Arteriovenous Fistula Versus Graft Access Strategy in Older Adults Receiving Hemodialysis: A Pilot Randomized Trial

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Background: It is unclear whether surgical placement of an arteriovenous (AV) fistula (AVF) confers substantial clinical benefits over an AV graft (AVG) in older adults with end-stage kidney disease (ESKD). We report vascular access outcomes of a pilot clinical trial.

Study Design: Pilot randomized parallel-group open-label trial.

Setting & Participants: Patients 65 years and older with ESKD and no prior AV access receiving maintenance hemodialysis through a tunneled central venous catheter referred for AV access placement by their treating nephrologist.

Intervention: Participants were randomly assigned in a 1:1 ratio to surgical placement of an AVG or AVF.

Outcomes: Index AV access primary failure, successful cannulation, adjuvant interventions and infections.

Results: Of 122 older adults receiving hemodialysis and no prior AV access surgery, 24% died before (n = 18) or were too sick for (n = 11) referral for a permanent AV access. Of 46 eligible patients, 36 (78%) consented and were randomly assigned to AVG (n = 18) and AVF (n = 18) placement, of whom 13 (72%) and 16 (89%) underwent index AV access surgical placement, respectively. At a median follow-up of 321.0 days, primary AV access failure was noted in 31% in each group. The proportion of patients with successful cannulation was 62% (8 of 13) in the AVG and 50% (8 of 16) in the AVF group; median times to successful cannulation were 75.0 and 113.5 days, respectively. Endovascular procedures were recorded in 38% and 44%, and surgical reinterventions, in 23% and 25%, respectively. AV access infection was seen in 3 (23%) and 2 (13%) patients, respectively.

Limitations: Small sample size precludes statistical inference.

Conclusions: Almost one-quarter of older adults with incident ESKD and a central venous catheter as primary access were not referred for AV access placement due to medical reasons. Based on these limited results, there is little reason to favor either an AVF or AVG in this population until results from a larger randomized clinical trial become available.

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Visual Abstract included

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Each year, almost 750,000 people in the United States receive life-saving hemodialysis (HD) treatments for end-stage kidney disease (ESKD). Older adults (aged ≥65 years) make up half of this population.[1] In caring for these patients, timely placement of an arteriovenous (AV) vascular access (AV fistula [AVF] or AV graft [AVG]) for HD is desirable to limit the long-term use of tunneled central venous catheters (CVCs). Present clinical practice has followed a categorized order of preference for dialysis vascular access, with first, second, and last choice given to AVF, AVG, and CVC, respectively. Whether such a stereotypical approach to vascular access placement, fortified by current financial reimbursement models, benefits all HD patients is a point of growing contention. Although 7 decades ago, AVF placement suited a large proportion of patients started on HD for treatment of ESKD, the landscape of incident and prevalent patients with advanced kidney disease has vastly changed.[2] Treatment of ESKD with HD is now offered to an aging population with numerous comorbid conditions who may derive little benefit from the intervention of permanent vascular access placement.[3]

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Age is an important biological variable that affects vascular access outcomes. Compared with younger adults, older patients have 50% to 65% higher risk for primary AVF failure.[4] Recent registry-based studies have also indicated that older adults do not accrue the benefits of AVF use (ie, longer patency) and may retain the benefits associated with placement of an AVG (ie, shorter time to maturation).[5-9] In patients who convert from a CVC to an AV-based access, we and others have shown that >60% will revert back to use of a CVC.[10-12]

Studies suggesting equivocal clinical results between AVF and AVG strategies in this population have been complicated because these studies have relied on observational data and retrospective analyses, which have an

PLAIN-LANGUAGE SUMMARY

Randomized clinical trials to compare arteriovenous fistula and arteriovenous graft vascular access strategies in patients receiving hemodialysis are lacking. We performed a pilot clinical trial of fistula-first versus graft-first access placement in older adults with end-stage kidney disease who were started on hemodialysis with a catheter and had no prior access surgeries. Our study identified the presence of a large morbidity and mortality burden that prevented surgical placement of an arteriovenous access. Small sample size and limited follow-up precluded rigorous statistical comparison between the 2 access strategies. The pilot trial helped refine study design (eligibility criteria, primary outcome, population set analysis, and covariate adjustment) and study team organizational structure (strategic and operational components) for successful execution of a future multicenter randomized trial.

inherent risk for harboring residual confounders. To date, no randomized prospective studies comparing clinical outcomes between an approach of AVF-first and AVG-first in older patients have been conducted. High-quality data are critically needed to resolve the emerging notion that placement of an AVG is a better choice than an AVF-first strategy for older HD patients with ESKD and to identify preoperative predictors of successful AV access development to mitigate the burden of unsuccessful vascular surgeries.

Given the paucity of robust data and clinical trials, we conducted a pilot trial to evaluate the feasibility of randomly assigning older adults with ESKD or advanced chronic kidney disease and no prior AV access to a strategy of AVF-first or AVG-first access placement.[12] Feasibility results were reported in a separate report.[13,14] Here, we report the clinical outcome data collected in this pilot trial of older adults in the patient population who had ESKD at the time of enrollment and were randomly assigned to an AVG (intervention group) versus AVF (comparator group) AV vascular access strategy.

METHODS

Trial Design

The trial was a bicenter, prospective, randomized, open-label, pilot feasibility trial that was conducted at 2 hospitals and 16 metropolitan and rural dialysis units affiliated with Wake Forest School of Medicine in North Carolina. The protocol was approved by the Institutional Review Board of Wake Forest School of Medicine (IRB00050577), registered at ClinicalTrials.gov (NCT03545113), and published previously.[12]

Participants

Patients were screened for eligibility at the time of HD initiation and/or at the time of evaluation for AV access placement by vascular surgery after duplex vascular mapping. Patients were included if they were 65 years or older with ESKD receiving long-term HD through a CVC or had advanced chronic kidney disease expected to require HD initiation within 90 days of AV access placement. This report includes only patients who had ESKD at the time of enrollment. Patients also had to have native vasculature suitable for placement of an AVF or AVG assessed using duplex vascular mapping and be medically and surgically eligible to undergo surgery for placement of either an AVF or AVG. Patients with previous surgical interventions for AV access placement, imminent kidney transplantation (expected within 6 months), or anticipated life expectancy less than 9 months were excluded. All participants provided written informed consent.

Surgical AV Access Placement

The participant's vascular suitability and surgical eligibility for AVF or AVG creation was based on the overall assessment of a board-certified vascular surgeon after evaluation of all preoperative findings. All operations were performed in the operating room under regional anesthesia. The surgical configuration of the anastomosis and anatomical location of the access was at the discretion of the surgeon. Participants were seen 7 to 14 days postoperatively and then at 4 to 6 weeks to assess for adequate access maturation and cannulation suitability.

Outcomes

Vascular access outcomes included time to index AV access creation, time to successful AV access cannulation, adjuvant interventions on the AV access, and access-related infections. The incidence rate of primary AV access failure was also evaluated. Time to first AV access cannulation, time to successful AV access cannulation, and duration of follow-up are reported from the date of the index AV access placement. Adjuvant endovascular interventions included percutaneous angiography with angioplasty, thrombectomy, or intra-access stent placement. Surgical reintervention included ligation of collateral vein(s), second-stage procedures in a transposed AVF, revision or arterial angioplasty for steal syndrome, and AVG removal for access infection.

The success or failure of an AV access is contingent on whether it is functional for HD. Vascular access outcomes were defined according to accepted reporting standards.[13,15] Primary failure of an AV access was defined as permanent failure of the fistula or graft before HD suitability and included immediate vascular access failure in an access that had either no appearance or loss of bruit or thrill within 72 hours of creation. It also included early and late dialysis suitability failure. Early and late dialysis suitability failure occurred in an access when despite

interventions (radiologic or surgical), it was not possible to use the access successfully for HD by the third (early) or sixth (late) month following its creation.

We defined successful cannulation when the access became the primary access for HD (the access had been cannulated with two 16- or 15-gauge needles for ≥3 consecutive dialysis sessions and the CVC was removed). Unassisted access maturation was defined as an AV access that was able to be successfully cannulated without a preceding adjuvant intervention. An AV access requiring 1 or more preceding adjuvant interventions before successful cannulation was recorded as assisted access maturation.

Statistical Analyses

This is the first study with this type of complex access intervention and there is no precedent to base power calculations. The primary purpose of this pilot study was to evaluate feasibility rather than detect specific intervention effects. Therefore, the sample size for this study was based on recommendations for pilot and feasibility studies in which samples provide data required for the design of a larger randomized trial with 90% power and 2-sided 5% significance to detect intervention effect for standardized effect sizes that are small (0.2), medium (0.5), or large (0.8), respectively.[16] We targeted enrollment of 50 patients (25 per arm), inclusive of advanced chronic kidney disease and ESKD, during an 18-month enrollment period.

We report data for patients who had ESKD at the time of enrollment. Results are presented using descriptive statistics. Tests for statistical significance were not conducted due to the small sample size. We present baseline characteristics of patients who consented for study participation as excerpted from the medical history and review of electronic medical records. Outcomes are described for those who underwent AV access surgical placement according to the intervention assigned. Kaplan-Meier data were used to show the cumulative incidence of time-to-event outcomes for primary access failure and successful access cannulation in the study groups.

RESULTS

Participants

Between September 1, 2018, and February 29, 2020, a total of 156 patients 65 years and older with ESKD were started on HD through a CVC at one of the participating research sites and were screened for study eligibility (Fig 1). Of these, 34 (22%) had previous AV access surgery. Of the remaining 122 patients with no prior AV access surgery, 18 (15%) relocated care outside the Wake

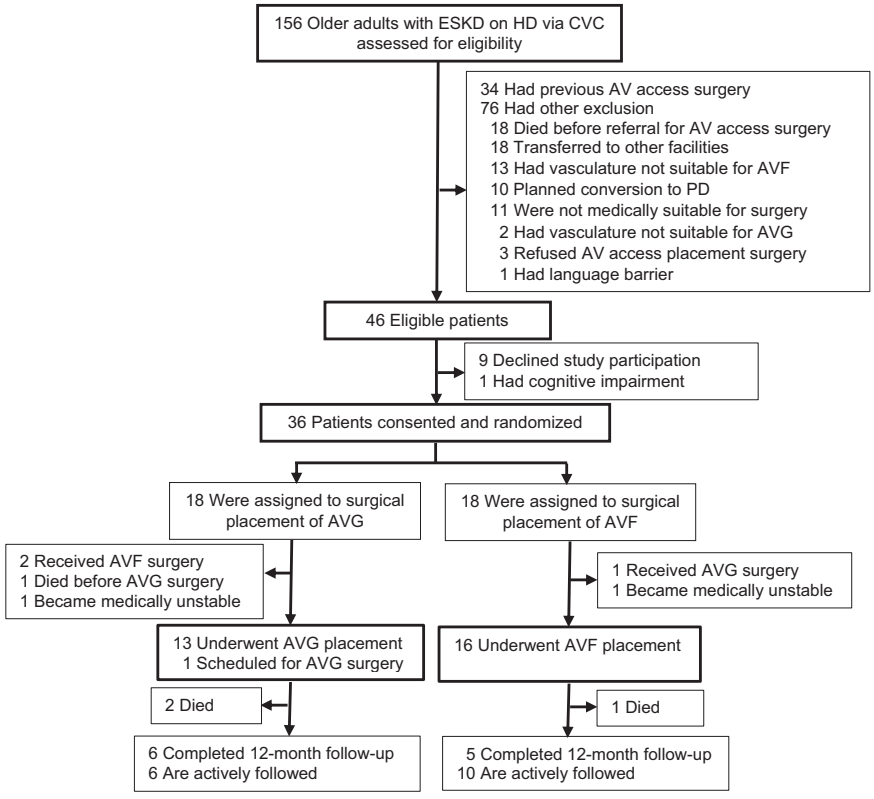

Figure 1. Flow diagram. Screening and randomization between September 1, 2018, and February 29, 2020. Abbreviations: AV, arteriovenous; AVF, arteriovenous fistula; AVG, arteriovenous graft; CVC, central venous catheter; ESKD, end-stage kidney disease; HD, hemodialysis; PD, peritoneal dialysis.

Forest Baptist Health System network, 10 (8%) elected to switch treatment to peritoneal dialysis, 11 (9%) had a short survival expectancy and were not referred for AV access placement, 18 (15%) died before being referred to vascular surgery, and 3 (2%) refused referral to vascular surgery for access placement. Sixty-two (51%) were referred to and evaluated by vascular surgery for AV access placement, of which the upper extremity vasculature was not suitable for placement of either an AVF or AVG in 13 (21%) and 2 (3%) patients, respectively. Forty-six patients (29% of all screened patients) were approached for study participation, of whom 9 (20%) declined to participate and 1 (2%) had cognitive impairment that impeded obtaining research consent. In total, 36 older adults (78% of eligible patients or 23% of all screened patients) with ESKD met all eligibility criteria and were enrolled and randomly assigned to either AVF-first (n = 18) or AVG-first (n = 18) placement.

Baseline characteristics of the patients enrolled are listed in Table 1. Participant age ranged from 65 to 92 years. Eleven percent were living at a skilled nursing facility. The racial distribution and burden of comorbid conditions were similar between the groups with the exception of cerebrovascular disease and dementia, which were more common in patients randomly assigned to AVG placement. Elements of predialysis nephrology care and HD prescription are recorded in Table 1.

Index AV Access Surgery

Three (8%) participants dropped out from the study before surgical intervention due to becoming medically unstable (n = 2) or sudden death (n = 1) before AV access placement. Patients who were enrolled but underwent placement of an AV access that was different from the assigned intervention were withdrawn from the study. This included 3 (8%) participants: 2 in the AVG-first group who received an AVF and 1 in the AVF-first group who received an AVG. The decision to place a vascular access that differed from the assigned intervention was made intraoperatively by the surgeon.

At the time of data lock, 13 (72%) and 16 (89%) participants underwent the assigned access placement of AVG first or AVF first, respectively. One patient in the AVG-first group was scheduled but had not yet had surgery. Median time to index AV access surgical placement across the 29 participants who underwent surgery as assigned, calculated from the date of HD initiation, was 146 (range, 7-403; interquartile range [IQR], 73-230) days. There was a longer time to surgery observed in the AVG group (176.5; IQR, 57-292.5 days) than in the AVF group (118; IQR, 78-183 days).

The AVG group included forearm loop AVGs with brachial artery to cephalic vein (n = 3), basilic vein (n = 1), or median cubital vein (n = 1) configurations. In the upper arm, configurations were brachial artery to brachial vein (n = 3) or axillary vein (n = 3). In the AVF group, surgical anastomotic configurations were as follows: radial artery to cephalic vein (n = 5), ulnar artery to cephalic vein (n = 2), brachial artery to basilic vein (n = 2), brachial artery to cephalic vein (n = 4), or brachial artery to brachial vein (n = 3).

Index AV Access Outcomes

Primary AV Access Failure

Table 2 summarizes vascular access outcomes. At the median follow-up of 321 days, the cumulative primary AV access failure rate was 31% for both groups (4 of 13 in the AVG-first group and 5 of 16 in the AVF-first group). All primary AVG access failure events were early failures, within 3 months of placement. In contrast, the AVF group experienced more late access failures, 120 to 244 days after placement (Fig 2). Four patients with primary AV access failure (2 AVGs and 2 AVFs) underwent percutaneous angioplasty (with or without thrombectomy) before their access was abandoned.

Percutaneous interventions were performed on the index AV access in 41% of cases and surgical reinterventions were performed in 24% of cases. The median time to first percutaneous access intervention and surgical reintervention from the index access placement date was 56.0 (range, 35.0-91.0) days and 41.0 (range, 20.0-99.0) days, respectively. Two patients in the AVF-first group underwent surgical intervention on their index AVF (evacuation of antecubital hematoma and ligation of collateral vein) to assist access development; neither experienced successful cannulation by day 180 after the index surgical date.

At the time of data lock, 4 participants who underwent index AV access placement did not have their access outcomes declared: 1 patient in the AVG-first group and 1 patient in the AVF-first group underwent access placement 12 and 10 days before data lock, respectively; and 2 patients in the AVF-first group did not have an attempt at access cannulation by 132 and 151 days, respectively, after access placement.

AV Access Cannulation

Twenty-one (72%) patients underwent AV access cannulation. The first attempt at access cannulation took place at a median of 51.5 days after the index access placement, with a shorter time to first cannulation seen in those who underwent AVG placement (39.5 days) than those who underwent AVF placement (63.5 days). Sixteen (55%) patients who underwent AV access creation experienced successful access cannulation, encompassing 62% of those who received an AVG and 50% of those who had an AVF placed. Time to successful access cannulation occurred after a median of 95 days from access creation, with a shorter time to successful cannulation seen in those with an AVG (75 days) versus an AVF (113.5 days; Fig 3).

Unassisted and Assisted AV Access Maturation

Of the 16 participants who experienced successful AV access cannulation, unassisted access maturation took place

Table 1. Baseline Characteristics of Patients Who Consented to Study Participation

Characteristic	All (N = 36)	AVG-First (n = 18)	AVF-First (n = 18)
Age, y	76.5 (7.2)	77.5 (7.5)	75.4 (7.1)
Female sex	12 (33%)	8 (44%)	4 (22%)
Race			
Black	9 (25%)	4 (22%)	5 (28%)
White	27 (75%)	14 (78%)	13 (72%)
Marital status			
Single	5 (14%)	4 (22%)	1 (6%)
Married	25 (69%)	10 (56%)	15 (82%)
Widowed	4 (11%)	3 (17%)	1 (6%)
Divorced	2 (6%)	1 (6%)	1 (6%)
Living arrangement			
Alone	2 (6%)	2 (11%)	0 (0%)
With other members (family or friend)	30 (83%)	14 (78%)	16 (89%)
Assisted facility	0 (0.0%)	0 (0.0%)	0 (0%)
Nursing home	4 (11%)	2 (11%)	2 (11%)
Body mass index, kg/m^2	28.9 (6.1)	30.3 (6.6)	27.6 (5.6)
Duration of ESKD, d	45.0 (22.5, 73.3)	46.0 (7.8, 118.8)	44.5 (25.0, 56.0)
HD prescription			
Treatment time, min	201.0 (23.5)	201.8 (21.2)	200.0 (21.2)
Blood flow, mL/min	334.7 (35.5)	336.1 (37.6)	333.3 (34.3)
Dialysate flow, mL/min	570.0 (86.5)	554.5 (82.0)	588.9 (92.8)
Target weight, kg	80.1 (16.8)	83.8 (16.8)	75.6 (16.6)
Single-pool Kt/V_{urea}	1.32 (0.39)	1.3 (0.4)	1.4 (0.4)
Urea reduction ratio, %	67.6 (10.1)	68.0 (10.3)	67.2 (10.3)
Albumin, g/dL	3.4 (0.4)	3.3 (0.4)	3.5 (0.4)
Hemoglobin, g/dL	9.6 (1.3)	9.5 (1.4)	9.6 (1.3)
Ferritin, ng/mL	496.7 (281.8)	449.1 (283.0)	544.3 (316.4)
Transferrin saturation, %	26.2 (9.9)	24.9 (9.9)	27.5 (10.1)
Calcium, mg/dL	8.7 (0.7)	8.7 (0.8)	8.8 (0.6)
Phosphorus, mg/dL	4.6 (1.3)	4.5 (0.8)	4.6 (1.7)
Intact PTH, pg/mL	384.1 (256.7)	362.7 (202.5)	405.5 (309.5)
Coexisting medical conditions			
Diabetes and complications of diabetes	22 (61%)	10 (56%)	12 (67%)
Hypertension	31 (86%)	15 (82%)	16 (89%)
Cardiovascular disease	18 (50%)	10 (56%)	8 (44%)
Congestive heart failure	6 (17%)	2 (11%)	4 (22%)
Peripheral arterial disease	7 (19%)	4 (22%)	3 (17%)
Cerebrovascular disease	13 (36%)	9 (50%)	4 (22%)
History of tumor without metastases	8 (22%)	4 (22%)	4 (22%)
Chronic pulmonary disease	5 (14%)	2 (11%)	3 (17%)
Liver disease	2 (6%)	1 (6%)	1 (6%)
Dementia	2 (6%)	2 (11%)	0 (0%)
Outpatient nephrology care[a]			
First visit before enrollment, y	3.7 (2.0, 5.3)	4.4 (1.8, 7.1)	3.5 (2.0, 4.4)
No. of outpatient visits	8.5 (4.8, 18.8)	9.5 (5.0, 22.0)	8.0 (4.8, 14.3)

Note: Baseline data were collected at the time of patient enrollment. Data are presented as number of participants (percent) for categorical variables and mean (standard deviation) or median (1st, 3rd quartile) for continuous variables.
Abbreviations: AVF, arteriovenous fistula; AVG, arteriovenous graft; ESKD, end-stage kidney disease; HD, hemodialysis; PTH, parathyroid hormone.
[a]Outpatient nephrology care was calculated from the date of first outpatient nephrology office visit to the date of HD initiation. Race or ethnic group was self-reported. Body mass index is weight in kilograms divided by the square of height in meters.

in 6 (46%) AVG patients and 2 (13%) AVF patients. Two patients who underwent brachiobasilic AVF placement underwent second-stage transposition of the basilic vein before successful cannulation. Adjuvant interventions before successful access maturation took place in 3 (19%) patients with an AVF who underwent 5 interventions (1 surgical intervention for ligation of collateral veins and 4 percutaneous interventions for angioplasty with or

Table 2. Vascular Access Outcomes in Patients who Underwent the Assigned Surgery for AV Access Placement

Outcome	All (N = 29)	AVG-First (n = 13)	AVF-First (n = 16)
Primary, early AV access failure[a]	5 (17%)	4 (31%)	1 (6%)
Time to early AV access failure, d	57.0 (22.0-85.0)	47.5 (22.0-79.0)	85.0 (-)
Primary, late AV access failure[b]	4 (14%)	0 (0%)	4 (25%)
Time to late AV access failure, d	128.0 (120.0-244.0)	—	128.0 (120.0-244.0)
First AV access cannulation[c]	21 (72%)	10 (77%)	11 (69%)
Time to first AV access cannulation, d	51.5 (36.0, 66.0)	39.5 (35.0, 55.0)	63.5 (45.8, 75.0)
Successful AV access cannulation	16 (55%)	8 (62%)	8 (50%)
Time to successful AV access cannulation,[c] d	95.0 (66.5, 151.0)	75.0 (53.3, 108.0)	113.5 (89.0, 181.5)
Endovascular interventions on index AV access[d,e]	12 (41%); 16	5 (38%); 7	7 (44%); 9
Surgical re-intervention on index AV access[e,f]	7 (24%); 8	3 (23%); 3	4 (25%); 5
CVC exchange over wire due to malfunction or thrombosis[e]	5 (17%); 6	3 (23%); 4	2 (13%); 2
Follow-up,[g] d	321.0 (181.0, 365.0)	327.0 (202.0, 365.0)	321.0 (168.5, 365.0)

Note: Data are reported as number of patients (percent), median (1st, 3rd quartile), or median (range).
Abbreviations: AV, arteriovenous; AVF, arteriovenous fistula; AVG, arteriovenous graft; CVC, central venous catheter.
[a]Early primary AV access failure was defined as index AV access failure within 3 months of surgical placement and no successful cannulation.
[b]Late primary AV access failure was defined as lack of successful AV access cannulation within 6 months of surgical placement and does not include counts of early primary failure.
[c]Time to first or successful AV access cannulation and duration of follow-up are reported from the date of the index AV access placement.
[d]Adjuvant percutaneous interventions included percutaneous angiography, with or without thrombectomy, angioplasty, or stent placement.
[e]Represents total number of events.
[f]Surgical reintervention included ligation of collateral vein(s), second-stage procedure in transposed brachiobasilic AVF, revision or arterial angioplasty for steal syndrome, and AVG removal for access infection.
[g]Follow-up is calculated from the date of surgical placement of the index AV access.

without thrombolysis) and 1 (8%) patient with an AVG who underwent 2 interventions (percutaneous angioplasty with or without thrombolysis). After successful cannulation, 3 (19%) patients with an AVF and 2 (15%) patients with an AVG underwent percutaneous salvage access procedures to maintain access functionality.

Adverse Events

The adverse events seen among patients who underwent index AV access placement are shown in Table 3. Three deaths were recorded, of which 1 was in the AVF group and 2 were in the AVG group. A total of 44 hospitalizations were observed in 23 (79%) of the 29 participants who

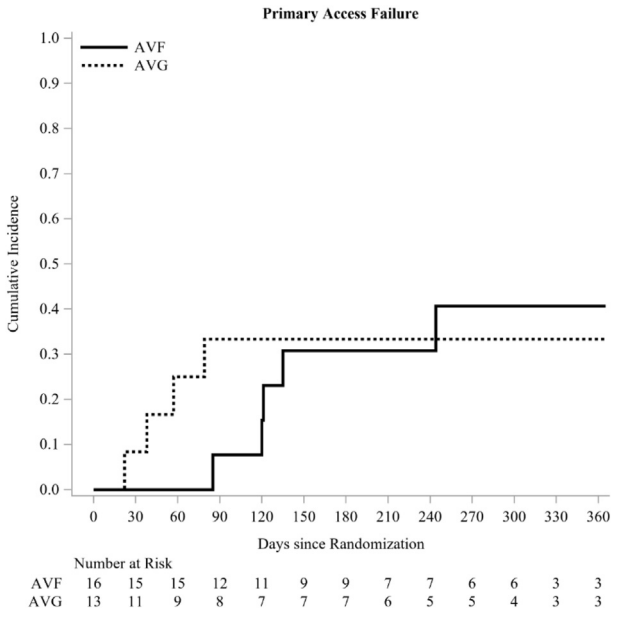

Figure 2. Cumulative incidence of primary access failure. Shown are Kaplan-Meier event curves for the outcome of primary access failure in the arteriovenous fistula (AVF)-first and arteriovenous graft (AVG)-first groups.

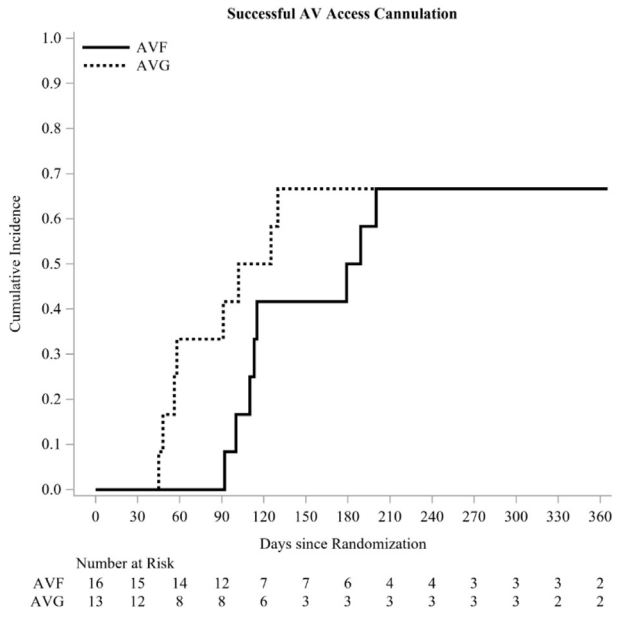

Figure 3. Cumulative incidence of successful access cannulation. Shown are Kaplan-Meier event curves for the outcome of successful access cannulation in the arteriovenous (AV) fistula (AVF)-first and arteriovenous graft (AVG)-first groups.

Table 3. Adverse Events

Outcome	All (N = 29)	AVG-First (n = 13)	AVF-First (n = 16)
Death	3 (10%)	2 (15%)	1 (6%)
Participants hospitalized	23 (79%)	11 (85%)	12 (75%)
All hospitalization events	44	23	21
Cause-specific hospitalization events, of all hospitalization events			
Cardiovascular- and cerebrovascular-related	14 (32%)	8 (35%)	6 (29%)
Infection, not related to CVC or index AV access	7 (16%)	4 (17%)	3 (14%)
Infection, related to index AV access	4 (9%)	2 (9%)	2 (10%)
Infection, related to CVC	5 (11%)	3 (13%)	2 (10%)
Other	14 (32%)	6 (26%)	8 (38%)
Hospitalization length, d	2.0 (1.0, 5.3)	2.5 (1.0, 4.0)	3.0 (2.0, 5.0)
Time to first hospitalization, d	56.0 (23.0, 122.0)	64.54 (20.0, 106.5)	56 (32.0, 128)
CVC exit-site infection	3 (10%)	2 (15%)	1 (6%)
CVC-related bacteremia	6 (21%)	4 (31%)	2 (13%)
Steal syndrome	3 (10%)	2 (15%)	1 (6%)
AV access infection	5 (17%)	3 (23%)	2 (13%)
AV access infiltration	7 (24%)	2 (15%)	5 (31%)
AV access hematoma	3 (10%)	1 (8%)	2 (13%)

Note: Categorical variables are reported as number or number (percent) and continuous variables as median (1st, 3rd quartile). Hospitalizations are reported as total number of events. A similar but separate event on a same participant was recounted and added to the total number of events.
Abbreviations: AV, arteriovenous; AVF, arteriovenous fistula; AVG, arteriovenous graft; CVC, central venous catheter.

received the assigned AV access. Most hospitalizations were related to a cardiovascular, cerebrovascular, or noninfectious event. Bacteremia related to index AV access infection was noted in 2 (15%) patients who underwent AVG placement; these patients had the AVG surgically removed. Cellulitis at the site of the index AV access was recorded in 2 (13%) patients who received an AVF and 3 (23%) patients who underwent AVG placement. Symptoms related to steal syndrome were noted in 2 (15%) patients with an AVG and 1 (6%) patient with an AVF; these patients had mild to moderate manifestations that resolved after arterial angioplasty of the radial artery in 2 patients and subclavian artery in 1 patient. Six events of catheter-related bacteremia were noted, of which 2 events required hospitalization. Numerically, there were more events of catheter-related bacteremia noted among patients who underwent placement of an AVG.

DISCUSSION

In this pilot randomized trial, our primary intent was to determine the feasibility of randomly assigning older patients with ESKD to either AVF or AVG surgical creation as a first permanent vascular access strategy.[14] In this report, clinical outcomes between the AVF and AVG groups are presented. Whereas prior studies have been mainly observational, this trial's primary strength is that it is the first to test the "Fistula First" approach in a randomized fashion. Despite the small number of participants, our results revealed several important findings that can inform future investigations.

First, the enrollment to screening ratio was 0.23. At the end of the enrollment period, 72% of the original recruitment target consisted of patients with ESKD. This provided an opportunity to identify variables that limited the enrollment rate. For a future trial, we propose the inclusion of patients with prevalent ESKD and patients with failed AV access receiving HD through a CVC.

Second, the study intervention rate was 81%. For a larger trial, we propose the primary analysis to be based on the entire cohort of randomly assigned patients according to the intention-to-treat principle, with sensitivity analysis performed on a per-protocol population set.

Third, a mix of AV access subtypes was present in each intervention group. Many eligible patients had suitable vascular anatomy in the forearm for one type of AV access and in the upper arm for the other type of AV access. This indicates that stratified randomization by anatomical location (forearm vs upper arm) is impractical. Statistical analyses in a larger clinical trial will need to adjust for vascular access location and include prespecified subgroup analyses to compare forearm AVFs with forearm loop AVGs and arm AVFs (including brachiobasilic AVFs) with brachioaxillary AVGs.

Fourth, this pilot study revealed a high patient morbidity and mortality rate in the screening and preintervention phase of the study, as discussed next. This underscores the need for setting realistic recruitment targets for each clinical center in a multicenter trial.

Finally, the execution of this pilot study helped improve the organizational structure of the study team in both its strategic and operational components.

In this pilot trial, 24% (29 of 122) of older patients with ESKD who were started on HD with a CVC died (n = 18) or were too sick (n = 11) to be referred for AV access placement. Among patients enrolled in the study, there

was an additional 8% morbidity rate (3 of 36) that prevented AV access surgery due to death or worsening clinical status before the scheduled date of AV access placement. In a retrospective analysis, this high morbidity and mortality that precluded AV access surgery would have been associated with CVC use. Furthermore, the mortality rate of 10% (3 of 29) at a median follow-up of 321.0 days among patients who underwent AV access placement was lower than the previously reported mortality rates of 25% to 60% in the first year of HD in older adults.[17-19] Overall, these results lend significant support to recent studies that have suggested that patient-specific factors, rather than the vascular access itself, explains at least two-thirds of the mortality benefit historically credited to AVFs.[20,21]

Several access-related outcomes deserve further discussion. Primary access failure was similar between the groups. When an access experienced primary failure, this tended to occur earlier in the AVG cohort and later in those who received an AVF. In patients randomly assigned to an AVG, the first successful cannulation occurred earlier when compared with AVFs. Whether earlier successful cannulation in those with an AVG imparts a benefit to older patients with more comorbid illness will need to be examined in future trials. Both AVGs and AVFs required similar endovascular and surgical reintervention to augment maturation. Access-related infection was numerically more common in the AVG group, and 2 patients required surgical AVG removal for infection related to the index procedure.

The major limitation of this pilot study is, by design, a small sample size that limits generalizability and prohibits rigorous between-group difference assessments. For this reason, statistical calculations to determine significance were not computed and the findings must be interpreted with caution. We note that the primary failure rate and time to successful cannulation in the AVG group were higher than expected, whereas the AVF primary failure rate was perhaps lower than expected. Given that these results were derived from a small cohort at a single health system and not inclusive of the overarching picture of access-related outcomes in older adults (ie, proportion of CVC-free days during dialysis life span after access placement), at this stage we do not consider them of significant impact on vascular access decision making.

Moreover, the short follow-up duration in this pilot limited a thorough comparison of adjuvant access procedures. Studies have shown that although AVFs require more interventions in the immediate postoperative period to facilitate maturation, AVGs require more interventions in the later postoperative period to maintain patency.[7,9,22] A short follow-up of less than 1 year may skew results in favor of AVGs by not capturing the entire scale of adjuvant interventions expected to occur later in patients using AVGs. Larger randomized clinical trials spanning more than 1 health system with longer follow-up and all-encompassing access-related and patient outcomes will be necessary to fully analyze clinically significant differences between an AVF and AVG vascular access strategy.

The recently published update of the National Kidney Foundation Dialysis Outcomes Quality Initiative (K-DOQI) clinical practice guidelines for vascular access aims to replace the AVF-centered approach with a more individualized patient-centric paradigm that places the focus on the "right access, in the right patient, at the right time, for the right reasons" as it fits within an ESKD life-plan for each patient.[21] A key present and future challenge will be how to transition to this new case management model in which providers should engage and work together with patients to decide the optimal vascular access. This ongoing discussion will be distinctly relevant as the fabric of the dialysis population continues to evolve, including older patients with a higher burden of comorbid disease. Well-powered multicenter clinical trials are necessary to guide decision makers in this area and elucidate which patient factors will predict outcomes.

ARTICLE INFORMATION

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Data Sharing: Individual participant data that underlie the results reported in this article (text, tables, and figure) will be shared after deidentification, beginning 9 months and ending 36 months following article publication, with investigators whose proposed use of the data has been approved by an independent review

committee. Proposals may be submitted up to 36 months following article publication and should be directed to the corresponding author.

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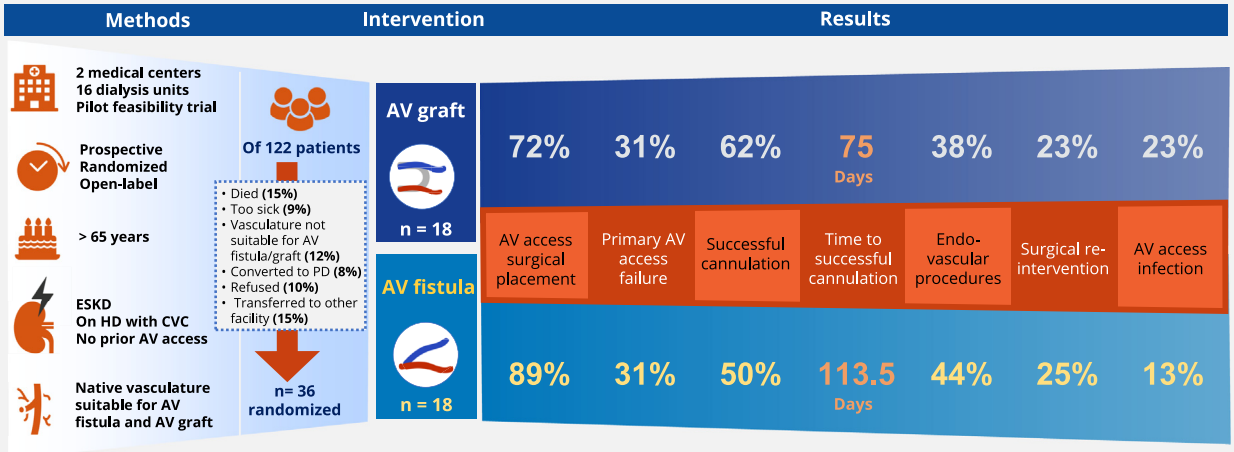
Do AV fistulas have benefits over AV grafts in older adults receiving hemodialysis?

Kidney Medicine



Conclusion: Almost one quarter of older patients with ESKD and no prior AV access, receiving HD with a CVC, were not referred for AV access placement due to medical reasons. Based on these limited results, there is little reason to favor either AV fistula or AV graft in this population until results from a larger RCT become available.

Reference: Robinson T, Geary R, and Murea M et al. Arteriovenous fistula versus graft access strategy in older adults receiving hemodialysis: a pilot randomized trial. *Kidney Medicine*, 2021.

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