a lower eGFR. Finally, the small size of our cohort may have limited our ability to find statistical significance for certain variables found to be significant in other studies.

**Table 5. Logistic regression model for central venous catheter with arteriovenous fistula present vs arteriovenous fistula at initial dialysis**

| | Model 1[a] | | | Model 2[b] | | | Model 3[c] | | |
|---|---|---|---|---|---|---|---|---|---|
| **Variable** | **OR** | **95% CI** | **p value** | **OR** | **95% CI** | **p value** | **OR** | **95% CI** | **p value** |
| Sex (men, reference) | 1.67 | 1.14-2.47 | 0.009 | 1.73 | 1.10-2.71 | 0.02 | 1.76 | 1.14- 2.72 | 0.01 |
| CHF | 1.59 | 1.08-2.35 | 0.02 | 1.06 | 0.64-1.74 | 0.83 | — | — | — |
| Diabetes | 1.28 | 0.84-1.97 | 0.25 | 1.05 | 0.63-1.75 | 0.85 | — | — | — |
| History of AKI | 0.70 | 0.47-1.04 | 0.08 | 0.86 | 0.54-1.37 | 0.53 | — | — | — |
| PVD | 1.48 | 0.95-2.29 | 0.08 | 1.14 | 0.67-1.95 | 0.63 | — | — | — |
| Hospitalizations | 1.05 | 1.01-1.10 | 0.02 | 1.04 | 0.99-1.09 | 0.11 | — | — | — |
| Length of predialysis care, mo | 0.99 | 0.98-0.99 | 0.003 | 1.00 | 0.99-1.01 | 0.67 | — | — | — |
| Proteinuria[d] | — | — | 0.01 | — | — | 0.01 | — | — | 0.02 |
| Absent (reference) | — | — | — | — | — | — | — | — | — |
| Low grade | 0.51 | 0.21-1.20 | 0.13 | 0.71 | 0.28-1.84 | 0.48 | 0.71 | 0.28-1.81 | 0.48 |
| Midgrade | 0.37 | 0.19. 0.73 | 0.003 | 0.38 | 0.18-0.82 | 0.01 | 0.37 | 0.18-0.78 | 0.009 |
| High grade | 0.85 | 0.44-1.67 | 0.64 | 0.77 | 0.34-1.71 | 0.51 | 0.65 | 0.31-1.36 | 0.25 |
| Age groups, y[d] | — | — | 0.12 | — | — | 0.12 | — | — | — |
| < 50 | 0.79 | 0.43-1.43 | 0.46 | 0.77 | 0.36-1.63 | 0.49 | — | — | — |
| 50-70 | 0.65 | 0.43-0.99 | 0.04 | 0.59 | 0.36-0.98 | 0.04 | — | — | — |
| > 70 (reference) | — | — | — | — | — | — | — | — | — |
| Race[d] | — | — | 0.23 | — | — | 0.23 | — | — | — |
| White (reference) | — | — | — | — | — | — | — | — | — |
| Native American | 0.46 | 0.07-1.81 | 0.32 | 0.36 | 0.05-1.82 | 0.26 | — | — | — |
| Asian | 0.61 | 0.20-1.57 | 0.34 | 0.60 | 0.17-1.83 | 0.40 | — | — | — |
| Black | 0.85 | 0.41-1.68 | 0.66 | 0.89 | 0.39-2.03 | 0.78 | — | — | — |
| Timing of AVF placement, mo[d] | — | — | < 0.001 | — | — | < 0.001 | — | — | < 0.001 |
| 0-3 | 7.51 | 4.01-14.80 | < 0.001 | 7.00 | 3.26-15.03 | < 0.001 | 7.21 | 3.64-14.26 | < 0.001 |
| 3-6 | 1.56 | 0.74-3.34 | 0.24 | 1.49 | 0.65-3.38 | 0.34 | 1.42 | 0.66-3.08 | 0.37 |
| 6-9 | 0.70 | 0.25-1.77 | 0.46 | 0.62 | 0.22-1.71 | 0.36 | 0.64 | 0.24-1.71 | 0.37 |
| 9-12 | 1.50 | 0.55-3.87 | 0.41 | 1.61 | 0.57-4.53 | 0.37 | 1.63 | 0.61-4.38 | 0.33 |
| 12-24 | 1.78 | 0.84-3.87 | 0.14 | 1.79 | 0.80-4.01 | 0.16 | 1.76 | 0.80-3.85 | 0.16 |
| > 24 (reference) | — | — | — | — | — | — | — | — | — |

[a] Model 1: Univariate logistic regression.
[b] Model 2: Multivariate logistic regression with all variables.
[c] Model 3: Multivariate logistic regression with only covariates after removing nonsignificant variables in step wise selection.
[d] Likelihood ratio test between model with categorical variable and model without.
AKI = acute kidney injury; AVF = arteriovenous fistula; CHF = congestive heart failure; CI = confidence interval; OR = odds ratio; PVD = peripheral vascular disease.

## CONCLUSION

We found that proteinuria was associated with starting dialysis with a CVC and with patients who had midgrade proteinuria having the best vascular access outcome for starting dialysis. However, we did not find that increasing proteinuria was associated with higher CVC rates as we had expected. Surprisingly, patients with low or absent proteinuria also had higher rates of CVC use comparable to patients with high-grade proteinuria. Our findings suggest that the relationship of proteinuria with CVC use is more complex, and current prediction models may miss older patients with lower-grade proteinuria who progress to ESRD. Future prospective studies looking at refinement of these models in this group of patients would be of interest in helping reduce CVC rates at initial dialysis. ❖

**Disclosure Statement**

*The author(s) have no conflicts of interest to disclose.*

**Acknowledgments**

*No financial support was received for this study. We thank Amy Ronfeld, Jill Walker, and Carolyn Beall for collecting vascular access information.*

*Kathleen Louden, ELS, of Louden Health Communications provided editorial assistance.*

**How to Cite this Article**

Park KJ, Johnson ES, Smith N, Mosen DM, Thorp ML. Association of proteinuria with central venous catheter use at initial hemodialysis. Perm J 2018;22:16-194. DOI: https://doi.org/10.7812/TPP/16-194

**References**

1. United States Renal Data System. USRDS 2015 annual data report: Atlas of chronic kidney disease and end-stage renal disease in the United States [Internet]. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2015 [cited 2017 Aug 29]. Available from: www.usrds.org/2015/view/Default.aspx.
2. Pisoni RL, Arrington CJ, Albert JM, et al. Facility hemodialysis vascular access use and mortality in countries participating in DOPPS: An instrumental variable analysis. Am J Kidney Dis 2009 Mar;53(3):475-91. DOI: https://doi.org/10.1053/j.ajkd.2008.10.043.
3. Lee T, Barker J, Allon M. Associations with predialysis vascular access management. Am J Kidney Dis 2004 Jun;43(6):1008-13. DOI: https://doi.org/10.1053/j.ajkd.2004.02.013.
4. Hod T, Desilva RN, Patibandla BK, Vin Y, Brown RS, Goldfarb-Rumyantzev AS. Factors predicting failure of AV "fistula first" policy in the elderly. Hemodial Int 2014 Apr;18(2):507-15. DOI: https://doi.org/10.1111/hdi.12106.
5. Xue JL, Dahl D, Ebben JP, Collins AJ. The association of initial hemodialysis access type with mortality outcomes in elderly Medicare ESRD patients. Am J Kidney Dis 2003 Nov;42(5):1013-9. DOI: https://doi.org/10.1053/S0272-6386(03)01015-1.
6. Dhingra RK, Young EW, Hulbert-Shearon TE, Leavey SF, Port FK. Type of vascular access and mortality in US hemodialysis patients. Kidney Int 2001 Oct;60(4):1443-51. DOI: https://doi.org/10.1046/j.1523-1755.2001.00947.x.
7. CMS; ESRD Network. Fistula first breakthrough initiative. Arteriovenous fistula first: The first choice for hemodialysis [Internet]. Baltimore, MD: Centers for Medicare & Medicaid Services; 2003 Jul [cited 2016 Dec 18]. Available from: www.fistulafirst.org.
8. Oliver MJ, Rothwell DM, Fung K, Hux JE, Lok CE. Late creation of vascular access for hemodialysis and increased risk of sepsis. J Am Soc Nephrol 2004 Jul;15(7):1936-42. DOI: https://doi.org/10.1097/01.ASN.0000131524.52012.F8.
9. Chronic Kidney Disease, HealthyPeople.gov [Internet]. Washington, DC: US Department of Health and Human Services, Office of Disease Prevention and Health Promotion; updated 2017 Aug 29 [cited 2016 Dec 18]. Available from: www.healthypeople.gov/2020/topics-objectives/topic/chronic-kidney-disease/objectives.
10. United States Renal Data System. USRDS 2013 annual data report: Atlas of chronic kidney disease and end-stage renal disease in the United States [Internet]. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2013 [cited 2017 Aug 30]. p 1-26. Available from: www.usrds.org/atlas13.aspx.
11. Lee T, Thamer M, Zhang Y, Zhang Q, Allon M. Outcomes of elderly patients after predialysis vascular access creation. J Am Soc Nephrol 2015 Dec;26(12):3133-40. DOI: https://doi.org/10.1681/ASN.2014090938.
12. Allon M, Ornt DB, Schwab SJ, et al. Factors associated with the prevalence of arteriovenous fistulas in hemodialysis patients in the HEMO study. Hemodialysis (HEMO) Study Group. Kidney Int 2000 Nov;58(5):2178-85. DOI: https://doi.org/10.1111/j.1523-1755.2000.00391.x.
13. Peterson WJ, Barker J, Allon M. Disparities in fistula maturation persist despite preoperative vascular mapping. Clin J Am Soc Nephrol 2008 Mar;3(2):437-41. DOI: https://doi.org/10.2215/CJN.03480807.
14. Hirth RA, Turenne MN, Woods JD, et al. Predictors of type of vascular access in hemodialysis patients. JAMA 1996 Oct 23-30;276(16):1303-8. DOI: https://doi.org/10.1001/jama.1996.03540160025028.
15. Astor BC, Eustace JA, Powe NR, et al. Timing of nephrologist referral and arteriovenous access use: The CHOICE Study. Am J Kidney Dis 2001 Sep;38(3):494-501. DOI: https://doi.org/10.1053/ajkd.2001.26833.
16. Allon M, Robbin ML. Increasing arteriovenous fistulas in hemodialysis patients: Problems and solutions. Kidney Int 2002 Oct;62(4):1109-24. DOI: https://doi.org/10.1111/j.1523-1755.2002.kid551.x.
17. Lok CE, Allon M, Moist L, Oliver MJ, Shah H, Zimmerman D. Risk equation determining unsuccessful cannulation events and failure to maturation in arteriovenous fistulas (REDUCE FTM I). J Am Soc Nephrol 2006 Nov;17(11):3204-12. DOI: https://doi.org/10.1681/ASN.2006030190.
18. DeSilva RN, Patibandla BK, Vin Y, et al. Fistula first is not always the best strategy for the elderly. J Am Soc Nephrol 2013 Jul;24(8):1297-304. DOI: https://doi.org/10.1681/ASN.2012060632.
19. Patibandla BK, Narra A, Desilva R, et al. Disparities in arteriovenous fistula placement in older hemodialysis patients. Hemodial Int 2014 Jan;18(1):118-26. DOI: https://doi.org/10.1111/hdi.12099.
20. Levey AS, de Jong PE, Coresh J, et al. The definition, classification, and prognosis of chronic kidney disease: A KDIGO Controversies Conference report. Kidney Int 2011 Jul;80(1):17-28. DOI: https://doi.org/10.1038/ki.2010.483.
21. Stoumpos S, Stevens KK, Aitken E, et al. Predictors of sustained arteriovenous access use for haemodialysis. Am J Nephrol 2014;39(6):491-8. DOI: https://doi.org/10.1159/000362744.
22. Al-Balas A, Lee T, Young CJ, Barker-Finkel J, Allon M. Predictors of initiation for predialysis arteriovenous fistula. Clin J Am Soc Nephrol 2016 Oct 7;11(10):1802-8. DOI: https://doi.org/10.2215/CJN.00700116.
23. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International Supplements 2013 Jan;1(3):1-150.
24. Levey AS, Stevens LA, Schmid CH, et al; CKD-EPI (Chronic Kidney Diseae Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. Ann Intern Med 2009 May 5;150(9):604-12. DOI: https://doi.org/10.7326/0003-4819-150-9-200905050-00006. Erratum in: Ann Intern Med 2011 Sep 20;155(6):408. DOI: https://doi.org/10.7326/0003-4819-155-6-201109200-00024.
25. O'Hare AM, Choi AI, Bertenthal D, et al. Age affects outcomes in chronic kidney disease. J Am Soc Nephrol 2007 Oct;18(10):2758-65. DOI: https://doi.org/10.1681/ASN.2007040422.
26. O'Hare AM, Kaufman JS, Covinsky KE, Landefeld CS, McFarland LV, Larson EB. Current guidelines for using angiotensin-converting enzyme inhibitors and angiotensin II-receptor antagonists in chronic kidney disease: Is the evidence base relevant to older adults? Ann Intern Med 2009 May 19;150(10):717-24. DOI: https://doi.org/10.7326/0003-4819-150-10-200905190-00010.
27. Al-Jaishi AA, Lok CE, Garg AX, Zhang JC, Moist LM. Vascular access creation before hemodialysis initiation and use: A population-based cohort study. Clin J Am Soc Nephrol 2015 Mar 6;10(3):418-27. DOI: https://doi.org/10.2215/CJN.06220614.
28. Richardson AI 2nd, Leake A, Schmieder GC, et al. Should fistulas really be first in the elderly patient? J Vasc Access 2009 Jul-Sep;10(3):199-202. DOI: https://doi.org/10.5301/JVA.2009.3240.
29. National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) [Internet]. New York, NY: National Kidney Foundation; c2017 [cited 2017 Aug 30]. Available from: www.kidney.org/professionals/guidelines.
30. Canadian Society of Nephrology home [Internet]. Montreal, Quebec, Canada: Canadian Society of Nephrology; c2017 [cited 2017 Aug 30]. Available from: www.csnscn.ca/.
31. ERBP (European Renal Best Practice) [Internet]. Glasgow, Scotland: European Renal Best Practice; c2017 [cited 2017 AAug 30]. Available from: www.european-renal-best-practice.org/.
32. Hod T, Patibandla BK, Vin Y, Brown RS, Goldfarb-Rumyantzev AS. Arteriovenous fistula placement in the elderly: When is the optimal time? J Am Soc Nephrol 2015 Feb;26(2):448-56. DOI: https://doi.org/10.1681/ASN.2013070740.
33. Schroeder EB, Yang X, Thorp ML, et al. Predicting 5-year risk of RRT in stage 3 or 4 CKD: Development and external validation. Clin J Am Soc Nephrol 2017 Jan 6;12(1):87-94. DOI: https://doi.org/10.2215/CJN.01290216.
34. Tangri N, Stevens LA, Griffith J, et al. A predictive model for progression of chronic kidney disease to kidney failure. JAMA 2011 Apr 20;305(15):1553-9. DOI: https://doi.org/10.1001/jama.2011.451.
35. Cooper BA, Branley P, Bulfone L, et al; IDEAL study. A randomized, controlled trial of early versus late initiation of dialysis. N Engl J Med 2010 Aug 12;363(7):609-19. DOI: https://doi.org/10.1056/NEJMoa1000552.