

The Case Against Chronic Venous Hemodialysis Access

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The provision of adequate hemodialysis is dependent on repeated and reliable access to the central circulation. This access to the circulation is best provided by primary arteriovenous fistulas (AVF) and to a lesser extent by AV grafts (AVG). AVF have the lowest rates of infection and thrombosis and are therefore the access of choice whenever vascular anatomy allows (1,2). On the other hand, establishing primary AVF in an ever-aging end-stage renal disease (ESRD) patient population with a high prevalence of diabetes and vascular disease has proved a daunting task, at least in the United States. Late referrals to nephrologists make establishment of AVF more difficult. Therefore, our reliance on less desirable modes of vascular access such as synthetic (PTFE) grafts and tunneled, cuffed catheters (CVC) has increased. In fact, up to 60% of new patients and 30% of prevalent patients are using a catheter for dialysis access (3). These latter two accesses are more prone to both thrombosis and infection. Venous access in particular has emerged as a substantial cause of hemodialysis morbidity and mortality. Two articles in this issue of *JASN* deal with these dilemmas (4,5).

Catheter-related bacteremia remains the most common and potentially serious complication of long-term venous access (6–8). Initial reports of tunneled, cuffed catheters reported low rates of bacteremia, but these were maintained in patients for a relatively short duration. In our original description, for example, median catheter use was only 8 wk, ranging from 3 wk to 5.4 mo (9). In this early report, only one episode of bacteremia occurred in 80 dual lumen catheters. Two more recent studies each showed bacteremia to occur about once every 200 to 250 catheter-days. In the first study, Marr *et al.* (10) followed 102 patients with CVC for total of 16,081 catheter-days. Bacteremia occurred in this study at a rate of 3.9/1000 catheter-days. Similar to Marr's data, Saad described a mean bacteremia rate of 5.5/1000 catheter-days (11).

In our experience, metastatic complications, such as vertebral osteomyelitis, septic arthritis, and endocarditis, have only rarely been seen among our patients in the absence of indwelling catheters. Kovalik *et al.* (12) demonstrated a significant increase in vertebral osteomyelitis and epidural abscess in patients with dialysis catheters *versus* AVG. Likewise, Robinson *et al.* (13) showed that endocarditis occurred at a much

higher rate in patients with catheters and was relatively rare in patients using synthetic grafts or AVF. Hence, dialysis with a catheter not only increases the rate of bacteremia but also appears to increase the rate of complications from an individual episode of bacteremia.

Furthermore, frequent problems maintaining catheter blood flow in CVC reduce dialysis efficiency and delivered Kt/V. Repeated studies have shown consistently lower delivered dialysis dose with catheters when compared with either grafts or fistulas. For instance, Sehgal *et al.* (14) demonstrated Kt/V of 1.37 and 1.31 with AVG and AVF, respectively, compared with 1.18 with CVC. Similarly, Dhingra *et al.* (15) reporting from the USRDS showed decreased Kt/V in patients receiving dialysis through a catheter compared with a fistula or graft.

Not surprisingly, this increased rate of infection along with the overall lower delivered dose of dialysis has been correlated with increased hospitalization rates and mortality in patients relying on catheters for vascular access. In a recent report from the USRDS, Wolfe *et al.* (16) reported that the standardized mortality rate and the standardized hospitalization rates were both correlated with the percentage of central venous catheters in individual dialysis units. There were increases of 4% in mortality and 5% in hospitalization for every 10% increase in tunneled dialysis catheters. Data were controlled for race, gender, age, and diabetes. Thus, the higher the prevalence of catheter use in an individual dialysis unit, the higher the hospitalization and mortality rates in that unit.

Because of this excess morbidity and mortality associated with catheter use, the Dialysis Outcomes Quality Initiatives put forth by the NKF have sought to standardize the vascular access practice nationally and limit catheter use (17). The DOQI states that cuffed, tunneled central venous catheters should be discouraged as permanent vascular access, and DOQI further recommends that primary AVF should be constructed in at least 50% of all new kidney failure patients and that 40% of prevalent patients should have a native fistula. For indwelling catheters, the committee has set a target of less than 10% of chronic maintenance hemodialysis patients maintained on catheters, defined as use of catheters for more than 3 mo in the absence of a maturing access.

Two articles in this issue of *JASN* address where we are in regards to meeting DOQI guidelines regarding vascular access and how we may be able to further reduce morbidity in those patients reliant on central venous catheters. In the first article, Reddan *et al.* (4) detail the information of the Clinical Performance Measures to examine predictors of clinical practice profiles 2 yr after the release of the DOQI guidelines. Only current vascular access could be listed; therefore, patients with a maturing AV access were not captured. Thus, maturing AVF

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not in use were not captured, causing this to represent a worst-case scenario. Nevertheless, only 28% were dialyzed through AVF, 49% through AVG, and 23% through catheters. Thirty percent of incident patients were dialyzed through CVC, and 22% of prevalent patients were dialyzed via CVC, roughly twice the goal set by DOQI. While this represents a substantial gain in AVF from the 21% use of 5 yr ago, it is offset by increased CVC use. Whether this reflects late referral of patients and concomitant use of CVC while AVF are maturing cannot be answered by their database.

Nonetheless, the progress toward more AVF in the United States is disappointing. In a recent observation by Oliver *et al.* (18), a major move toward upper arm AVF access is explored. The substantial failure to mature rates for Cimino fistulae and the huge accumulation of catheter time with these failures to mature should force us to place more upper arm AVF and to reevaluate and develop new techniques for determining when a fistula is likely to mature. The use of preoperative venous mapping in this regard appears promising (19). In like manner, the NIH Dialysis Access Consortium is exploring pharmacologic therapy to improve AVF survival rates.

In the second article, Dogra *et al.* (5) evaluate the utility of an antibiotic lock technique in reducing risk of CVC bacteremia. Antibiotic lock techniques have been previously described to have some efficacy in treating CVC bacteremia but have not been demonstrated to reduce bacteremia when used prophylactically. This article reports the results of a randomized trial comparing standard heparin flush to a gentamicin/citrate lock for indwelling catheters. Gentamicin was mixed at 40 mg/ml and instilled at a volume to fill the lumen. Citrate functioned well as an anticoagulant, and catheter dysfunction was actually more common in the group randomized to heparin. In the Gentamicin group, no episodes of bacteremia occurred with only one exit-site infection compared with seven episodes of bacteremia and four exit-site infections in the control group. Treatment with antibiotic lock resulted in reduction in infection rates from 4.2/1000 catheter-days to 0.3/1000 catheter-days. Mean infection-free survival increased from 180 d to 280 d, and relative risk of infection was reduced by 90%. In this article, antibiotic lock was a highly effective strategy to prevent CVC infection compared with standard care.

Although the study was done in a group of patients with very short duration of catheter use, rates of bacteremia and exit-site infection were both reduced in the group receiving antibiotic lock. One must wonder if antibiotic lock techniques would continue to prove useful when catheter use is extended. Also of concern with any prolonged antibiotic administration is the question of whether long-term use would result in antibiotic resistance or fungal infections. In the antibiotic lock treatment study recently reported from the University of Alabama, several fungal catheter infections were seen (20). In this article, nine cases of fungal superinfection (14%) were observed. The present study also raises concerns regarding the safety of aminoglycosides in this setting. Even with short duration of use and minimal overfill infusion, systemic toxicity was observed. Measurable levels of aminoglycoside were obtained, and ototoxic-

ity occurred. Median levels were 2.8 mg/L with levels as high as 3.5 mg/L in one patient. When used over a longer duration, these problems with ototoxicity would undoubtedly be magnified. Perhaps a lower dose of Gentamicin will be proven to be as equally efficacious without the risks associated with chronic aminoglycoside administration.

Despite these limitations, the case made for antibiotic lock techniques in this article are promising. However, antibiotics other than aminoglycosides will need to be used and anticoagulation other than citrate would be desirable. An antibiotic-heparin lock may ultimately prove most useful in our attempts to reduce bacteremia. Other possible advances include the use of subcutaneous venous hemodialysis access ports (21). A recent prospective randomized trial showed substantial reduction in bacteremia when the subcutaneous port was compared with a CVC (22). Thus, technology and new techniques may reduce the huge morbidity associated with venous hemodialysis access but will not eliminate it. Our best and wisest course for the future is to deal with the venous access conundrum by finding mechanisms to limit venous hemodialysis complications with new techniques and novel devices but also to use venous access less and for shorter periods of time.

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See related articles, “National Profile of Practice Patterns for Hemodialysis Vascular Access in the United States” on pages 2117–2124 and “Prevention of Tunneled Hemodialysis Catheter-Related Infections Using Catheter-Restricted Filling with Gentamicin and Citrate: A Randomized Controlled Study,” on pages 2133–2139.