Moving Points in Nephrology

Vascular Access Morbidity and Mortality: Trends of the Last Decade

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Summary

During the past decade, clear trends in the types of incident and prevalent hemodialysis vascular access can be observed. There has been a steady increase and recent stabilizaton of patients initiating hemodialysis with a central venous catheter, representing approximately 80% of all incident accesses. There has also been a steady increase in prevalent fistula use, currently greater than 50% within 4 months of hemodialysis initiation. Patient and vascular access related morbidity and mortality are reflected in the type of vascular access used at initiation and for long-term maintenance dialysis. There is a three- to fourfold increase in risk of infectious complications in patients initiating dialysis with a catheter compared with either a fistula or graft and a sevenfold higher risk when the catheter is used as a prevalent access. Procedure rates have increased two- to threefold for all types of access. There is a significant increased risk of mortality associated with catheter use, especially within the first year of dialysis initiation.

Clin J Am Soc Nephrol 8: 1213–1219, 2013. doi: 10.2215/CJN.01690213

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Introduction

More than 1 million North American patients initiated dialysis over the past decade. This significant achievement is possible with what the nephrology community considers routine processes. Yet we should not take for granted the need for a reliable vascular access, upon which long-term hemodialysis (HD) depends. Although this article reviews the trends in morbidity and mortality associated with HD vascular access over the past decade, it is worthwhile to begin by discussing early experiences of our pioneers that may shed light on modern-day vascular access challenges.

In 1948, Dr. Nils Alwall had the original idea to maintain arteriovenous (AV) access patency using a glass cannula, but he abandoned the idea because of complications of local infection and clotting (1). In 1960, Dr. Belding Scribner and Wayne Quinton (an engineer) described the original all-Teflon (polytetrafluoroethylene, or PTFE) Quinton Scribner AV shunt (2), which had an average life span of 2 months, similar to the glass cannulae that Dr. Alwall had described. Two years later, a simple modification of the Quinton Scribner shunt—which involved joining flexible silicon rubber tubing between the cannulated vessels with Teflon, the "silastic-Teflon shunt"—extended access lifespan to months and sometimes even years, similar to the present-day central venous catheter. However, it is the multidisciplinary efforts of Drs. Cimino, Brescia, and Appel (3) in 1962 that has stood the test of time. Their creation, the AV fistula, remains today's preferred HD vascular access because of the great longevity and low complication rate achievable once an AV fistula is successfully established and used for dialysis.

In 2010, the United States ESRD program treated 593,086 people, with 383,992 undergoing HD (64.7% of all patients with ESRD or 92.8% of all dialysis patients). The overall incident rate of ESRD was 348 per million population (105,923 HD patients), and the prevalent rate was 1752 per million population (383,992 HD patients). Although the annual incidence (absolute numbers of patients) has remained relatively stable (average annual increase ± SD, 2.3%±1.4%), the prevalence in 2010 was a 49% increase from 2000 (4). These seemingly simple data on incident and prevalent trends provide a window on performance of more complex CKD and ESRD management and assist with future resource allocation. The data are possible with the U.S. Renal Data System (USRDS). The USRDS, funded by the National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, is the national data registry that collects, analyzes, and distributes information on the ESRD population in the United States, including treatments and outcomes. All patients with ESRD, regardless of insurance coverage and age, are included in the USRDS database. However, claims analyses, such as hospitalizations, costs, and clinical services, are restricted to Medicare patients. Thus, the USRDS is a rich data repository for evaluation of and research on vascular access quality.

This review will summarize and explore the past decade's trends in USRDS data with regard to vascular access–related morbidity and mortality, implications for patient care and health care costs, and potential future directions. For consistency in interpretation of trends data, all data were derived from USRDS using their analytic methods, terminology, and definitions, unless otherwise specified (5).

Incidence and Prevalence

In 2010, 114,083 patients initiated dialysis and 105,923 of those were undergoing HD (91%) (6). HD continues to be the most common dialysis modality worldwide, with 70%–80% of patients initiating dialysis with HD (7). In some countries, peritoneal dialysis is the dominant modality; for example, 76% of dialysis patients in Hong Kong and more than 50% in Mexico use peritoneal dialysis (7). Compared with other countries, the United States has the highest incident rate of dialysis at 369 per million population, followed by Taiwan and Japan at 361 and 288 per million, respectively. The United States incident HD rate has increased 24.4% over a decade.

The Kidney Disease Outcomes Quality Initiative target for incident vascular access is to initiate 50% of patients with an AV fistula (8). Yet vascular access use at dialysis initiation as determined by the Medical Evidence form on day 1 of Medicare eligibility shows that approximately 80% of 2010 incident HD patients initiated dialysis with central venous catheter access, 16.3% started with an AV fistula, and 3.2% initiated with an AV graft. Trends from USRDS are depicted in Figure 1. The distribution of vascular access use at dialysis initiation has remained unchanged over the past half decade.

Many reasons for the high catheter use rates at HD initiation have been suggested, including both nonmodifiable and modifiable factors. Such factors include inherent patient characteristics and CKD practice processes. For example, in terms of modern-day characteristics, the incident dialysis patient has an average age of 62.8 years, is probably white (66%), and often has diabetes mellitus as the primary cause of ESRD (45%). It can be argued that, to a great extent, a patient's clinical characteristics, clinical and social situation, and financial circumstances dictate both the dialysis modality and the type of HD vascular access used. Data from USRDS suggest that these factors do indeed contribute. Between 2000 and 2010, the average age of a patient initiating dialysis and the proportion of patients with diabetes were remarkably consistent: 62.8 years and 44.8%, respectively, in 2010 compared with 62.6 years and 44.1% in 2000 (7,9). This is in contrast to the dialysis population encountered by our dialysis forefathers, where the majority of patients had renal limited disease, with no diabetes (a prior exclusion criterion for dialysis), and were substantially younger (by approximately 20 years) (3).

Studies have demonstrated several clinical factors contributing to AV fistula success or failure, with older age, diabetes, and their associated complications (*e.g.*, cardiac and peripheral vascular disease) as strong predictors of failure (10–12). In the first described AV fistulas, the failure rate was 12.5% (3), but it is as high as 40% today (13,14), probably reflecting the effect of an older dialysis population with greater comorbidity. Indeed, the Fistula First initiative was developed primarily from available data attained before 2000. It was during the time period between 1982 and 2000 when the steepest increase in the population older than 65 years occurred; the numbers in that age group have stabilized over the past decade (Figure 2). Concurrently, the number of black/African American patients older than 60 years has increased. Some studies showed nonwhite ethnicity to be a risk factor for AV fistula failure (10,15) (Figure 3). The consequences of attempting to create AV fistulas in more patients who may not fit the optimal eligibility characteristics noted in the first reports might be reflected in the high numbers of patients initiating HD with a central venous catheter, despite having been seen by a nephrologist beforehand.

In terms of process issues that contribute to increased catheter use at dialysis initiation, delayed referral by nonnephrologists to nephrologists (and access surgery) with the consequence of inadequate predialysis preparation time is a logical and commonly cited reason (16–18). Yet this provides only a partial explanation. Even among HD patients seen by a nephrologist for more than a year before starting dialysis, 41.8% initiated dialysis with a catheter (6). However, it is also these patients with >1 year nephrology care who have the greatest likelihood of having an AV fistula or at least have a maturing AV fistula present at HD initiation, at 26.3% and 17.1%, respectively. Forty-three percent of patients starting ESRD therapy in 2010 had not seen a

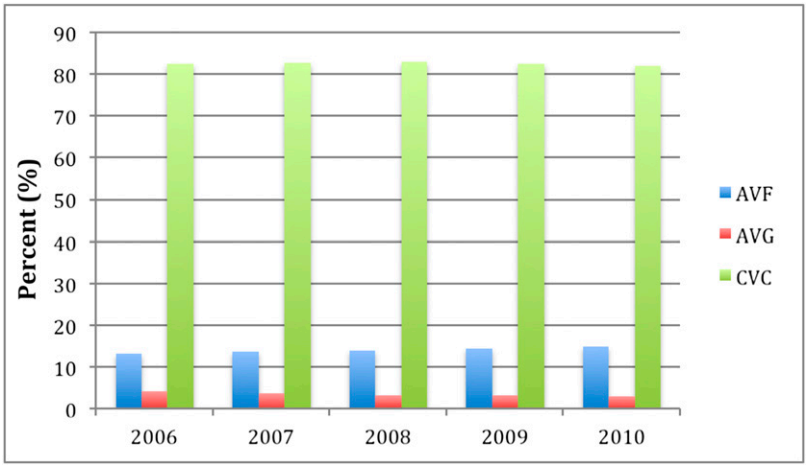

Figure 1. | Trends in vascular access type at hemodialysis initiation according to the U.S. Renal Data System. AVF, arteriovenous fistula; AVG, arteriovenous graft; CVC, central venous catheter.

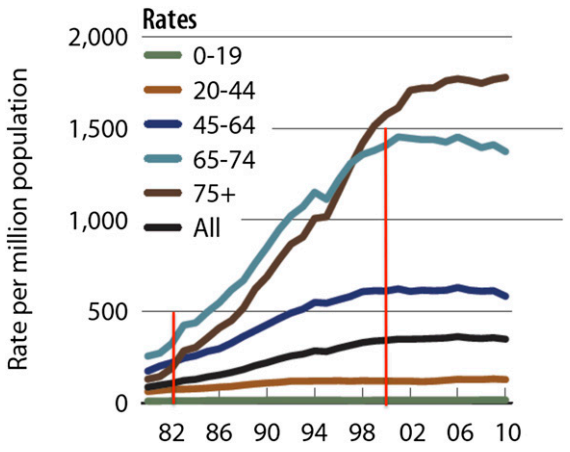

Figure 2. | Greatest growth in incident patients older than age 65 years between red bars (1982–2000). Adapted with permission from *USRDS 2012 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health*, Chapter 2, Figure 1.4.

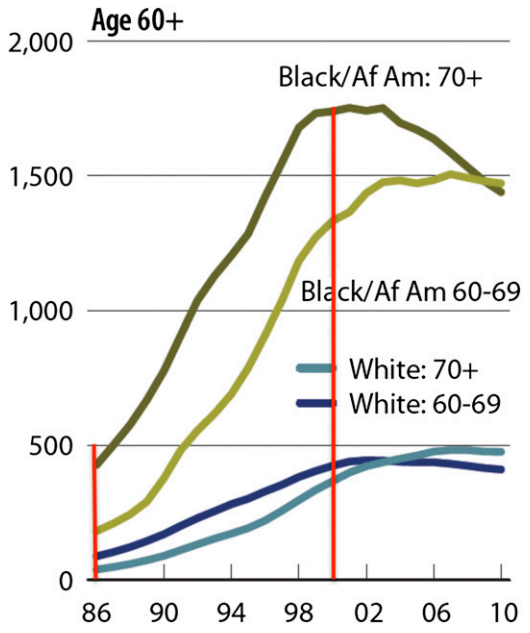

Figure 3. | Concurrent increase in African American (Af Am)/black hemodialysis population older than age 60 years between red bars (1986–2000). Adapted with permission from *USRDS 2012 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health*, Chapter 2, Figure 1.4.

nephrologist before initiation. Not surprisingly, of these patients, 89% initiated HD with a catheter, only 3% had a mature AV fistula, and 13% had a maturing internal access (4). It is impossible to accurately know how many patients with established progressive CKD have not been appropriately assessed and managed by a nephrologist, although prospective CKD cohort studies are ongoing (19,20).

Yet many factors are beyond the nephrologists' control. For example, nephrologists consult in-hospital on patients with AKI who are deemed to need a "temporary" catheter for temporary dialysis; however, many such patients never recover kidney function and require permanent dialysis. Thus, the "temporary" catheter becomes the permanent catheter—indeed, it is the vascular access the patient has now become accustomed to as she or he transitions from inpatient to outpatient dialysis services. The current reimbursement system does not allow simultaneous payment for an AV fistula or AV graft placement during the same hospitalization, serving as a disincentive for our surgical colleagues to create the necessary surgical permanent access with which to initiate long-term dialysis (21).

Nephrologists are all too familiar with the "urgent start" patient: a patient who has established, stable CKD with the same GFR for months to years who then unexpectedly sustains an acute event that destabilizes and escalates their "nonprogressive" renal function to an urgent need for dialysis—with a catheter. Often that patient's nephrologist may not even be involved in the patient's dialysis initiation, depending on the circumstances of the acute kidney-damaging medical, surgical, or traumatic event.

Finally, there are patients who truly have unknown CKD or were never referred appropriately and require acute dialysis initiation. Because these patients are usually first diagnosed during a crisis situation in an emergency department, the proper course of action is to insert a central venous catheter to provide the necessary dialysis. Currently, no long-term administrative data distinguish patients with known versus unknown CKD or planned versus "urgent" dialysis starts in order to determine trends in renal replacement modality initiation or care, vascular access, or dialysis outcomes.

International comparisons of the prevalence of ESRD in 2010 demonstrate that rates in the United States, Taiwan, and Japan were 1870, 2584, and 2260 per million, respectively (7). The United States prevalent rate has increased 20.4% over a half decade (prevalent rate of ESRD in 2004 was 1553 per million [7]). The current Fistula First target is to have 66% of prevalent patients undergoing HD with an AV fistula (8). Trends in prevalent AV fistula use have progressively improved over the past decade, while it appears that catheters are replacing AV grafts. Although data on vascular access initiation indicates an area of much-needed improvement, by month 4 (day 91) of dialysis initiation, claims data show rates of AV fistula, catheter, and AV graft use to be 52.6% 16.7%, and 5.9%, respectively.

Further, patterns of prevalent vascular access use are associated with several patient characteristics, such as age, sex, and ethnicity. The greatest relative increase in prevalent catheters from 1999 to 2007 was seen in patients age 45–64 years (48%). The greatest relative increase in AV fistulas (151% increase) and reduction in AV grafts (56% reduction) occurred in patients older than age 65 years. Women had a 45% relative increase in catheter use compared with 21% in men but also a 167% increase in AV fistulas compared with 68% in men. African Americans and Native Americans have the greatest increase in prevalent catheter use: 44% and 59%, respectively. Native Americans had the lowest increase in prevalent AV fistulas, although AV fistula prevalence increased in all ethnic populations. AV graft use also decreased in all ethnic groups, with the greatest relative drop observed in white race/ethnicity of 60%, compared with a 45% reduction seen in African Americans.

Complications

All types of vascular access have the potential for complications. Complications can range from events that are inconvenient to patients, such as prolonged dialysis duration due to the need for a thrombolytic installation for a malfunctioning catheter, an extra trip outside their daily routine to undergo access angioplasty, or loss of their access that necessitates replacement by another. All complications are costly, regardless of whether they are associated with hospitalization or not. Over the past decade, clear trends according to vascular access type can be demonstrated by USRDS data.

The most frequent serious vascular access complications are infection and sepsis. Vascular access–related infection and sepsis remain a major cause of morbidity and mortality in dialysis patients (22). Rates of hospitalization for infection (adjusted for age, sex, race, and primary diagnosis) in the HD population have increased 43% since 1993, and the use of dialysis catheters continues to have the largest associated risk (23). Compared with 2000, hospitalizations for infections were 19.5% higher in 2005 and 14.2% higher in 2010. Admissions for vascular access infection rose steadily from 1993 until 2005, but since have fallen 24%, to 103 per 1000 patient-years in 2010. Admissions for bacteremia and sepsis remain highest for HD patients, at 116 per 1000 patient years in 2010 (23). This represents a 12.6% increase since 2005 and a 45% increase since 2000. Regardless of access type, sepsis is more common than infection. For example, in 2007, the rate of sepsis in patients with a catheter was 1.6 times higher than the rate of infection (6). It is likely that more "minor" types of vascular access–related infections (without requiring hospitalizations or invasive intervention), such as exit-site infections, are not consistently captured, leading to an underreporting of the true vascular access–related infection rate (6). Clearly, sepsis is clinically more life-threatening than infection is; vascular access–related infections can include (but are not restricted to) catheter exit-site infections, AV fistula buttonhole infections, or AV graft infections, all of which can progress to full-blown sepsis. Indeed, recent analysis of USRDS data demonstrate that mortality within 3 months of initiating dialysis attributed to septicemia was 4.3 times greater in patients who initiated dialysis with a catheter compared with an AV fistula.

As of 2010, dialysis providers are required to report the type of vascular access used for dialysis on a monthly basis and to report whether a vascular access infection occurred. A recent analysis by USRDS evaluated 11,290 incident and 177,875 prevalent HD patients to determine vascular access type and their associated infections (24). Patients who had an incident catheter were 3.8 times more likely to have a catheter-associated infection than those with an AV fistula (1.6%) or AV graft (1.6%). Although the proportion of prevalent patients analyzed who used a catheter only was just 10%, these patients had a seven-fold higher likelihood of having an access-related infection compared with prevalent patients who had an AV fistula (0.9%) or AV graft (0.9%). A more recent analysis of USRDS data (n=118,517) found that hospitalization due to septicemia within 3 and 12 months of initiating dialysis was 3.2 and 2.5 times higher, respectively, for catheters compared with fistulas.

Rehospitalization within 30 days of a hospital discharge has not changed over the last decade (36.3% in 2010 in prevalent HD patients). Rehospitalizations occurred in 34% and 31% of original hospitalizations for overall infection and vascular access infections, respectively. Rehospitalization for overall infection and vascular access infection, respectively, followed 13% and 6% of discharges from index hospitalizations of the same category, compared with 8% and <2% of discharges from all-cause index hospitalizations. The new "bundled" payment system, begun in January 2011, may be an additional incentive to reduce infections and related hospitalizations to further reduce the total hospital days per year for each patient and dialysis facility.

Another too common but important complication that has been analyzed in conjunction with hospitalization is vascular access interventions (replacements/removals, revisions, angioplasties, declotting procedures). Overall, the patient counts for the combination of needing a vascular access intervention and hospitalization has increased over the past decade for catheters and AV fistulas and declined for AV grafts (Table 1). The proportion of patients with catheters requiring interventions reduced from 14.4% (2000) to 11.9% (2008), suggesting an increase in catheter-related hospitalizations, probably due to bacteremia and sepsis. The proportion of patients requiring interventions has remained stable with AV fistulas (0.3% in 2000 and 0.4% in 2008) and reduced with AV grafts (1.5% in 2000 and 1.1% in 2008). Of those prevalent patients requiring interventions, the greatest increase trend is replacement with another access, typically replacement with a catheter rather than an internal access (Figure 4). More catheters are being replaced (25.1% in 2000 and 30.0% in 2008) compared with AV fistulas (1.1% in 2000 and 0.4% in 2008) or AV grafts (1.6% in 2000 and 0.9% in 2008). However, overall the trend over time is in the right direction, with more catheters being replaced by AV fistulas or AV grafts and fewer AV fistulas and AV grafts replaced by catheters.

Specific vascular access interventions worthy of note include angioplasty and declotting procedures. The rate of angioplasty for AV fistulas has nearly tripled over the decade and doubled for AV grafts; conversely, the rate of declotting has doubled for AV fistulas and tripled for grafts (6). The timing of these procedures in relation to when an access is created, cannulated, or lost is unknown in USRDS analysis and an area of future investigation.

The Timing of Access Placement

In contrast to the uncertainty of timing of angioplasty and declotting, USRDS data can inform on the relationships between the placement of various vascular access types, dialysis vintage, and corresponding anticipated clinical events, particularly as a patient survives longer on dialysis. For example, it is not surprising that more catheters and AV

Table 1. Number of patients for vascular access interventions and hospitalizations

Variable	2000	2008
Central venous catheter	610	776
Arteriovenous fistula	1555	2451
Arteriovenous graft	2254	1256

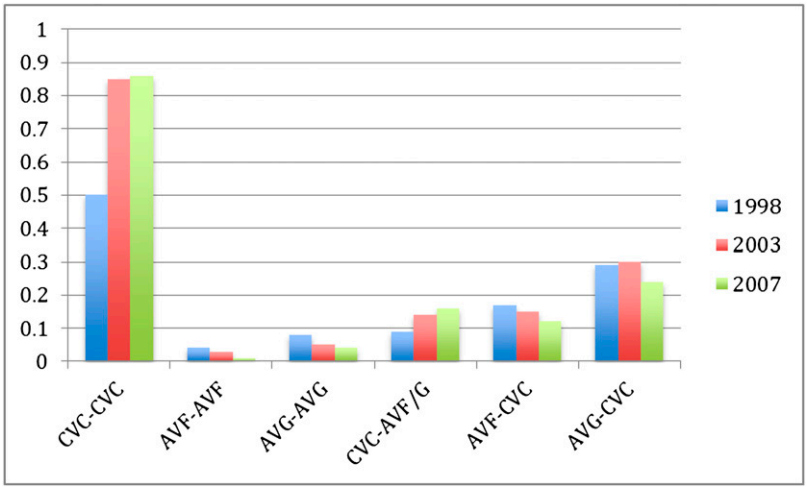

Figure 4. | Trends in vascular access replacements. AVF, arteriovenous fistula; AVG, arteriovenous graft; CVC, central venous catheter.

fistulas will be placed within the first 6 months of dialysis initiation. As AV fistulas mature, catheters will be removed and fewer AV fistulas will be placed because of their longevity once successfully used for dialysis. If the AV fistula does not mature within the first 6 months, AV grafts may increase in an attempt to reduce catheter use. Indeed, the USRDS 2012 Annual Data Report (which reflects data collected in 2010) demonstrates that of the accesses placed within the first 6 months, 53% are catheters, 35% are AV fistulas, and 11% are AV grafts. Between 6 and 12 months, of the accesses that are placed, 58% are catheters, followed by 16% AV grafts. Catheters continue to predominate as the main access type placed at 68% after a patient has been undergoing dialysis for >5 years compared with 16% each for AV fistulas and AV grafts. Of note, the catheter placement rate dramatically drops from 828/1000 patient-years in the first 6 months to 271/1000 patient-years in years 2–5. The rate of AV grafts decreases from 177/1000 patient-years in the first 6 months to 60/1000 patient-years between years 2 and 5, then increases again to 71/1000 patient-years. This pattern may reflect the desire to avoid catheter use, but over time while receiving dialysis, the patient may lose the vasculature required for AV fistula creation and the relative rate of AV graft creation slightly increases.

Implications

Although clinical associations of vascular access trends are noted above, USRDS trend data also suggest resource implications. For example, in the United States, the new dialysis bundle payment by the Centers for Medicare & Medicaid Services provides a fixed reimbursement per patient per dialysis treatment (25); however, commonly used medications, such as tissue plasminogen activator to resolve catheter malfunction, are not separately reimbursed. This might motivate dialysis care providers to reduce catheter use and appropriately select patients for an AV fistula or AV graft, depending on their likelihood of successful AV fistula creation, maturation, and use. Since 2010, of the approximate 80% of patients who initiated dialysis with a catheter, 50% who had a maturing AV fistula or AV graft at initiation will transition to use that access approximately 4 months after HD initiation. In contrast, almost double the time (7 months) is required for 50% of patients who initiated dialysis without a maturing surgically created access to transition to an internal access (26). Thus, the problem remains that 50% in each of these groups continue to undergo dialysis with a catheter after these specified time points.

The costs of catheter maintenance (*e.g.*, use of tissue plasminogen activator), complications, and catheter exchanges during this time, or any time, are unknown but not trivial. For example, recent USRDS data of patients older than age 67 years indicate that 7% of patients with a catheter are hospitalized for septicemia within 3 months. If 2010 data are examined (6), 86,856 patients initiated dialysis with a catheter (82% of 105,923), with an estimated 6080 patients hospitalized for septicemia. A conservative cost estimate is $24,000 for managing an episode of catheter-related septicemia (22), resulting in $145,920,000 USD spent within the first 3 months of dialysis initiation to manage a single catheter-related complication. The risks associated with catheters remain as long as they are in place, although the degree of risk might change over time, depending on the complication.

It is unknown whether the subset of catheter patients who take longer to transition to an internal access differs from those who quickly and successfully transition in terms of infections, procedural complications, hospitalizations, and costs. What is clear, however, is the high cost of catheter use to both the patient's health outcomes and health care resources, and the need to urgently reduce catheter use.

Subsequent Access

Previously, data raised appropriate concerns regarding AV graft use, such as the risk of infection, need for greater intervention, and reduced cumulative survival compared with AV fistulas. These concerns should be re-examined in light of new data that emphasize the significant morbidity and mortality associated with catheter use and more recent data on AV fistula and AV graft outcomes (13,27–30), particularly for patients at risk of long-term catheter exposure.

Recent evidence has demonstrated a significantly increased hazard of death (hazard ratio > 2.0) if a patient converts from an AV fistula or an AV graft to a catheter (31). The most appropriate subsequent vascular access requires multidisciplinary patient-focused attention (32), particularly given that the patient's clinical characteristics and circumstances would have been known to HD care providers at the time of the first failing access, be it an AV fistula, AV graft, or catheter.

Mortality

Mortality in the dialysis population remains 10 times greater than among Medicare patients of similar age without kidney disease; however, mortality has declined by 19% in the prevalent ESRD population since 2000. Yet only 51% of dialysis patients are still alive 3 years after the start of dialysis. Compared with persons in the general population age 65 and older who have diabetes, cancer, congestive heart failure, cerebrovascular disease (stroke or transient ischemic attack), or myocardial infarction, a dialysis patient of the same age has twice the mortality (33). Most of the mortality occurs in the first year of HD. Death due to cardiovascular disease and infection peak in the second month after HD initiation; For example, in 2009, all-cause mortality (adjusted for age, sex, race, Hispanic ethnicity, and primary diagnosis) was 435/1000 patient-years at 2 months, then fell to 206/1000 patient-years by the end of the first year. The rates of cardiovascular and infection-related death were at 169/1000 patient-years and 43/1000 patient-years at month 2. Both cardiovascular and infection-related deaths have been associated with catheter use (22,34–36). There is consistent evidence that mortality is reduced when dialysis patients convert their catheters to an AV fistula or an AV graft within the first year of dialysis (31,37). In 2010, of 509,947 patients studied *via* USRDS, the 3-month mortality significantly differed according to vascular access type at dialysis initiation: 9.7% (catheters), 4.8% (AV grafts), and 3.1% (AV fistulas). Of even greater concern, 26% of patients who initiated dialysis with a catheter died within 12 months, compared with 11% and 16% in patients who initiated dialysis with an AV fistula and AV graft, respectively. A sustained effort for reduced catheter use may result in continued and sustained improvement in survival after the first year of dialysis.

Challenges and Future Direction

Attaining the right vascular access in the right patient at the right time in the right circumstances is challenging. Such "right" alignments depend on specific patient, facility, administrative, and resources factors. Administrative USRDS data can provide important supporting information on broad population-based trends; however, many confounders cannot be accounted for in analysis, and changes in trends, such as reducing the percentage of patients initiating HD with a catheter, can be made only at the patient level with patient-level information. USRDS cannot inform on some critical variables that may affect change, such as patient preferences, expected patient survival (38,39), or changes in clinical practice (*e.g.*, the emergence of vascular access centers and the growing field of interventional nephrology). Such changes in practice may affect both the quality and cost of care and are an area of ongoing research. Indeed, both the indirect and direct costs of complications and care associated with vascular access require focused attention given the rising costs of health care. This is particularly relevant to the first year of dialysis, when hospitalization and mortality rates are high.

Until recently, USRDS data on initial vascular access were limited to the first outpatient dialysis using the Centers for Medicare & Medicaid Services 2728 form. A recent validation exercise using an incident cohort of all HD patients in 2010 older than age 67 years who received Medicare coverage before admission and at least one dialysis claim (n=9812) was very good but found over-reporting of AV fistulas at HD initiation by approximately 11%–12%, when, in fact, the patient started dialysis with a catheter (26). Such validation exercises help determine where possible gaps in knowledge, process, and data documentation exist and improvements can be made. For example, the over-reporting of initial AV fistulas may reduce because facilities are now required to report vascular access type and the presence of a vascular access–related infection on a monthly basis. Collecting longitudinal vascular access data will allow more granular analysis that will provide better information on trends in vascular access types and their effect on patient morbidity, mortality, and cost of care.

Disclosures

Dr. Lok has no disclosures to report related to the manuscript content. The following disclosures are unrelated to the manuscript content: Research funding: Astellas; honoraria and consultancy agreements: Roche, Gore, Terumo, Atrium. Dr. Foley has no disclosures to report.

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Published online ahead of print. Publication date available at www.cjasn.org.