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Catheter-Related Mortality among ESRD Patients

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Abstract

Hemodialysis access-related complications remain one of the most important sources of morbidity and cost among persons with end-stage renal disease, with total annual costs exceeding $1 billion annually. In this context, the creation and maintenance of an effective hemodialysis vascular access is essential for safe and adequate hemodialysis therapy. Multiple reports have documented the type of vascular access used for dialysis and associated risk of infection and mortality. Undoubtedly, the central venous catheter (CVC) is associated with the greatest risk of infection-related and all-cause mortality compared with the autogenous arteriovenous fistula (AVF) or synthetic graft (AVG). The AVF has the lowest risk of infection, longer patency rates, greater quality of life, and lower all-cause mortality compared with the AVG or CVC. It is for these reasons that the National Kidney Foundation's Kidney Disease Outcome Quality Initiative Clinical Practice Guidelines for Vascular Access recommend the early placement and use of the AVF among at least 50% of incident hemodialysis patients. This report presents catheter-related mortality and calls for heightened awareness of catheter-related complications.

Creation and maintenance of an effective hemodialysis vascular access is essential for safe and adequate hemodialysis therapy. Unfortunately, access-related complications remain one of themost important sources of morbidity and cost among persons with end-stage renal disease (ESRD), with total annual costs exceeding $1 billion annually (1–3). The type of hemodialysis vascular access used at dialysis initiation is associated with subsequent risk of infection and mortality. The central venous catheter (CVC) is associated with the greatest risk of infection-related and all-cause mortality compared with the autogenous arteriovenous fistula (AVF) or synthetic graft (AVG) (4–7).

In an effort to curtail CVC use and increase AVF use, the National Kidney Foundation's Kidney Disease Outcome Quality Initiative (NKF K/DOQI) Clinical Practice Guidelines for Vascular Access recommend the early placement and use of the AVF among at least 50% of incident hemodialysis patients (8). The AVF has longer patency, fewer infectious complications, greater quality of life, and is associated with lower all-cause mortality compared with the AVG or CVC (4–7,9–11). However, despite these recommendations, approximately 15% of incident patients in the United States initiate dialysis with an AVF, while >60% do so using a catheter (12,13).

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Risk Factors for CVC Use

CVC use at dialysis initiation among incident ESRD patients ranges from 56.8% to 71% in the United States (5,7,13,14). Patients using a CVC at the start of dialysis tend to be female, are less likely to be obese or receive pre-ESRD erythropoietin, and are more likely to have ischemic heart disease, hypoalbuminemia and anemia prior to ESRD than those starting dialysis with a permanent form of vascular access (AVF or AVG) (5,13,14). In addition, patients with fewer than three nephrology visits prior to maintenance hemodialysis are 40% more likely to start dialysis with a catheter (15).

A majority (59.4%) of individuals in a national, random sample of incident patients initiating dialysis with a CVC remain CVC dependent 90 days after starting dialysis. Among those who transition to a permanent vascular access, the majority receive an AVG (25.4%), while only 15.2% have a functioning AVF. Patient characteristics independently associated with protracted CVC use include older age, black race, female gender, ischemic heart disease, and peripheral vascular disease (14).

It is unclear why high rates of CVC use persist among hemodialysis patients in the United States in view of the clear disadvantages and evidence-based practice guidelines to the contrary. However, high rates of CVC use may occur for several reasons, including limited access to medical care for many patients in need of chronic hemodialysis, limited patient education regarding optimal access type, failure of an AVF to mature, inadequate surgical training of local surgeons in AVF construction, and delayed referral to a nephrologist.

While several reports have linked delayed nephrology referral to lower AVF use, it is interesting to note that a single-center study found that even when patients were referred for vascular access creation as early as 1 year prior to dialysis initiation, a majority of patients (65%) did not start dialysis with a permanent vascular access (15–17). This largely occurred because of repeatedly missed access-related appointments, despite adequate provision of patient transportation. Only the presence of diabetes was predictive of permanent access rather than CVC use at dialysis initiation, possibly due to greater nephrology referral by endocrinologists (17). This suggests a role for early predialysis vascular access education among chronic kidney disease patients.

Complications of CVC Use

While CVCs have the advantage of immediate use for dialysis after placement, they are associated with a host of complications. Compared with patients who receive an AVF, patients with a CVC may experience poorer clearance of blood toxins secondary to unreliable blood flow, central vein scarring with subsequent vein occlusion, and antibiotic resistance (18–23). Patients with a CVC may have higher rates of anemia, and require greater doses of intravenous iron and recombinant human erythropoietin compared with patients with AVFs or grafts (21,23). In addition, CVC use is associated with greater rates of infection, including bacteremia, endocarditis, septic shock, septic arthritis, and epidural abscess (18–20). Half of catheter-related infections are managed on an outpatient basis, and patients with a CVC tend to receive multiple series of intravenous antibiotics for catheter-related bacteremia from their outpatient dialysis facility, placing them at greater risk for antibiotic resistance (22,24). Finally, studies demonstrate that CVC use is independently associated with an increased rate of infectious, cardiovascular and all-cause death compared with AVF use (1,4–6,10,23,25,26).

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Infection-Related Mortality

CVC use is strongly associated with an increased risk of infection-related mortality among both incident and prevalent ESRD patients, primarily as a result of CVC-related bacteremia and sepsis (6,27,28). When prospectively comparing the incidence of bacteremic episodes among ESRD patients undergoing dialysis at hospital-based facilities, 84.8% of episodes occurred among patients with a CVC compared with 15.2% among patients with permanent AV access ($p < 0.001$). *Staphylococcus aureus* and coagulase-negative staphylococcus accounted for themajority of infections (29).

Diabetic and nondiabetic ESRD patients who use a tunneled CVC are reported to have between a two- to threefold greater risk of death due to infection compared with patients using an AVF, and nontunneled catheters have the highest rate of infection (4,6,19). The risk of hospitalization for sepsis and mortality in the first year following initiation of dialysis is reduced if permanent access placement occurs greater than 4 months prior to ESRD, primarily by reducing the use of CVCs (28).

Among the multiple risk factors for catheter-related bacteremia are early bacterial colonization of the catheter lumen, biofilm formation, nasal carriage of *S. aureus*, the presence of diabetes, frequency of catheter manipulation, and catheter duration (26,30).

Cardiovascular-Related Mortality

Beyond the increased risk of infection, CVC use has been linked to a greater risk of cardiovascular death compared with AVF use. In the USRDS Morbidity and Mortality Study Wave 1, prevalent diabetic ESRD patients with a CVC were 47% more likely to experience a cardiovascular-related death than diabetic patients using an AVF, while nondiabetic patients using a CVC had a 38% greater risk of cardiovascular-related death compared with AVF patients (6).

Even when patients have a similar burden of co-morbid conditions, those using an AVF experience significantly lower cardiovascular mortality compared with patients using a CVC. We recently found that AVF use 90 days after the initiation of hemodialysis is associated with a 31% reduction in cardiovascular mortality, independent of known risk factors, when compared with CVC use. Decreased cardiovascular-related death was associated with black race, younger age, and pre-ESRD erythropoietin use while patients with low pre-ERD serum albumin, diabetes, ischemic heart disease, and congestive heart failure had a greater risk of CV-related and all-cause death (31).

Multiple possible explanations may exist for the association between AVF use and decreased risk of cardiovascular-related death. These may include greater delivered dose of dialysis due to better blood flow rates among patients with AVF use, reduced risk of infection, and lower levels of inflammatory factors which may be responsible for cardiovascular-mediated disease (4,7,26,32–34).

All-Cause Mortality from CVC Use

Compared with AVF use, incident and prevalent CVC use is associated with greater all-cause mortality among ESRD patients. Reports indicate that CVC use is associated with a 40–70% increased risk of death from any cause compared with AVF use (4–7).

The first study to estimate the association of vascular access type and death used national data and evaluated death by infection and all-causes among incident and prevalent ESRD patients with and without diabetes (6). Both prevalent diabetic and nondiabetic patients with

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an AVF had better all-cause survival through the 2-year follow-up than those with an AVG and CVC. Prevalent diabetic patients with a CVC were 54% more likely to die compared with patients with an AVF, while prevalent nondiabetic patients with a CVC were 70% more likely to die from any cause compared with those with an AVF. A similar trend was observed among incident ESRD patients but was not statistically significant.

This study was subsequently followed by a report among patients in the Southeast United States (ESRD Network 6),which reported that prevalent hemodialysis patients with a CVC were 40% more likely to die of any cause than those using an AVF (4). Elderly ESRD patients using a CVC at the start of dialysis have a significantly greater risk of death during the first year of dialysis. The risk of death was observed to be greatest 90 days following dialysis initiation, and at first year, patients using a CVC had a 70% greater likelihood of death compared with AVF users (5). Finally, among incident ESRD patients followed up for 3 years, the estimated annual mortality rates were significantly greater (16.1%) among patients using a CVC compared with those using an AVF (11.7%), and patients using a CVC had a 50% greater risk of death from all-causes compared with patients using an AVF (7).

Conclusion

Vascular access type influences mortality, and the use of a CVC is associated with greater infectious, cardiovascular and all–cause-related death compared with AVF use. Additional investigation is needed to determine the impact of specific factors such as predialysis vascular access education emphasizing AVF use at dialysis initiation, timely access to surgery, and early assessment of nonmaturing AVFs on CVC use among ESRD patients.

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