

Reassessing Recommendations for Choice of Vascular Access

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Optimizing vascular access outcomes remains a major challenge, despite the accumulation of consensus guidelines during the past 20 years. The initial Kidney Disease Outcomes Quality Initiative guidelines published in 1997 (1) and updated in 2001 (2) and 2006 (3) as well as the “Fistula First Initiative” in 2003 (4) have consistently recommended preferential placement of arteriovenous fistulas (AVFs) over arteriovenous grafts (AVGs). There has been a gratifying increase in AVF use among patients on prevalent hemodialysis in the United States from 35% in 2003 to 63% in 2017 (4). Unfortunately, central vein catheter (CVC) use remains high at about 20% in patients on prevalent hemodialysis and 80% among patients on incident hemodialysis (4). There has also been an alarming increase in the frequency of percutaneous and surgical interventions to promote AVF maturation and maintain their long-term patency for hemodialysis (5).

Several rationales for preferring AVFs over AVGs have been proposed: (1) AVFs have better longevity (6), (2) AVFs require fewer interventions to maintain long-term patency for hemodialysis (6), (3) patients dialyzing with an AVF have a lower mortality than those dialyzing with an AVG (7), and (4) patients with AVFs incur lower access-related costs (6,8). Recent publications have suggested that the purported advantages of AVFs over AVGs may be overstated, because they hold true only if the AVF successfully matures for dialysis use. AVFs fail to mature at higher rates than AVGs and require longer maturation times (6,8). A systematic review of observational studies published from 1996 to 2002 reported that approximately one third (20%–50%) of new AVFs failed to mature successfully for dialysis use (6). Subsequently, the Dialysis Access Consortium Fistula Study, a multicenter trial enrolling 877 United States patients on hemodialysis, reported in 2008 that 60% of new AVFs failed to mature successfully for dialysis within 6 months (9). Most recently, the Hemodialysis Fistula Maturation Study observed an unassisted AVF maturation rate of only 44% in 602 patients (10). As a consequence of their high nonmaturation rates, AVFs have a secondary patency similar to that of AVGs in an “intention-to-treat analysis” (11). Additionally, AVFs requiring interventions to promote maturation have shorter patency and require more frequent interventions to maintain their patency compared with AVFs that mature without an intervention

(5,12). In fact, AVFs requiring an intervention before successful use have a shorter survival than AVGs used without a prior intervention (5). Importantly, any delay in using the AVF for hemodialysis prolongs CVC dependence and its potential for causing catheter-related bacteremia.

Two studies by Ravani *et al.* (13) and Hall *et al.* (14) appearing in this issue of *Clinical Journal of the American Society of Nephrology* further challenge the current paradigm that AVFs are preferred to AVGs in all hemodialysis populations in terms of patient survival and cost-effectiveness. Ravani *et al.* (13) studied 6119 patients enrolled in the Dialysis Outcomes and Practice Patterns Study who initiated hemodialysis with an AVF (37%), an AVG (13%), or a CVC (50%). As expected, access type predicted likelihood of access complications (highest with CVC, intermediate with AVG, and lowest with AVF), and both access type and access complications predicted patient mortality. However, the mortality risk associated with different access types was similar in models including or excluding access complications. These findings suggest that the higher mortality in patients with AVGs and CVCs is not mediated by the higher rate of access complications but rather, is attributable to the higher comorbidity burden of patients receiving these access types. This conclusion is consistent with two recent studies that reported a lower mortality in patients starting hemodialysis with a CVC who underwent prior AVF creation compared with patients without prior AVF surgery, even if the AVF was never used (15,16). It is also in keeping with the observation that only 2.3% of all deaths in patients on incident hemodialysis are access related (15). Ravani *et al.* (13) recognized the limitations of observational studies and advocated for a definitive randomized, controlled trial to determine whether vascular access complications mediate the association between access type and mortality.

Hall *et al.* (14) constructed a Markov model to estimate the cost-effectiveness of placing an AVF or AVG or continued CVC use in a hypothetical cohort of elderly (age ≥ 65 years old) patients initiating hemodialysis with a CVC. Costs, quality of adjusted life-months, and incremental cost-effectiveness ratios were estimated for patients in different age groups and quartiles of life expectancy. Placement of an AVF was more cost effective than continued CVC use for all age

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and life expectancy groups except 85–89 year olds in the lowest life expectancy quartile. AVFs were more cost effective than AVGs for all quartiles of life expectancy among the 65- to 69-year-old age group. However, the cost-effectiveness of the AVF relative to the AVG option diminished with increasing age. In other words, both patient age and life expectancy determine the cost-effectiveness of AVF placement. Three recent analyses also concluded that the cost-effectiveness of AVFs was attenuated in older patients (17–19). The conclusions by Hall *et al.* (14) should be interpreted with caution, because their model incorporated several key assumptions that may differ from routine clinical practice. (1) After failure of an initial access, a patient would undergo only one additional access placement, which would always be of the same type as the first access. (2) All vascular access infections require hospitalization. (3) Fifty percent of procedures to re-establish vascular access patency require hospitalization. To the extent that clinical practice differs from these assumptions, the cost-effectiveness calculations may differ.

Why is the benefit of AVFs less clear among older patients on hemodialysis? Older age is associated with both a lower likelihood of AVF maturation (20) and a shorter life expectancy. In other words, older patients are likely to have a longer duration of catheter dependence before they achieve a usable AVF and may not live long enough to realize the benefits of dialyzing with an AVF. The combined effect of these two factors was highlighted in a single-center report by Richardson *et al.* (20). Among patients ≥ 70 years old undergoing AVF creation, only 39% of AVFs were patent at 1 year, and only 50% of patients were alive at 18 months (20). As a consequence, only 35% of patients who died ever used their AVF (20). It is also likely that AVF creation is not cost effective in patients with a poor functional status (which is more common in elderly patients). Thus, for example, in a study of 3702 nursing home patients initiating hemodialysis, only 42% survived 1 year (21).

A definitive answer about the relative merits of AVFs and AVGs in terms of patient survival, frequency of hospitalizations, and access-related costs would require large, multicenter, randomized clinical trials (RCTs), in which patients are allocated to receive one of these vascular access types. Until such RCTs are available, the choice of optimal vascular access placement depends on the clinical judgment of nephrologists and surgeons caring for these patients. A patient on dialysis with a functional AVF may be better off than a patient with a functional AVG. However, a patient with a functional AVG is better off than a patient with an immature AVF and prolonged CVC dependence. An ongoing challenge in vascular access selection is the difficulty in predicting which AVFs will successfully mature for dialysis and which ones will require one or more interventions to promote their maturation. Clinical considerations relevant to access choice may include (1) whether the patient is already using a CVC for dialysis (increasing the risk of catheter-related bacteremia), (2) the likelihood of successful AVF maturation, (3) the outcomes of a previous vascular access, and (4) the patient's life expectancy and quality of life (22). Even if RCTs comparing different vascular access types are performed, they cannot possibly address every patient scenario, incorporating multiple factors including age, vascular disease, body mass index, functional status,

and preoperative arterial and venous diameters. In this regard, a recent study used the RAND/UCLA Appropriateness Method to assess the appropriateness of an AVF or an AVG in a large number of scenarios (23). Eleven vascular access experts assessed the appropriateness of each access type in 864 clinical scenarios and concluded that an AVG was appropriate in 36% of them (23).

Rather than pursuing an unquestioning "Fistula First" strategy, it is time for clinicians to adopt a "patient-centered" approach that considers individual patient risks of death before need of dialysis, life expectancy after initiating dialysis, and risks of complications with CVC versus AVF (24). Ultimately, nephrologists should assist patients with vascular access decision the basis of making an individualized evaluation of risks and benefits of specific access types, while also considering the patients' beliefs, values, and preferences (24). To provide care that is truly centered on the individual patient, we must focus on not only traditional metrics (*e.g.*, proportion of patients with AVF, AVG, and CVC use) but also, metrics that capture the process of vascular access selection and support the goals and preferences of the individual patient (25). Ultimately, such an approach will result in choosing "the right access, in the right patient, at the right time, and in the right circumstance" (7).

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- See related articles, “Choice of Hemodialysis Access in Older Adults: A Cost-Effectiveness Analysis,” and “Examining the Association between Hemodialysis Access Type and Mortality: The Role of Access Complications,” on pages 947–954 and 955–964, respectively.