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Arteriovenous Fistula Maturation in Prevalent Hemodialysis Patients in the United States: A National Study

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Abstract

Background—Arteriovenous fistulae (AVFs) are the preferred form of hemodialysis vascular access, but maturation failures occur frequently, often resulting in prolonged catheter use. We sought to characterize AVF maturation among a national sample of prevalent hemodialysis patients in the United States.

Study Design—Nonconcurrent observational cohort study.

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Supplementary Material
Supplementary Material Descriptive Text for Online Delivery
Supplementary Figure S1 (PDF). Adjusted probability of first use of AVF placed in 2013 by age, race, sex, dialysis vintage, and vascular access type at incidence.
Supplementary Figure S1 (PDF). Adjusted probability of first use of AVF placed in 2013 by comorbidity at incidence.
Supplementary Item S1 (PDF). Cause-specific HRs of time to first AVF use (with follow-up through the end of 2014).

Setting & Participants—Prevalent hemodialysis patients having had at least one new AVF placed during 2013, as identified via Medicare claims data in the United States Renal Data System (USRDS).

Predictors—Demographics, geographic location, dialysis vintage, comorbidities.

Outcomes—Successful maturation following placement defined by subsequent use identified using monthly CROWNWeb data.

Measurements—Rates of AVF maturation were compared across strata of predictors. Patients were followed until the earliest evidence of death, AVF maturation, or the end of 2014.

Results—In the study period, 45,087 new AVFs were placed in 39,820 prevalent hemodialysis patients. No evidence of use was identified for 36.2% of AVFs. Only 54.7% of AVFs were used within four months of placement, with maturation rates varying considerably across end-stage renal disease (ESRD) networks. Older age was associated with lower AVF maturation rates. Female sex, black race, some comorbidities (cardiovascular disease, peripheral artery disease, diabetes, needing assistance, or institutionalized status), dialysis vintage >1 year, and catheter or arteriovenous graft use at ESRD incidence were also associated with lower rates of successful AVF maturation. In contrast, hypertension and prior AVF placement at ESRD incidence were associated with higher rates of successful AVF maturation.

Limitations—This study relies on administrative data, with monthly recording of access use.

Conclusions—We identified numerous associations between AVF maturation and patient-level factors in a recent national sample of United States hemodialysis patients. After accounting for these patient factors, we observed substantial differences in AVF maturation across some ESRD Networks—indicating a need for additional study of the provider, practice, and regional factors that explain AVF maturation.

Keywords

Arteriovenous anastomosis; Arteriovenous fistula (AVF); AVF maturation; Arteriovenous shunt; Cannulation; Registry; Renal dialysis; Risk factors; US Renal Data System (USRDS); Vascular access; fistula first; end-stage renal disease (ESRD); hemodialysis (HD)

Introduction

Compared to other forms of vascular access, arteriovenous fistulas (AVFs) are viewed as the best vascular access for most long-term hemodialysis patients, displaying better long-term outcomes and lower rates of thrombosis, infection, hospitalization, and mortality.[1–5] Despite many potential advantages of the AVF, the United States (US) has historically relied heavily on arteriovenous grafts (AVGs) and central venous catheters. More recently, US clinical guidelines, such as the National Kidney Foundation - Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) and the Fistula First Breakthrough Initiative (FFBI) have prioritized AVF over AVG, attempting to minimize central venous catheters.[6, 7] In the United States, AVF use among prevalent long-term dialysis patients increased from 32% in 2003 to 65% in 2014.[8] Despite these efforts, 80% of incident dialysis patients initiate with a catheter, with only a quarter of those patients having maturing AVF or AVG in place.

Successful establishment of an optimally functioning AVF is a highly desirable outcome that can directly improve patient outcomes and lower the cost of care. However, despite gradual improvement in historically low rates of AVF placement in the US, suboptimal AVF maturation rates are increasingly problematic.[8,9] Prior work has credited the improvement to the key roles of preoperative planning and surgical techniques,[10–12] as well as the dedication and training of those responsible for both vascular access monitoring[13] and placement.[14] Motivated by this topic's critical importance and paucity of relevant national data, we sought to characterize time-to-first use of AVF after surgical placement as a surrogate of successful 'maturation.' In particular, we explored factors associated with time-to-first successful AVF using newer data from CROWNWeb available from the United States Renal Data System (USRDS). CROWNWeb is a web-based data collection system that was implemented across all Medicare-certified dialysis facilities throughout the US in June 2012, and has replaced the Standard Information Management System (SIMS). CROWNWeb incorporates a number of clinical data elements, including monthly information on dialysis vascular access usage. We previously brought attention to the much longer times to first cannulation of AVF in the US compared to other countries.[15] Now, we hypothesize that, in addition to patient-level factors, regional differences may exist with respect to time to AVF maturation, and that rates of successful AVF maturation might be reflective of national practice variations.

Methods

Study Population and Data Sources

The study population included 39,820 hemodialysis patients with AVF placement in 2013, as identified in Medicare claims. The Centers for Medicare & Medicaid Services (CMS) Medical Evidence Form 2728 was used to ascertain dialysis initiation date and comorbidities at dialysis incidence. All Medicare claims among prevalent hemodialysis patients in 2013 were explored to identify procedure codes for AVF placements. Monthly CROWNWeb data for the study period of January 1, 2013, to December 31, 2014, were analyzed to determine vascular access 'in use.' In order to be included in the analyses, patients were required to have vascular access use data in CROWNWeb following the fistula placement procedure. Patients were excluded if such vascular access use follow-up data were not available at any point during the study period. We did not formally censor the patients at modality switch. However, as the patient is not in CROWNWeb after a modality switch, they would be treated as "lost to follow-up," so should not overly influence the outcome. In the merged CROWNWeb-Medicare dataset, 1.12% of records were missing data on access type. The analyses were limited to vascular accesses placed among prevalent hemodialysis patients, as non-dialysis-dependent patients would not need to have their AVF cannulated, and likely would not have the same clinical urgency for timely AVF use. Medicare claims and CROWNWeb data were linked via a patient identifier, allowing us to determine the first month in which the AVF was being used for HD (defined by successful 2-needle cannulation) subsequent to the AVF placement date, which reflects clinical AVF maturation.

Statistical Analysis

AVF placement was identified through inpatient, outpatient, and physician and supplier Medicare claims using the following International Classification of Diseases 9th Revision

(ICD-9) procedure codes: 36818, 36819, 36820, 36821, and 36825. Subsequent first use of the placed fistula, defined in CROWNWeb as successful access use with both input and output needles, was obtained from CROWNWeb through the end of 2014. As data on direct clinical assessment is not available in the databases, whether, and when, maturation occurred was determined using the date of AVF placement in Medicare claims and the date of first use of the AVF in CROWNWeb. If CROWNWeb data indicated the AVF was used following the placement, without evidence of any intervening new AVF or AVG placements, the fistula was considered to have successfully matured for use.

A patient could contribute more than one record to the analysis if he or she had more than one AVF placed. For each patient-AVF record, follow-up started at placement and finished at the earliest of maturation, death, subsequent AVF placement, or end of the study period (December 31, 2014). The set-up is consistent with the classical competing risks structure;[16] in our case, the competing risks are maturation, death, or subsequent AVF or AVG placements. We analyzed the cause-specific hazard of maturation[16, 17], which amounts to the AVF maturation rate among patients who are alive and have not had a subsequent AVF or AVG placement. Naturally, for a given patient-AVF-placement combination (i.e., for a given record used in our analysis), successful AVF maturation (per our above described definition) can only occur prior to death and prior to subsequent AVF or AVG placement. From this perspective, the cause-specific hazard of maturation, which we refer to as the “maturation rate,” estimates the rate of AVF maturation counting only the follow-up time when maturation could actually occur.

The maturation rate (cause-specific hazard of maturation) was modeled using cause-specific hazards models. The model included the following covariates: age, race, sex, comorbidities at incidence (for results shown in Figure 2 and Table S1), dialysis vintage (time since declaration of ESRD, or time on dialysis) at AVF creation, vascular access type in use at incidence, and ESRD Network region. We used a robust (sandwich estimator) for the variance to take care of the correlation across records with patient. The relationship of each covariate on the outcome was estimated by its cause-specific hazard ratio (HR). For example, the HR for females would represent the maturation rate for females, divided by the maturation rate for males, with the comparison being between a hypothetical female and male, with all other covariates being equal. A HR >1 reflects faster maturation, while HR <1 corresponds to slower maturation rates. Statistical significance was defined as $p < 0.05$.

As a supplementary descriptive analysis, we present cumulative incidence curves for AVF maturation. Within each panel of the supplementary figures, the curves were generated by running separate Fine and Gray models[18], stratified by the panel-specific patient characteristic of interest. Note that this model is the Cox regression analog applicable to the hazard function corresponding to cumulative incidence. In contrast to the afore-described models for the cause-specific maturation hazard, subjects essentially continued follow-up after death or graft placement, to get the risk sets to align with cumulative incidence computation. For the purposes of creating the US map, cause-specific hazard ratios by ESRD Network were calculated using separate Cox regression models with the geographic indicator as the only adjustor.

Statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC). This study was performed under the USRDS Coordinating Center contract with the NIH-NIDDK; research as part of the contract has been approved by the University of Michigan Institutional Review Board (HUM0086162). As data for the USRDS components are collected by federal mandate, there are no individual patient consent requirements.

Results

Among 39,820 prevalent hemodialysis patients, 45,087 AVF placements were identified in Medicare claims and had follow-up data in CROWNWeb (Table 1). A mean of 1.13 (95% CI, 1.128–1.13) AVFs were placed per patient, with 79.5% of patients contributing one AVF, 17.8% contributing two AVFs, and 2.7% contributing three or more AVFs. Diabetic and hypertensive kidney disease were the most commonly assigned primary causes of ESRD in the study population. Cumulative probability of successful AVF first use is shown in Figure 1. No evidence of use during the study period (ending December 31, 2014) was found for 36.2% of the AVF placements, with 12.5% and 4.7% of patients subsequently undergoing another AVF or an AVG placement, respectively, and 16.2% of patients were no longer followed in CROWNWeb due to death prior to access use. Among successfully used AVF, the median time to first reported use in CROWNWeb was 111 days. Of those successfully utilized, 54.7% were accessed within four months, with another 23.1% accessed by six months (Table 2). Of these successfully used AVFs, 83.7% were recorded as in use the month following initial use, with 95.4% having at least two months of consecutive use during the study period.

Older age groups were incrementally associated with longer time to maturation and lower rates of successful AVF use, while patients who were ≤44 years of age had the shortest maturation times and the highest rate of successful AVF use (Figure 2, Figure S1, Table S1). Similarly, males were observed to have earlier and more successful AVF maturation than females. Asians and Native Americans were more likely to experience successful AVF maturation than whites, while blacks had the lowest maturation rates. Dialysis vintage ≥1 year was associated with greater difficulty in successfully establishing an AVF. Greater successful maturation was seen for AVF placements in prevalent dialysis patients who at HD initiation had used an AVF or a catheter but had a maturing AVF in place, compared to AVF placements in prevalent HD patients who initiated HD with a catheter only. AVF maturation was poorest for AVF placements in prevalent patients who had an AVG, either in use or maturing with a catheter in place, at HD initiation. Cardiovascular disease, peripheral arterial disease, diabetes, institutionalization, and poor functional status were associated with a slower rate of AVF maturation, while a diagnosis of hypertension was associated with a somewhat greater maturation rate (Figure 2, Figure S2, Table S1).

AVF maturation rates differed considerably across ESRD Networks in analyses adjusted for patient case-mix differences (Figures 2–3, Table S1). Network 11 (Minnesota, Michigan, North Dakota, South Dakota, and Wisconsin) displayed the highest adjusted AVF maturation rate, followed by Networks 16 (Alaska, Idaho, Montana, Oregon, and Washington) and 18 (Southern California). In contrast, Networks 3 (New Jersey, Puerto Rico, and the Virgin

Islands) and 9 (Indiana, Kentucky, and Ohio) displayed AVF maturation rates that were significantly lower ($p<0.05$) than the national average.

Discussion

AVF use rates among prevalent dialysis patients in the US rose from 32% in 2003 to 65% in 2014.[8] However, these improvements did not occur without substantial effort, as there are a number of barriers to successfully establishing AVF. AVF often require several weeks to mature, and even after that time, can subsequently fail. NKF-KDOQI recommends timely referral to allow time to complete preoperative vein mapping, placement, and maturation.[6] However, patients with shorter duration of nephrology care prior to initiation of dialysis are unlikely to have a usable AVF at initiation for logistic reasons. Hence, 60% of US incident dialysis patients have only a catheter at initiation, while another 20% have a maturing AVF or AVG requiring a catheter at initiation. Furthermore, progression of chronic kidney disease (CKD) to ESRD requiring dialysis can be difficult to predict,[20, 21] thresholds for dialysis initiation vary,[22, 23] and patients may express reluctance toward access placement consistent with clinical expediency.[24] Timely vascular access planning and placement is thus fraught with multiple barriers. Similar issues occur for kidney transplant patients with failing allografts[25, 26], which suggests that many of these problems may stem from more than simply a lack of early nephrology or surgical care. For example, despite high rates of hospitalized central venous catheter-related infections[27, 28] and pre-existing nephrology care for 93.5% of the patients with failing kidney transplants, 65% of such patients returned to dialysis utilizing a catheter. In the case of patients with cystic kidney disease, who often experience earlier referral for nephrology care and may be less likely to have utilized arm veins for other medical care, a greater proportion—43.6%—were observed to have started hemodialysis with an AVF, with 52.5% utilizing a catheter at initiation.[8]

In our study, a number of comorbidities were associated with prolonged time to, or failure of, AVF usage and maturation. We found that older age, need for assistance, and institutionalization were associated with prolonged AVF maturation and higher failure. Interestingly, using Medicare billing data from patients ≥66 years of age, Woo *et al.* found that, even though mortality was somewhat lower in patients using an AVF compared to AVG (28.2% versus 29.9%, $p = 0.03$), the one-year repeat fistula, graft, or catheter-free survival was lower after AVF creation than AVG creation; 44.4% of AVF patients required a subsequent access, while only 33.7% of AVG patients did ($p < 0.001$).[29]

The Dialysis Outcomes and Practice Patterns Study (DOPPS) has demonstrated that both older age[4] and lower functional status[30] are also associated with early mortality following hemodialysis initiation. Furthermore, elderly nursing home residents are observed to experience a sustained decline in functional status after initiation of dialysis, [31] further compounding maturation difficulty. As there is high mortality during the first few months of hemodialysis,[8] and older patients on hemodialysis tend to be more frail,[30] a focus on this group in future investigations is warranted. It has been proposed that elderly patients may benefit from more liberal use of AVG placement, as AVGs are associated with earlier catheter removal and fewer catheter days in the first year following dialysis initiation.[33] However, it is possible that there is additional unaccounted for time following AVG failure,

as AVGs have historically had shorter functional life expectancies than AVFs.[34–37] However, there have been recent improvements in secondary patency for AVGs, which suggests that interventional techniques may improve their viability as an access option[38]. However, given that “steal syndrome”---more common with AVGs[39, 40]---can result in significant morbidity and loss of quality of life, it remains unclear whether such a policy approach is reasonable. A patient-centered approach to preoperative planning and intraoperative plan modifications that take into account the likelihood of AVF success may have improved utility and outcomes.[41–43]

Consistent with previous studies,[8, 25, 34, 42, 44, 45] we found that for females, blacks, and those with peripheral arterial disease, there was more difficulty successfully establishing AVF. Interestingly, hypertension was associated with higher rates of successful AVF maturation. While our study focused on prevalent patients, Zarkowsky *et al.,* similarly found that female gender, black race, or presence of peripheral arterial disease decreased the likelihood of initiating hemodialysis with an AVF. In their study, they also observed that hypertension is associated with greater likelihood of achieving a successful AVF at dialysis start.[45] In that study, as well as in ours, diabetes was associated with lower AVF maturation. However, the prospective Hemodialysis Fistula Maturation Study recently reported lower frequency of early thrombosis among diabetic patients, suggesting that screening and preoperative planning may allow for improved outcomes among diabetics. The regional variation with respect to time to AVF maturation may reflect known geographic variation in timing of provider visits and first cannulation attempts.[46, 47] However, the geographic heterogeneity with respect to AVF maturation requires further investigation, and may reveal unrecognized practice variations.

Dialysis vintage >1 year was associated with a lower rate of AVF maturation, as was dialysis access initiation with an AVG. Prevalent HD patients with an AVF at initiation were more likely to develop a future AVF, compared to those with a catheter at initiation, consistent with prior observations.[19] As the percentage of prevalent patients with AVFs continues to rise, coupled with a fall in AVG use,[8] it is likely that improvements in maintaining the AVFs have been successfully developed. However, given the more recent guidelines for universal preoperative vein mapping for operative planning,[6] it is not surprising that those with previous AVFs may have usable veins, while those who previously required an AVG may have had poorer vasculature near the time of HD initiation, with a lower likelihood of later AVF development if subsequently attempted.

We found that only 17.1% of patients with successful AVFs were cannulated by two months, with 54.7% by four months (Table 2). The 2015 USRDS Annual Data Report (ADR) reported a median of 112 days (IQR 74 to 171 days) between AVF placement and first use.[8] In contrast, in a 2004 DOPPS report, Saran *et al.* found that 36% of AVFs in the US were cannulated by two months, which contrasted with 79% in Europe, and 98% in Japan.[15] Since that time, there has been increasing AVF in the US.[8] It is possible that more tenuous fistulae require even more time to mature, but these differences may also reflect provider practice differences with respect to first cannulation. There are also significant differences between blood flow rates in the US and Japan (400 versus 200 mL/min), which might explain the lower threshold for AVF failure in the US. Furthermore, there are meaningful

differences in the comorbidities of the dialysis population, access to predialysis CKD care, and in the organization of ESRD care among these countries.[2, 15, 46, 48, 49] These data suggest that there is more to early cannulation than merely early needle placement. Additional attention to training for both the nephrologist and surgeon are likely beneficial.[13, 14, 50] Dialysis access coordinators can improve access to care.[7, 34, 51] Vascular access placement reimbursement is significantly lower than other vascular operations,[52] which likely result in lower priority for scarce operating time. Expanded pre-dialysis CKD and early ESRD care, with expanded patient educational efforts addressing vascular access prior to the surgical evaluation, may also be of benefit[7, 47, 53, 54], particularly as patients may be resistant to access placement,[24, 55] resulting in patient-related factors delaying work-up, surgical evaluation, and scheduling.

This study has limitations. The USRDS ESRD database relies on administrative data submitted by dialysis providers. As such, it is dependent upon the accuracy and completeness of data submitted by the dialysis community. Furthermore, CROWNWeb accuracy for specific months post-initiation has not been determined. However, at least for incident patients, vascular access data from the CMS Medical Evidence Form 2728 and CROWNWeb frequently agree, with a kappa statistic of 0.88 for the first month of dialysis,[56] suggesting that vascular access data reporting is reasonably accurate. With regard to Medicare billing data, CPT coding errors are not uncommon in other procedural specialties.[57] As there are a number of CPT codes for dialysis access, there is certainly the possibility of systemic miscoding. Furthermore, CPT codes for AVF placement are not very specific, particularly in regards to anatomic location. For example, for two stage basilic vein transpositions or cephalic vein AVFs that are deep enough to require superficialization or transposition, the CPT code for the second stage falls under the general AVF revision code. In those particular instances they should not have been coded as a new AVF, although such an undetected errors may have been made in some instances. CROWNWeb is limited to ESRD patients on dialysis, with mandatory participation by Medicare-certified dialysis centers but with select participation by other ESRD-care providers.[54] The ideal AVF placement should occur prior to dialysis initiation;[6, 7] AVFs placed prior to initiation of dialysis are not directly addressed by this study and merit further investigation. In addition, CROWNWeb records access use at monthly intervals, introducing potential bias towards a median of ~15 days longer for maturation by this approach or for inaccurate reporting for those with partial month usage before failure. While it is unlikely that the distribution of monthly temporal differences among patients would have a significant bias, it is not inconceivable. We utilized a modified, ‘functional’ definition of AVF maturation (i.e., time to first use of AVF, as indicated in CROWNWeb), rather than a clinical or radiological determination of true AVF maturity, as the USRDS lacks this type of data pertaining to AVFs. This can be obtained in the setting of a prospective observational study such as the Hemodialysis Fistula Maturation Study. This surrogate definition for AVF maturation necessarily biases the study toward longer time to maturation. Finally, the reason for delay of cannulation cannot be ascertained from the database. For example, if a patient refused cannulation, if the AVF was deep due to high BMI, or the dialysis unit technician was not experienced and had difficulty with cannulation, these would appear as any noncannulated AVF.

We have characterized AVF maturation in a recent national US sample and identified important associations with multiple patient-level factors utilizing the newly added CROWNWeb component of the USRDS database. Longer AVF maturation times are associated with a number of risk factors such as age, race, comorbidities including cardiovascular or peripheral arterial disease, need for assistance, dialysis vintage, and previous access history. After accounting for these patient factors, substantial differences in AVF maturation were seen across some ESRD Networks. Research is urgently required into the importance of patient, provider, region, and practice factors that could improve AVF placement rates and successful maturation, decrease central venous catheter use, and improve patient outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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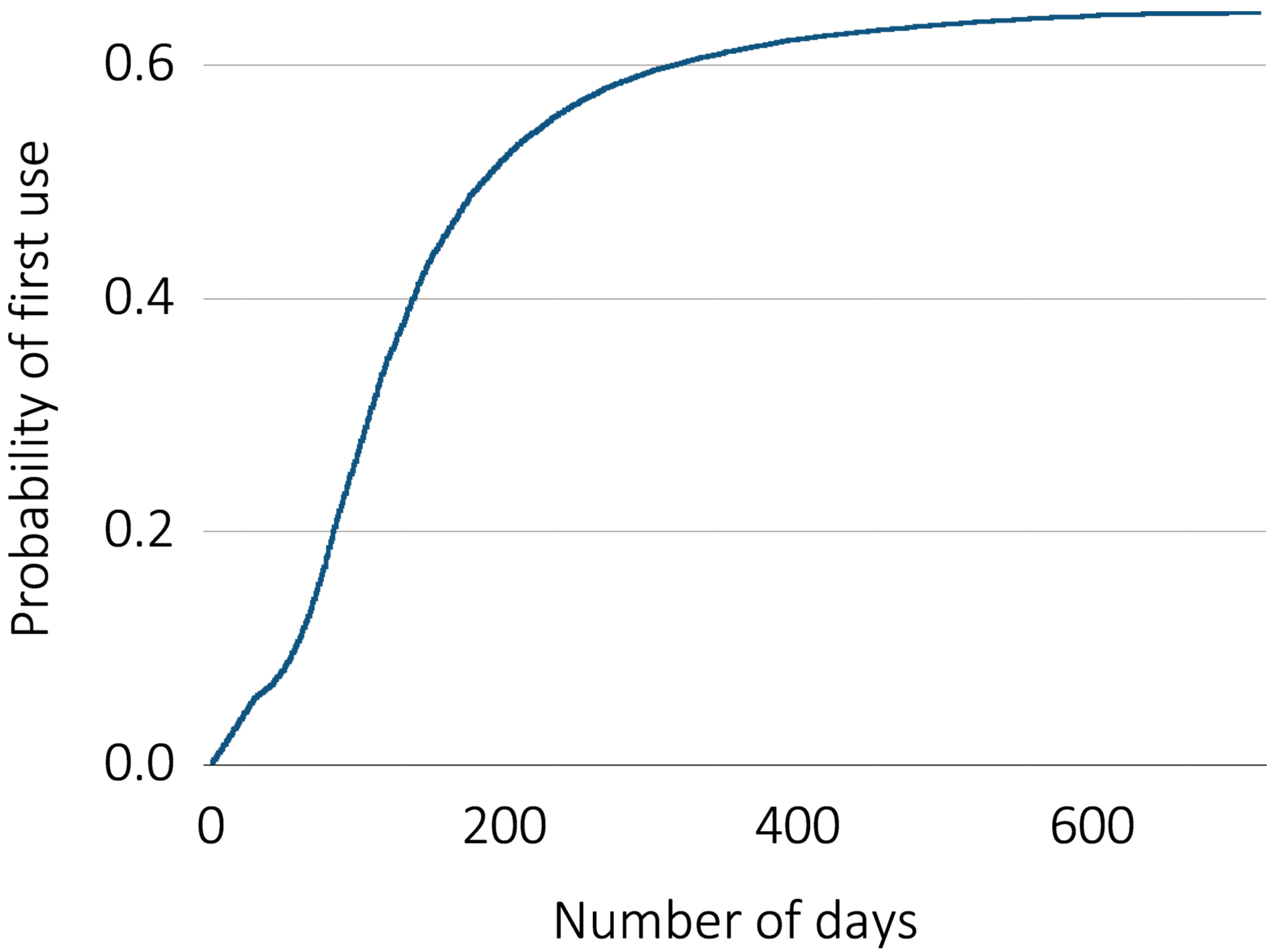

Figure 1.
Cumulative probability of first-use of AVFs placed among prevalent hemodialysis patients in the United States in 2013.

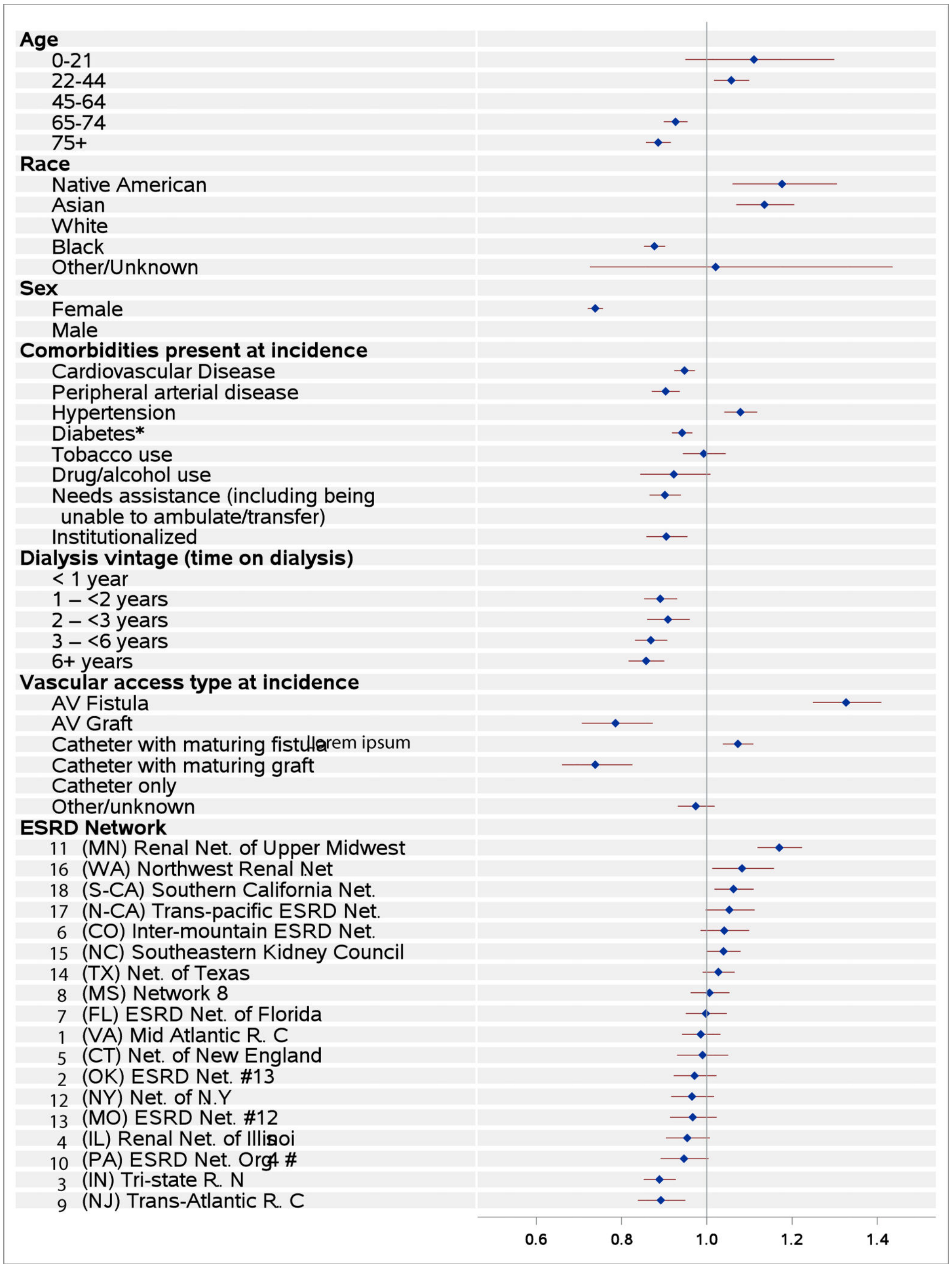

Figure 2.
Forest plot of cause-specific hazard ratios of time to first AVF use.

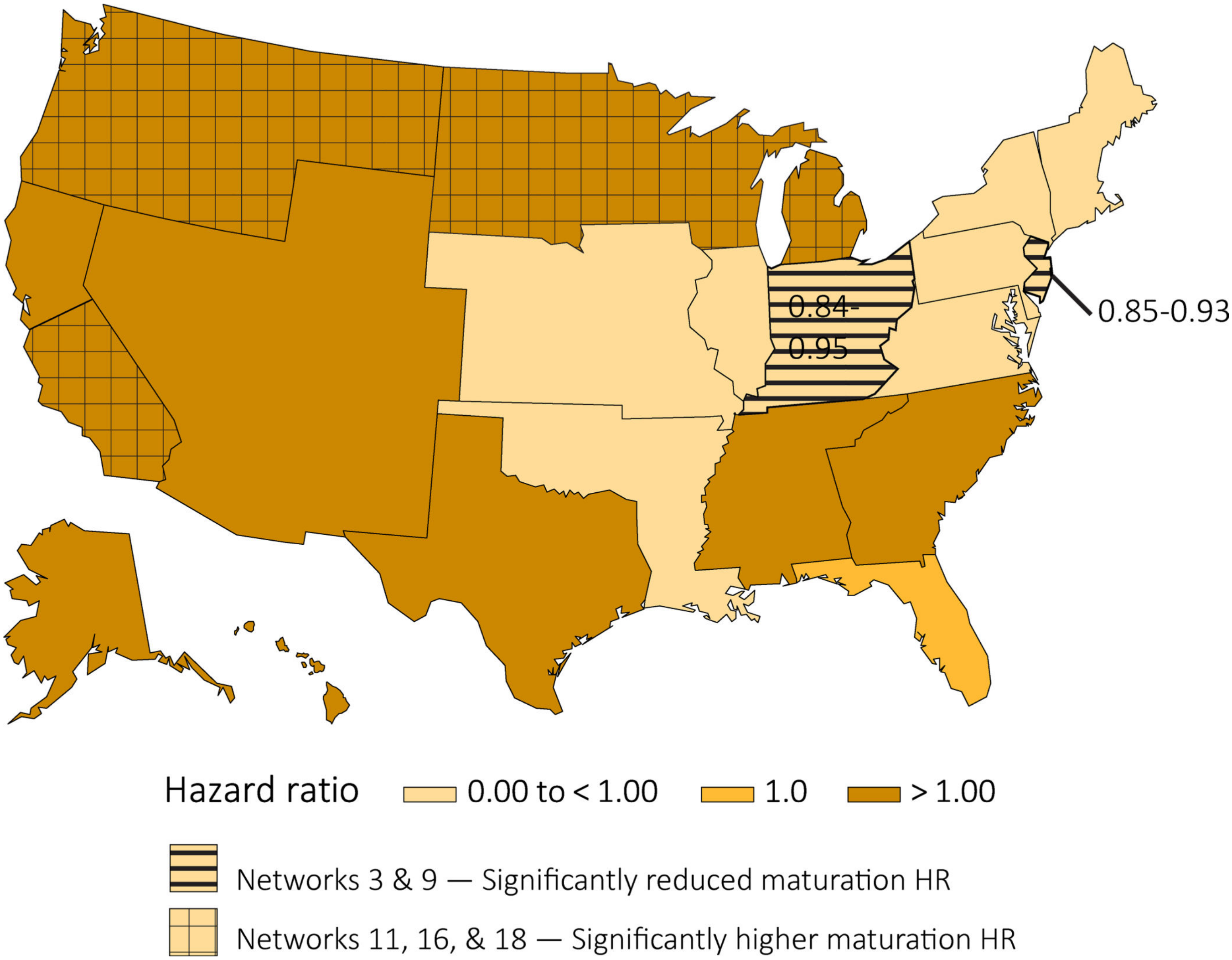

Figure 3.

Cause-specific hazard ratios for AVF maturation from univariate Cox regression model with ESRD Networks.

Table 1.

Patient characteristics

	Value	
No. of AVF placements per patient	1.13 **	
Age category *		
0–21 y	210 (0.5%)	
22–44	4,832	12.1%
45–64	15,325	38.5%
65–74	10,596	26.6%
75+	8,857	22.2%
Race		
Native American	421	1.1%
Asian	1,637	4.1%
Black	12,546	31.5%
White	25,172	63.2%
Other/Unknown	44	0.1%
Sex		
Male	22,703	57.0%
Female	17,117	43.0%
Primary Cause of ESRD		
Diabetes	18,617	46.8%
Hypertension	11,999	30.1%
Glomerulonephritis	3,552	8.9%
Cystic kidney	645	1.6%
Other urologic	584	1.5%
Other cause	3,256	8.2%
Unknown cause	1,167	2.9%
ESRD Network		
1	1,238	3.1%
2	1,838	4.6%
3	1,460	3.7%
4	1,436	3.6%
5	2,468	6.2%
6	4,105	10.3%
7	2,352	5.9%
8	2,557	6.4%
9	3,052	7.7%
10	1,650	4.1%
11	2,653	6.7%

	Value	
12	1,614	4.1%
13	1,971	4.9%
14	4,015	10.1%
15	1,616	4.1%
16	1,150	2.9%
17	1,824	4.6%
18	2,821	7.1%

N = 39,820. Except as indicated, values given as count (percentage).

*Age as of January 1, 2013

**mean

AVF, arteriovenous fistula; ESRD, end-stage renal disease

Table 2.

Time from AVF placement by Medicare claims, to first reported use of AVF in CROWNWeb data

Time Between AVF Placement and First Reported Use	Count (Column Percentage)	
0 - <2 months	4,903 (17.1%)	
2 - <4 months	10,799	37.6
4 - <6 months	6,630	23.1
6 - <8 months	2,984	10.4
8 - <10 months	1,524	5.3
10+ months	1,901	6.6

AVF, arteriovenous fisula