

Can We Predict the Unpredictable after Vascular Access Creation?

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Establishing permanent vascular access is a significant management step in the clinical pathway for patients with progressive stages 4 and 5 CKD. Although clinical practice guidelines are unified in the recommendation for the native arteriovenous fistula (AVF) as the first choice vascular access for hemodialysis (1–4), the majority of patients throughout the Western world commence hemodialysis with a central venous catheter.

A key decision-making point in establishing AVF relates to the timing of vascular access surgery that will allow adequate maturation time for the AVF to be ready at dialysis commencement. If the AVF is placed too late, it will not be ready in time, thus requiring dialysis to commence *via* a central venous catheter. Placing an AVF too early diverts precious resources that could have been used for other patients or clinical areas and more importantly, can subject the patient to the risks and inconveniences of a procedure that may, in fact, be unnecessary. Thus, a fine balance must be achieved, and attaining the right timing for AVF creation requires careful clinical consideration, process coordination, and with our existing data, perhaps a bit of clairvoyance.

Factors that determine the timing of AVF creation can be broadly placed into three broad categories. First is the presence of patient characteristics that are associated with a higher likelihood of AVF primary failure and/or maturation failure, such as older age, the presence of vascular disease, and diabetes mellitus (5). In the presence of these factors, the nephrologist will likely refer the patient earlier for surgical assessment to allow a longer lead time to establish a functioning AVF. Second is the severity of kidney dysfunction and perhaps more importantly, the trajectory of kidney function decline. Although this second point could be thought as stating the obvious, there is a surprising lack of literature surrounding this issue. Recent work shows significant heterogeneity in the GFR decline of patients with advanced CKD (6). O'Hare *et al.* (6) assessed the trajectory of eGFR in the 2-year period before commencement of hemodialysis in >5000 patients. Of note, four distinct trajectory groups were found, ranging from the largest group (68% of patients) with persistent low eGFR and quite slow decline in eGFR to those with high starting eGFR and catastrophic loss of kidney function within 6 months (6). Indeed, the consequences of this rapid loss are

reflected by the 20%–30% or more of patients who crash start on dialysis and initiate with a central venous catheter, despite having appropriate referral and visits to a nephrologist (7). Third, to complicate matters more, underlying patient and provider process factors can further alter the trajectory to dialysis start (7). This clinical uncertainty and the paucity of data in the literature may be reflected in the heterogeneity of clinical practice guidelines and the simplicity of using the severity of kidney function (*e.g.*, specific level of GFR) to guide the timing of AVF placement without real reference to remaining residual renal function or rate of GFR loss, except in relationship to an “anticipated start of dialysis” or a statement referring to progression of CKD (1–4). More research and data informing the relationships between vascular access placement, kidney function decline, and dialysis start may provide clarity for future guidelines and help lift the shroud of clinical unpredictability currently present.

In this issue of the *Clinical Journal of the American Society of Nephrology*, Al-Balas *et al.* (8) shed additional light on this subject. They present a retrospective analysis of 308 patients in whom an AVF was created in anticipation of commencing hemodialysis and assess the potential of patient and laboratory variables collected at the time of AVF surgery in predicting whether the patient will commence hemodialysis within 2 years of the initial AVF surgery. Characteristics assessed included patient demographics and comorbidities known to be associated with AVF placement but also, the severity of kidney function at the time of surgery as well as the eGFR trajectory over the 12 months preceding the AVF surgery.

The study presents a number of important findings. First, significant heterogeneity in the decline of kidney function was evident, with only 68% of the patients commencing hemodialysis over the 2-year follow-up period. Of the remaining 32%, 16% had not yet commenced dialysis, with the remainder of patients dying before commencement. Second, when assessing factors that predicted the likelihood of dialysis commencement, severity of CKD at the time AVF placement was important but did not on its own adequately predict whether a patient would commence dialysis over the follow-up period. Significantly, of the 145 subjects with stage 5 CKD at AVF placement, 19% did

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not commence dialysis in the ensuing 2 years. The addition of the presence of diabetes mellitus, the degree of proteinuria, and the eGFR trajectory in the preceding year, significantly improved the model beyond the severity of CKD, providing moderate prediction of dialysis commencement. Third, among those patients who commenced hemodialysis, less than one half (47%) did so with a functioning permanent vascular access, indicating that, despite the best efforts of the treating team, a majority of patients still needed a central venous catheter at dialysis commencement.

Previous studies have highlighted the difficulties in timing of AVF placement. In a similar study to this one, Oliver *et al.* (9) found that 30% and 10% of AVFs were placed >1 and >2 years, respectively, before the commencement of hemodialysis. However, although considerably larger than the study by Al-Balas *et al.* (8), no information was available on level of kidney function and/or trajectory of its decline before AVF creation. What is clear, however, is the ongoing difficulties in decision making between creating an AVF in a patient who may never commence dialysis and doing it too late with the need to commence hemodialysis with a central venous catheter.

A couple of important limitations of the study by Al-Balas *et al.* (8) need highlighting. The study is retrospective from a single center and thus, would need to be confirmed in a larger multicenter study. This is particularly important for external generalizability. For example, the majority of patients studied were of black race (69%), and the rate of decline in kidney function was a significant variable in predicting dialysis commencement, which improved the overall model. However, racial and ethnic differences have been associated with differences in rates of kidney decline, with more rapid decline in blacks (10). Although the trajectory of kidney decline had a significant effect, one wonders if there might there be an interaction of CKD severity or cause of ESRD at the time of surgery and the eGFR trajectory. This may have clinical implications for timing of AVF creation; for example, the effect on prediction of eGFR decline may differ according to different etiologies of CKD. It is unclear whether such interactions were tested for in this study. Additionally, a number of patients (17% of the potential study cohort) was excluded because of missing eGFR data at the time of AVF surgery. Despite the demonstrated similarities between those excluded and those included in the study, both observed and unobserved differences remain, and therefore, the possibility of residual confounding remains.

How might these data be used in clinical practice? Data from this study and the work of O'Hare *et al.* (6) show that, although severity of kidney function is an important determinant of commencing dialysis, the trajectory of kidney function loss is equally and likely, more important. This may be related to the degree of kidney damage reflected by the presence of albuminuria or proteinuria. This presence of albuminuria has been shown to be related to CKD progression as indicated in the updated CKD staging system (11) and a recent widely validated model for predicting CKD progression (12). This is consistent with this study's finding of the level of proteinuria (assessed by a protein-to-creatinine ratio) as a significant predictor in their model. Although this seems an obvious point to the practicing clinician, incorporation of GFR trajectories and a measure of

albuminuria/proteinuria in predialysis clinical pathways that include patient education is likely to be important. This resonates especially in resource-stressed health systems, where the avoidance of unnecessary health interventions is not just important for the individual patients but will have a wider effect on the ability of hospitals and networks to deliver timely care to all patients within their jurisdiction. However, it is clear that further work needs to be done for such data to be truly useful to the practicing clinician. For example, one could envisage that a predictive scoring system could be developed from a larger multicenter study, whereby the nephrologist could allocate a score to an individual that predicts the likelihood of dialysis commencement with a relatively short timeframe of 6–12 months to help enable decision making on the timing of AVF placement (similar to current models predicting progressive CKD [12]).

It is clear that the timing of AVF creation before dialysis commencement is important to optimize patient outcomes and health care resources; however, this is dependent on the challenging task of the nephrologists and multidisciplinary teams to predict when a patient will need to start dialysis under individual and typically complex circumstances. Al-Balas *et al.* (8) have highlighted this complexity and the need to consider not only a singular level of kidney function but also, the trajectory of its decline in planning AVF creation in relation to anticipated dialysis commencement. This important work has potential clinical implications but will require further study and confirmation in larger multicenter studies.

Disclosures

None.

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