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Gender Disparities in Vascular Access Surgical Outcomes in Elderly Hemodialysis Patients

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Abstract

Background: Despite national vascular access guidelines promoting use of arteriovenous fistulas (AVF) over arteriovenous grafts (AVG) for dialysis, AVF use is substantially lower in females. To assess clinically relevant AVF and AVG surgical outcomes in elderly male and female patients initiating hemodialysis with a central venous catheter (CVC).

Methods: Using the United States Renal Data System standard analytic files linked with Medicare claims, we assessed incident hemodialysis patients in the United States, 9,458 elderly patients (> 67 years) (4,927 males and 4,531 females) initiating hemodialysis from July 2010 to June 2011 with a catheter, and had an AVF or AVG placed within 6 months. We evaluated vascular access placement, successful use for dialysis, assisted use (requiring an intervention before successful use), abandonment after successful use, and rate of interventions after successful use.

Results: Females were less likely than males to receive an AVF (adjusted likelihood 0.57, 95% confidence interval [CI] 0.52–0.63). Among patients receiving an AVF, females had higher adjusted likelihoods of unsuccessful AVF use (HR 1.46, 95% CI 1.36–1.56), assisted AVF use (OR 1.34, 95% CI 1.17–1.54), and AVF abandonment (HR 1.28, 95% CI 1.10–1.50), but similar relative rate of AVF interventions after successful use (RR 1.01, 95% CI 0.94–1.08). Among patients receiving an AVG, females had a lower likelihood of unsuccessful AVG use (HR 0.83, 95% CI 0.73–0.94), similar rates of assisted AVG use (OR 1.05, 95% CI 0.78–1.40) and AVG

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Author Contributions

TL, MT, JQ, and MA designed the study

MT, JQ, TL, and MA analyzed the data

JQ made the figures

TL, MT and MA drafted and revised the paper

All authors approved the final version of the manuscript

Conflict of Interests

Dr. Lee is a consultant for Proteon Therapeutics, Boston Scientific, and Merck. Dr. Allon is a consultant for CorMedix. Dr. Thamer is a consultant for Proteon Therapeutics.

Statement of Ethics

This study was deemed exempt from the University of Alabama at Birmingham Institutional Review Board because we used deidentified information.

abandonment, and greater relative rate of interventions after successful AVG use (RR 1.16, 95% CI, 1.01–1.33).

Conclusions: While AVFs should be considered the preferred vascular access in most circumstances, clinical AVF surgical outcomes are uniformly worse in females. Clinicians should also consider AVGs as a viable alternative in elderly female patients initiating hemodialysis with a CVC to avoid extended CVC-dependence.

Keywords

End stage renal disease; Hemodialysis; Vascular access intervention Arteriovenous fistula; Arteriovenous graft; Central venous catheter

INTRODUCTION

Although current national vascular access guidelines promote arteriovenous fistulas (AVFs) over arteriovenous grafts (AVGs) as the preferred type of vascular access for hemodialysis[1,2], AVF use is substantially lower in female than male patients in the United States[3,4]. In broad terms, AVF use is a reflection of three distinct and sequential processes of care: AVF creation, AVF maturation that allows successful cannulation and use for dialysis, and AVF survival following successful use[5]. Thus, a lower prevalence of AVF use among female hemodialysis patients may be a consequence of suboptimal outcomes in one or more of these processes of care (e.g., less frequent AVF creation, less frequent successful use of AVFs that have been created, or shorter AVF survival after its successful use for dialysis). Additional processes of care may indirectly impact these AVF outcomes. For example, percutaneous interventions (e.g. angioplasty or surgical revisions) are frequently necessary prior to successful AVF use (“assisted use”), but such interventions may decrease long term AVF patency and/or increase the frequency of interventions to maintain AVF patency after successful use [6,7]. Although many publications have compared isolated vascular access processes of care in female vs male hemodialysis patients[7–16], none have addressed comprehensively the individual contributions of each of these processes of care to gender disparities in AVF use in a national cohort of patients. In addition, there is sparse information on the relative outcomes of AVGs in male and female hemodialysis patients. Finally, the current study focused on patients who initiated dialysis with a CVC, and subsequently received an AVF or AVG, as they represent 80% of new dialysis starts, and are at risk for prolonged CVC-dependence and its associated complications[7].

The present study systematically compared the interconnected series of vascular access processes of care and surgical outcomes among a recent national cohort of elderly male and female hemodialysis patients initiating hemodialysis with a CVC. We utilized data from the United States Renal Data System (USRDS) linked with Medicare claims to analyze the three key vascular access processes of care (creation, vascular access use, and abandonment), and compared the following surgical AVF and AVG outcomes between males and females: (1) AVF vs AVG creation, (2) unsuccessful AVF and AVG use, (3) assisted AVF and AVG use, (4) AVF and AVG abandonment after successful use, and (5) frequency of AVF and AVG interventions after successful use. Collectively, understanding differences in these surgical

vascular access outcomes may provide objective evidence to develop strategies that improve vascular access outcomes among female hemodialysis patients.

MATERIAL AND METHODS

Data Sources and Study Population

This study was deemed exempt from the University of Alabama at Birmingham Institutional Review Board because we used deidentified information. Our primary data source was derived from the USRDS standard analytic files between 7/1/2010 to 12/31/2013, as previously described by our group[17]. Briefly, we identified 100,441 patients who initiated hemodialysis from 7/1/2010 to 6/30/2011. Among these patients, we included 29,178 patients who started dialysis at age ≥ 67 years (in order to have pre-dialysis information), initiated hemodialysis with a CVC (representing ~60% of all dialysis patients and are at highest risk of long-term CVC use and adverse outcomes), and did not have a AVF or AVG placed prior to dialysis initiation (no decision on a permanent VA had been made prior to dialysis initiation). Our analysis focused on the elderly hemodialysis subpopulation since 97% of them have health insurance at the time of dialysis initiation. This feature permitted us to have comprehensive baseline information on co-morbidities and severity of illness, as well as vascular access procedures and outcomes from the first day of dialysis. We excluded patients (1) without pre-ESRD Medicare claims, (2) who had an AVF or AVG creation before dialysis initiation, (3) who did not have an AVF or AVG creation within 6 months of hemodialysis initiation, and (4) who had switched to peritoneal dialysis or received kidney transplantation at any point in the study. Our final study cohort included 9,458 patients initiating hemodialysis with a CVC and having a subsequent AVF (n=7,433) or AVG (n=2,025) placed within 6 months. Baseline clinical and comorbidity data in the two years prior to reaching ESRD were extracted from pre-ESRD Medicare data [17,18].

Variables of Interest

The main study exposure was patient gender, available for all patients in the study. Beginning July 2010, all dialysis units were mandated by the Centers for Medicare & Medicaid Services to ascertain monthly vascular access in use for all hemodialysis patients using one of three vascular access modifiers: V5 (CVC), V6 (AVG), or V7 (AVF). These monthly reports were used to determine when an AVF or AVG was initially used for dialysis, and when it was abandoned.

Several clinical vascular access outcomes were compared between male and female hemodialysis patients, using the following definitions:

1. Vascular access type created: AVF or AVG
2. Unsuccessful vascular access use: A vascular access which was not successfully used for dialysis within 6 months of its surgical creation, as ascertained from the vascular access modifier codes.
3. Assisted use: Whether the patient required an intervention of AVF/AVG prior to its successful use. Patients were considered to have assisted AVF/AVG use if

they underwent an access intervention prior to successful use, and to have unassisted use if they did not undergo such an intervention.

4. Access abandonment at 1 year: Access abandonment at 1 year was determined as the time from successful AVF/AVG use until it was abandoned. We defined abandonment as use of CVC for three consecutive months or placement of new AVF/AVG.
5. Frequency of access interventions during the first year. The analysis included any percutaneous or surgical interventions during the one-year period following successful vascular access use, as previously described[19].

The Medical Evidence Form was used to extract patient demographics, co-morbidities, and functional status at hemodialysis initiation. For all outcomes, we used the same baseline, defined as hemodialysis initiation. Start of follow-up was defined as vascular access creation date for both AVG and AVF patients.

Statistical Analysis

Baseline patient characteristics were compared between male and female patients, using Pearson's chi-square tests for categorical variables, and Student's t-test or nonparametric Wilcoxon rank-sum test for continuous variables. We identified duration of CVC-dependency prior to successful vascular access use by month and used Kruskal-Wallis test to compare them across gender groups. A multivariable logistic regression analysis adjusted for age, race, stroke, CAD (any history of MI, coronary revascularization, or CHF), history of stroke, and Liu's co-morbidity index was conducted to explore the possible association between patient gender and three vascular access outcomes: 6-month unsuccessful use, 6-month assisted use, and 12-month abandonment. The final vascular access study outcome, 12-month frequency of interventions after successful use, was compared using log-binomial regression analyses across gender groups, adjusted for age, race, stroke, CAD, history of stroke, and Liu's co-morbidity index. All analyses were done separately for AVF and AVG patients. Statistical analyses were performed using SAS (version 9.3; SAS institute, Cary, NC). All statistical tests were two-sided, and a p-value < 0.05 considered statistically significant. We used the STROBE guidelines to improve the reporting of our observational research study.

RESULTS

Baseline Characteristics of Overall Study Population by Gender

Table 1 compares the baseline demographics and comorbidities in elderly male and female patients who initiated hemodialysis with only a CVC, and had an AVF or AVG created during the ensuing 6 months. The mean age, 77 years, did not differ by patient gender. Several demographic and comorbidity factors differed significantly between male and female patients. Males were more likely to be of white race, have higher Liu co-morbidity index, and have more cardiovascular diseases and cancer ($p < 0.001$ for all comparisons). Females had a greater body mass index, and were more likely to have diabetes, inability to ambulate, depression, and dementia ($p < 0.001$ for all comparisons).

Unadjusted Vascular Access Outcomes by Gender

Overall, females were less likely than males to have an AVF created (74 vs. 83%, $p < 0.0001$). Figure 1A compares the major clinically relevant surgical vascular outcomes between male and female patients receiving an AVF. Females were more likely to have unsuccessful AVF use (57% vs 47%, $p < 0.0001$), to require assisted AVF use (47% vs 40%, $p < 0.0001$), and to experience AVF abandonment (21% vs 16%, $p = 0.002$). Figure 1B compares the same outcomes between men and women undergoing AVG placement. Females were less likely than males to have unsuccessful AVG use (42 vs 51%, $p < 0.0001$), but had a similar likelihood of assisted AVG use (24 vs 23%, $p = 0.70$) and AVG abandonment (25 vs 23%, $p = 0.32$).

Adjusted Vascular Access Outcomes by Gender

Females were less likely than males to receive an AVF (adjusted likelihood 0.57, 95% CI 0.52–0.63). Among patients receiving an AVF, females had higher likelihoods of unsuccessful AVF use (HR 1.46, 95% CI 1.36–1.56), assisted AVF use (OR 1.34, 95% CI 1.17–1.54), and AVF abandonment during a one-year follow-up after successful use (HR 1.28, 95% CI 1.10–1.50) (Figure 2A). In contrast, the relative rate of AVF interventions in the first year after successful use (HR 1.01, 95% CI 0.94–1.08) was similar between the two genders (Figure 2A).

Among patients receiving an AVG, females had a lower adjusted likelihood of unsuccessful AVG use (HR 0.83, 95% CI 0.73–0.94), but a greater relative rate of interventions during the one-year period after successful AVG use (HR 1.16, 95% CI, 1.01–1.33) (Figure 2B). Other surgical clinical outcomes, including assisted AVG use (OR 1.05, 95% CI 0.78–1.40) and AVG abandonment (HR 1.12, 95% CI 0.87–1.45) did not differ significantly between females and males.

DISCUSSION

Our current study utilized a national administrative database that includes information on all Medicare-insured elderly dialysis patients (~97%) to examine gender disparities in vascular access surgical outcomes among patients initiating hemodialysis with a CVC who subsequently received an AVF or AVG. We found several important differences in vascular access surgical outcomes between male and female patients that could explain why female hemodialysis patients are less likely to use an AVF for hemodialysis. Specifically, females were less likely to have an AVF surgically created, less likely to have successful AVF use, more likely to require assisted AVF use, and more likely to experience AVF abandonment (despite a similar rate of interventions after successful use). In contrast, AVG outcomes were fairly similar between the genders, with unsuccessful AVG use being somewhat lower in women, the rate of AVG interventions being slightly lower in men, and assisted use and likelihood of abandonment at one year being similar in both genders. These observations have important clinical implications about the choice of vascular access type in elderly women initiating hemodialysis with a CVC.

The substantial gender disparity in AVF use among hemodialysis patients has been observed repeatedly for over 20 years. An analysis of 1824 patients enrolled from 1995 to 1999 in the HEMO Study reported AVF use in 22.4% of female patients vs 46.3% of males[8]. Similarly, the USRDS report from 1999 documented a strikingly lower rate of AVF use in prevalent female vs male hemodialysis patients in each of the 18 U.S. dialysis networks, with the absolute rate being approximately 20% lower in females[9]. Although the overall proportion of patients dialyzing with an AVF has increased greatly in both genders following the 2003 Fistula First Initiative[1], the gender discrepancy persists. The Dialysis Outcomes Practice Patterns Study (DOPPS) of prevalent U.S dialysis patients from 2010 to 2013 reported a lower use of AVFs in women than in men for both black patients (50 vs 65%) and non-blacks (65 vs 75%)[10]. Most recently, the 2017 USRDS report documented AVF use in 55.2% of female patients vs 68.8% of males, an absolute difference of 13.6%[11]. Our study utilizes recent data, looking at outcomes previously not examined and, for the first time, uses national data focusing on the elderly population.

These previous studies did not, however, provide the information needed to understand or mitigate gender disparities, since they did not elucidate the causes of the lower AVF use. Equally important, they did not address gender differences in the outcomes of AVGs, the alternative permanent vascular to AVFs. Among patients initiating dialysis with a CVC and subsequently receiving a permanent vascular access, successful and long-term AVF or AVG use reflects three distinct and sequential surgical processes of care[5]. First, an AVF or AVG has to be surgically created. Second, AVFs have to mature sufficiently for successful use for dialysis and often times requires multiple interventions to promote patency and AVGs require several weeks to heal following surgery before cannulation. Finally, the AVF or AVG has to maintain patency after successful use to provide a long-term conduit for thrice weekly dialysis sessions. Suboptimal outcomes in any of these interconnected steps will lead to a lower frequency of permanent vascular access use, whereas a concurrent deficiency in all three outcomes is likely to result in prolonged CVC use. The 2017 USRDS report highlights the impact of these vascular access processes of care on achieving a successful AVF after hemodialysis initiation. Fewer than 20% of patients of either gender use an AVF at hemodialysis initiation; the proportion of female and male patients using an AVF rises to 37.6 vs 50.9% at 6 months, and 56.7 vs 71.4% at 1 year, respectively[11]. In other words, the gender gap in AVF use is 15% after a full year to permit AVF creation, successful AVF use, and measures to prevent AVF abandonment after successful use. The following discussion examines empirical evidence from the existing literature for gender differences at each vascular access process of care.

Similar to our study, others have documented a lower likelihood of AVF creation in female vs male patients. A single center study reported that, even with routine preoperative vascular mapping, a measure postulated to increase AVF creation, AVFs were less likely to be placed in female than in male patients (50 vs 74%)[12]. In the Dialysis Access Consortium (DAC) Study, which enrolled 877 patients receiving a new AVF from 2003–2006, only 38% of the patients enrolled were female. Subsequently, in the Hemodialysis Fistula Maturation (HFM) Study, which enrolled 602 patients receiving a new AVF from 2010–2013, only 30% of the patients enrolled were female. Several previous studies have also reported female sex to be a risk factor for unsuccessful AVF use [13–15]. In particular, a single center study observed

greater unsuccessful AVF use in females than in males, despite routine preoperative mapping and more frequent interventions in females to salvage non-maturing AVFs[16]. There has been limited published information on the impact of gender on AVF survival after its successful use. A single center study found no significant association between patient gender and AVF abandonment[7]. In contrast, in the national cohort described in the present study, AVF abandonment was greater among female patients.

Notably, none of the previous studies have provided a head-to-head comparison of both AVF and AVG outcomes in both genders. A previous study reported that despite a preoperative vascular access mapping, successful AVF use was lower in females vs. males, females required more interventions to achieve successful AVF use, and these outcomes were similar in forearm and upper arm AVFs[16]. Moreover, the worse AVF outcomes seen in females were not explained by differences in preoperative vessel diameter[16]. A recent publication by the HFM Consortium evaluated the role of baseline vascular function prior to AVF creation[20]. This study showed higher brachial artery flow-mediated dilation (marker of endothelial-dependent vascular function) and brachial artery nitroglycerin-mediated dilation (marker of endothelial-independent vascular function) in females compared to males at baseline prior to AVF creation [20]. Thus, lower successful AVF use in females is likely not explained by preoperative vascular function tests. Additional research is needed to explore potential biological processes that impair successful AVF maturation and use and reduce AVF longevity in females (e.g., vessel remodeling or neointimal hyperplasia), and to identify the clinical and physiologic reasons associated with selection of permanent vascular type in female hemodialysis patients.

Surgical or percutaneous interventions that are often required to promote successful vascular access use, are also associated with adverse subsequent vascular access outcomes after successful use. Two previous small studies reported a requirement for assisted use in 44 to 50% of new AVFs, with a greater frequency observed in female patients[6,7], similar to our study findings. Assisted vascular access use in these studies was associated with higher rates of access abandonment and increased frequency of interventions to maintain access patency after successful use [6,7]. In the present study, AVF abandonment after successful use was also found to be greater in females than in males, despite a similar frequency of interventions after successful use, suggesting that such interventions are less successful in maintaining AVF patency in females. This observation is consistent with a single-center study reporting shorter AVF survival after angioplasty in female vs male patients[21].

In contrast to AVF outcomes, gender differences in AVG outcomes have received little attention. Two single center studies found no association between patient gender and AVG abandonment,[7,22] findings consistent with the current study of patients from a national hemodialysis patient cohort. There is a clear difference between AVF and AVG outcomes in female patients in the present study. Whereas AVF outcomes (unsuccessful use and abandonment) were distinctly inferior in females vs male patients, AVG outcomes were comparable or better (lower rates of unsuccessful AVG use and similar abandonment). These findings suggest that the current Fistula First recommendations may not be optimal for elderly female dialysis patients. Rather, more frequent creation of AVGs in females may in fact lead to better outcomes, as measured by use of a permanent vascular access for

hemodialysis that minimizes catheter use and its associated risks of catheter-related infections and mortality[23–28].

Although the current study analyzed a large recent national cohort of incident hemodialysis patients, it also has several limitations. First, it includes only elderly patients (≥ 67 years) who initiated hemodialysis, and the observed gender disparities findings may not generalize to the younger hemodialysis population. However, our study findings are relevant to the 40% of incident United States hemodialysis patients who are ≥ 65 years of age[29]. Second, since this study is observational and uses a national administrative database, clinical decisions guiding whether an AVF or AVG is placed, and/or the need to intervene on a vascular access, are not fully captured. Finally, it is also not possible to adequately adjust for all patient-based or systems-based factors that may impact our measured clinical vascular access outcomes.

CONCLUSIONS

Among elderly patients who initiate hemodialysis with a CVC, AVF outcomes are uniformly worse among female patients, as manifested by a lower likelihood of AVF creation, a lower likelihood of successful AVF use, a higher likelihood of assisted AVF use, and a higher likelihood of AVF abandonment. In contrast, AVG grafts had fairly comparable outcomes in both genders, with females having a lower rate of unsuccessful AVG use, a slightly higher rate of intervention after successful AVG use, and comparable likelihoods of assisted use and abandonment. Taken together, these findings suggest that an AVF may not be the preferred choice of vascular access in many elderly female hemodialysis patients initiating hemodialysis with a CVC. While AVFs should be considered the preferred vascular access in most circumstances, clinical AVF surgical outcomes are uniformly worse in females. Clinicians should also consider AVGs as a viable alternative in elderly female patients initiating hemodialysis with a CVC to avoid extended CVC-dependence.

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Figure 1A.
Flow diagram of study cohort initiating hemodialysis with a CVC with subsequent AVF placement.

Note: Grey shading indicates access outcome occurred.

Figure 1B.

Flow diagram of study cohort initiating hemodialysis with a CVC with subsequent AVG placement.

Figure 2A.

Forest plots of adjusted hazard and odds ratio of 95% confidence interval (CI) of unsuccessful AVF use (unsuccessful use within 6 months of placement); assisted use (requirement for an intervention prior to successful use); and access abandonment; and adjusted relative risk (RR) and 95% CI of frequency of access interventions in the first year after successful use. All models were adjusted for age, gender, race, coronary artery disease (combined history of myocardial infarction, coronary revascularization, heart failure), history of stroke, and Liu's co-morbidity index

Figure 2B.

Forest plots of adjusted hazard and odds ratio of 95% confidence interval (CI) of unsuccessful AVG use (unsuccessful use within 6 months of placement); assisted use (requirement for an intervention prior to successful use); and access abandonment; and adjusted relative risk (RR) and 95% CI of frequency of access interventions in the first year after successful use. All models were adjusted for age, gender, race, coronary artery disease (combined history of myocardial infarction, coronary revascularization, heart failure), history of stroke, and Liu's co-morbidity index

Table 1.

Characteristics of elderly patients who initiated hemodialysis with only a catheter between July 1, 2010 and June 30, 2011 and had subsequent fistula or graft placement within 6 months of dialysis initiation by gender.

	Male N(%)	Female N(%)	p-value
Total Cohort	4927	4531	
Age at dialysis initiation (mean±SD)	77±6.5	76.8±6.5	0.124
67-<75	1987(40.3)	1875(41.4)	0.255
75-<85	2244(45.5)	1988(43.9)	
85	696(14.1)	668(14.7)	
Race			
White	3830(77.7)	3154(69.6)	<0.0001
Black	861(17.5)	1116(24.6)	
Other/unknown	236(4.8)	261(5.8)	
Body mass index (kg/m ²)(mean±SD)	27.7±6.6	29.2±7.9	<0.0001
<18.5	139(2.8)	198(4.4)	<0.0001
18.5-<30	3333(68.1)	2556(56.8)	
30	1424(29.1)	1743(38.8)	
Comorbid conditions			
Liu co-morbidity index (mean±SD)	10.4±4.4	10.1±4.4	<0.0001
0-7	1007(20.4)	1006(22.2)	0.0003
7-13	2084(42.3)	2013(44.4)	
13	1836(37.3)	1512(33.4)	
Cardiovascular diseases			
Congestive heart failure	2720(55.2)	2579(56.9)	0.094
Ischemic heart disease	3422(69.5)	2718(60)	<0.0001
Coronary revascularization	609(12.4)	415(9.2)	<0.0001
Acute myocardial infarction	614(12.5)	448(9.9)	<0.0001
Cerebrovascular disease	1619(32.9)	1470(32.4)	0.666
History of stroke	931(18.9)	898(19.8)	0.256
Peripheral vascular disease	2794(56.7)	2516(55.5)	0.248
Amputation	177(3.6)	101(2.2)	<0.0001
Diabetes	3296(66.9)	3233(71.4)	<0.0001
Cancer	1267(25.7)	728(16.1)	<0.0001
Chronic obstructive pulmonary disease	1916(38.9)	1691(37.3)	0.117
Inability to ambulate/transfer	1152(23.4)	1280(28.3)	<0.0001
Depression	556(11.3)	775(17.1)	<0.0001
Dementia	449(9.1)	572(12.6)	<0.0001
Hospital days (6 months before ESRD)	17.2±17.3	18.7±18.4	0.002
Catheter dependency (days to VA surgery)	69.2±44.6	70±44.9	0.357
60	2329(47.3)	2078(45.9)	0.170

	Male N(%)	Female N(%)	<i>p</i> -value
>60	2598(52.7)	2453(54.1)	

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