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# Mortality benefits of different hemodialysis access types are age dependent

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***Objective:*** **Risk of death in dialysis patients is lowest with arteriovenous fistulas (AVFs), followed by arteriovenous grafts (AVGs) and then intravenous hemodialysis catheters (HCs). Our aim was to analyze the effects of age at hemodialysis initiation on mortality across different access types.**

***Methods:*** **All patients ≥18 years in the United States Renal Data System between the years 2006 and 2010 were analyzed. Spline modeling and risk-adjusted Cox proportional hazard models were used to analyze the effect of age on mortality for first dialysis access with AVF vs AVG vs HC.**

***Results:*** **The study analyzed 507,791 patients (63.4 ± 0.02 years; 56.5% male; 40.9% mortality; follow-up, 1.57 ± 1.36 years). Increasing age was a significant predictor of overall mortality (adjusted hazard ratio [aHR], 1.03; $P < .001$). Compared with patients with HCs (n = 418,932), overall risk-adjusted mortality was lowest in patients with AVFs (n = 71,316; aHR, 0.63; $P < .001$) followed by AVGs (n = 17,543; aHR, 0.83; $P < .001$). AVF was superior to both HC and AVG for all age groups ($P < .001$). However, there was a significant change in the relative efficacy of AVG at ages 48 years and 89 years based on spline modeling; there were no significant differences comparing adjusted mortality with AVG vs HC for patients aged 18 to 48 years or for patients >89 years, but AVG was superior to HC for patients 49 to 89 years of age (aHR, 0.811; $P < .001$). The mortality benefit of AVF was consistently superior to that of AVG and HC for patients of all ages (all, $P < .001$).**

***Conclusions:*** **AVF is superior to AVG and HC regardless of the patient's age, including in octogenarians. In contrast, the mortality benefit of AVG over HC may not apply to younger (18-48 years) or older (>89 years) age groups. All patients 18 to 48 years should receive AVF for dialysis access whenever possible. (J Vasc Surg 2015;61:449-56.)**

A number of prior studies have evaluated the benefits of initiating dialysis with an arteriovenous fistula (AVF) vs arteriovenous graft (AVG) or intravenous hemodialysis catheter (HC), demonstrating overwhelming favor of AVF.[1-8] As a result, the National Vascular Access Improvement Initiative, later renamed the Fistula First Breakthrough Initiative, was started in 2003 in an attempt to increase AVF use and to reduce HC use for dialysis access.[9] Consistent with this initiative, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative published guidelines in 2006 endorsing the creation of an AVF as the initial form of dialysis access.[10] When patients are deemed unsuitable for AVF placement, AVG placement is recommended.[11] Despite these initiatives, incident AVF prevalence in the United States remains less than 20%[12] and has shown minimal improvement in recent years (Malas et al, in press).

One potential reason that may be contributing to the low incident AVF rates is the perception that permanent dialysis access is not necessary within certain patient populations. For example, the Kidney Disease Outcomes Quality Initiative calls for permanent dialysis only among pediatric patients who are expected to require dialysis for longer than 1 year, with the thought that many young patients are listed for prompt renal transplantation and therefore can be bridged appropriately with an HC.[13] Similarly, AVFs are often avoided in older populations, with the thought that elderly patients have a higher risk of death before starting dialysis and on dialysis initiation, making the benefits of AVF over AVG or HC less clear.[14,15]

Although a handful of studies have investigated the mortality rates with different forms of dialysis access within specific young[16-20] and elderly populations,[4,21-24] there are minimal data evaluating variations in mortality across a wide range of ages. Our aim was to analyze the effects of age and initial dialysis access type on mortality.

## METHODS

This study was a retrospective review of data from the prospectively maintained United States Renal Data System

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(USRDS) database. The USRDS maintains a prospective database, tracking each end-stage renal disease (ESRD) patient receiving renal replacement therapy within the United States. Annual reports published since 1988 appear at usrds.org and provide information on epidemiology, hospitalization, mortality, and cost, among other parameters.[25] The USRDS maintains a robust database on every ESRD patient by integrating patient-specific data from the Centers for Medicare and Medicaid Services (CMS), Centers for Disease Control and Prevention, United Network for Organ Sharing, and ESRD networks. The Johns Hopkins Hospital Institutional Review Board and the USRDS approved this study before its initiation. Data from the USRDS are in the public domain, and thus informed consent was not required for this study.

All patients in the USRDS database aged $\geq 18$ years who initiated dialysis between 2006 and 2010 were included. Patients missing data pertaining to age or initial dialysis access type, as well as those who stated dialysis before 2006 or received a kidney transplant during the course of the study period (as determined by records from the United Network for Organ Sharing), were excluded. In addition, we excluded all patients who died within 90 days of initiating dialysis because it takes up to 90 days for patients to obtain complete Medicare coverage, resulting in a high likelihood that dialysis access type and mortality were skewed in this population. Data on patient characteristics, including baseline demographics, comorbidities, etiology of ESRD, access to nephrologist care, and initial dialysis access type, were collected from CMS Form 2728, End Stage Renal Disease Medical Evidence Report. Data on patient mortality were collected from CMS Form 2746, ESRD Death Notification Form.

**Statistical methods.** The aim of this study was to compare the association between age and initial dialysis access type with all-cause mortality. As such, all patients were classified into one of three study groups for analysis: AVF, AVG, and intravenous HC. Patients with HC and a maturing AVF or AVG at the time of dialysis initiation remained classified as HC on the basis of our prior work that demonstrated a significant mortality benefit with initial AVF or AVG over HC with maturing AVF or AVG (Malas et al, in press) and in accordance with prior work investigating mortality outcomes based on initial dialysis access used.[21] All patients were classified by an intention-to-treat approach, meaning that they were classified as AVF vs AVG vs HC by the type of dialysis access with which they initiated dialysis; changes in access type during the course of the study period were not accounted for.

Descriptive (mean ± standard error of the mean or count with percentage) and univariable (analysis of variance and Pearson $\chi^2$ tests) statistics were used to evaluate baseline characteristics and to compare overall mortality between study groups. The overall effect of age on mortality was assessed by univariable and multivariable Cox proportional hazard models. The covariates included in the adjusted models were predictive of mortality in the USRDS population on the basis of univariable analyses and likelihood ratio tests and included dialysis access type, gender, body mass index (BMI), insurance status before ESRD coverage, comorbidities (congestive heart failure, atherosclerotic heart disease, cerebrovascular disease, peripheral vascular disease, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, cancer), smoking history, alcohol and drug dependence, ability to ambulate, etiology of ESRD, and access to nephrologist care.

**Table I.** Distribution of dialysis access method by age category

| | *AVF (n = 71,316), No. (%)* | *AVG (n = 17,543), No. (%)* | *HC (n = 418,932), No. (%)* |
|---|---|---|---|
| Age category | | | |
| 18-34 years | 2070 (2.90) | 446 (2.54) | 20,723 (4.95) |
| 35-44 years | 4577 (6.42) | 929 (5.30) | 31,262 (7.46) |
| 45-54 years | 10,567 (14.8) | 2259 (12.9) | 62,789 (15.0) |
| 55-64 years | 17,175 (24.1) | 4073 (23.2) | 94,705 (22.6) |
| 65-74 years | 18,528 (26.0) | 4668 (26.6) | 97,559 (23.3) |
| 75-84 years | 14,962 (21.0) | 4137 (23.6) | 85,784 (20.5) |
| >84 years | 3437 (4.82) | 1031 (5.88) | 26,110 (6.23) |

*AVF,* Arteriovenous fistula; *AVG,* arteriovenous graft; *HC,* hemodialysis catheter.

To more fully explore the effects of age and dialysis access type on mortality, we used risk-adjusted Cox proportional hazard models to test the risk of mortality for AVF and AVG vs HC for incrementally increasing age groups as categorized by 10- and then 5-year increments. On the basis of an apparent interaction between age and mortality among younger and older patients, we then performed spline modeling to estimate the age at which the relative mortality benefits of different forms of dialysis access changed. The spline technique applies a piece-wise approach to the evaluation of points (knots) at which significant changes occur in the trend of the age-mortality function.[26] Differences in mortality at certain age cutoffs as identified by the spline model were explored with multivariable analyses of the slopes of the spline graph for each treatment before and after each designated age cutoff. Multivariable Cox proportional hazard models using moving averages $\pm 2$ years were then employed to estimate the precise age at which there was an inflection point in the mortality benefit of a specific treatment and to describe the adjusted hazard ratios (aHRs) for mortality for AVF and AVG vs HC over each age range. For all analyses, HC served as the reference group.

All data analyses were performed with Stata 12.1 statistical software (StataCorp, College Station, Tex), with a level of $P < .05$ denoting statistical significance.

## RESULTS

**Patient characteristics.** During the 5-year study period, 553,064 patients initiated dialysis in the USRDS database. Of these, 45,273 (8.19%; AVF, 2262; AVG, 874; HC, 41,773) died within 90 days and were excluded, leaving a total of 507,791 patients for analysis (mean age,