A Preponderance of Evidence Is Sufficient

Tom F. Parker, III

Awareness of a problem is the first step toward finding solutions. The nephrology community is increasingly aware of the extraordinary morbidity and mortality risks within the first year of renal replacement therapy (RRT), especially with in-center dialysis. However, this awareness has not yet been substantially translated to universal or even regional changes in care of patients—changes designed to address the recognized problems. Indeed, the trends associated with mortality and morbidity (hospitalizations) in dialysis forms of RRT have shown only minimal improvement in 20 years (1).

The authors of the paper “Early Outcomes among Those Initiating Dialysis in the United States” (8) remind us again of the problem and its complexity and offer further insights into how caregivers of patients undergoing dialytic RRT might focus their efforts to improve outcomes in incident patients. A database of over 300,000 patients is compelling, although the analysis is both complex and observational. The analysis has its inherent weaknesses, as acknowledged by the authors. Two omissions seem deserving of comment. For one, the serum creatinine (and calculated estimated GFR [eGFR]) at the time of initiation of dialysis was not studied. Because many observational studies have linked higher eGFR at dialysis initiation (early start) with higher subsequent mortality risk, this omission limits the conclusions (2). This is an important point because during the period covered by this analysis, such an “early start” of dialysis contributed almost all of the overall growth in incident dialysis in the United States (3). Also, the modus of death was not studied (from death certificate acquisition); thus we can only speculate on the details for the mortality event (e.g., sepsis, myocardial infarction, congestive heart failure, etc).

Nevertheless, this study clearly shows that incident dialysis patients are almost three times as likely to die in the first 2 weeks of care and are over twice as likely to enter the hospital compared with those who survive the first year of such therapy. This risk slightly lessens within the first 90 days and then begins to taper more rapidly. This is precisely the same observation suggested by a subset analysis of the United States Renal Data System (USRDS) (4). Even more concerning is the fact that 9% of deaths occurring in the first year do occur in first 2 weeks of dialytic treatment and 44% occur in the first 90 days. What is happening during this crucial period? More importantly, what might we do to alleviate this glaring problem of early postinitiation mortality and morbidity in dialysis patients?

Examination of the details of the study provides some clues to the answers to these questions. Excess mortality and morbidity was associated with certain clinical practices: initiating dialysis with a fistula decreased early mortality by 61%, and starting patients with peritoneal dialysis decreased early mortality by 87%, although the latter effect did not persist.

Although the picture is a rather gloomy one, areas worthy of a cheer are highlighted. Compared with 1997, there were slight improvements in 90-day and 1-year mortality. This was also confirmed by the USRDS (4). The lessons provided by this study, not provided by the USRDS observations, is that dicing and slicing the events into smaller temporal segments suggested associations with clinical patterns of care evolving over time, which might have a cause-and-effect relationship. Parenthetically, however, it is a bit shameful for our profession, or at least for me, that the improvements are so modest.

Allow dispensation of the obvious. It is very possible that many of these patients should not have initiated dialysis in the first place. Elderly, infirm subjects with advanced renal failure may not receive benefits from dialysis RRT. Likely, for many patients, palliative nondialysis care would have been of more comfort to the patient and the family. Sicker and older patients are more likely to require indwelling vascular access catheters, perhaps even appropriately so, but at a cost of enhanced infection and sepsis (5). Indeed, the serum albumin concentration was lower in those who died earlier, confirming, in part, this observation of lesser health and visceral malnutrition and/or chronic inflammation. Information on eGFR at the onset of dialysis, as mentioned above, would have provided additional clues concerning somatic malnutrition, because eGFR in advanced renal failure is more a reflection of sarcopenia than residual renal function. Caregivers who initiate dialysis as a “trial” might contribute to these kinds of data. We lack information on how many patients for whom such so-called therapeutic interventions have failed. Subjectively, I suspect that it might well be in excess of 50% in the first year. In this regard, data from the USRDS show that those over the age of 65 have a first-year survival on dialysis of only 20%, suggesting that such high mortality risk is a surrogate for elderly and...
infirm patients being placed on RRT as a trial (4). One major advantage of this study, worthy of emphasis, is the lack of censorship, which may explain some of the magnitude of differences in the data and those reported previously (6).

However, this editorialist is perplexed and unsettled by these observations. Given the multitude of clinical guidelines and clinical performance measures that we impose on our specialty and that regulators and payers expect facilities to follow, the availability of newer pharmaceuticals and a better understanding of usage of those that have been around for 20 years or more, the technology of equipment, preparation of patients during stages 3 through 5 of CKD, and our understanding and provision of “adequate” dialysis quantification, why do these poor outcomes persist, and why have there been such modest improvements over time?

Although not addressed in this study, clearly there are efforts being undertaken to change the results, offering promising interventions during the first year of dialytic RRT. Some of the same authors, in abstract form at the 2011 ASN meeting, will show a change in mortality and hospitalization rate using nutritional supplements in large populations of incident dialysis patients (personal communication, Raymond Hakim, MD).

Most importantly, four formal programs designed to alter the dismal outcome of the first 90 to 120 days of dialytic RRT are in various stages of implementation in the United States: (1) RightStart from Fresenius Medical Care; (2) Impact from DaVita; (3) PEAK from Kidney Care Partners; and (4) RVCare from Renal Ventures Management. (I am certain that there are others and beg apology for ignorance of them.) All of these programs use clinical managers, during the first 90 to 120 days, in person and by telephone, to more intensely manage these incident patients—providing immediate education for care and options, removal of vascular catheters, assessment of extracellular volume status and risks for volume overload, evaluation and correction of anemia, and comfort during this difficult transition period, including during episodes of major depression.

To my knowledge, only Wingard et al. (7), with RightStart, have published results showing a remarkable reduction in hospitalizations and mortality in the first year, even when expanded to a large population base. Unpublished data from RVCare have shown precisely this as well. Although both are uncontrolled and observational in character, we gain insight into what likely resulted in these significant improvements.

Clearly, most morbid and mortal events in the early postinitiation period of dialytic RRT are associated with at least two major factors: infection, predominantly from catheters, and cardiovascular events, mostly from poor control of fluid volume overload. This is succinctly confirmed by the USRDS, showing that well over 50% of adjusted rates of cause-specific mortality in the first months of dialytic care are due to infection (likely related to indwelling vascular catheters) and cardiovascular disease (mostly volume, not atherosclerotic cardiovascular disease [ASCVD], related) (4).

It is simple. Intensely working with dialysis staff, surgeons, and especially patients to control these two factors has had the greatest effect in the aforementioned programs. The latest USRDS data, at the time of this editorial, shows that 82% percent of patients initiate dialysis with a catheter, and well in excess of 20% prevalent patients have catheters as their functioning access. Even if a patient has seen a nephrologist several times, the incident patients have a greater than 60% probability of starting dialysis with an intravenous catheter. Clearly this iatrogenic problem is exquisitely vulnerable to a simple solution. Furthermore, 70 to 90% of patients initiate dialysis with evidence of left ventricular hypertrophy and accompanying fibrosis, with a propensity to volume overload and lethal arrhythmias, yet the principal attention of the caregiver is dialysis dose (Kt/V), and attention to achieving euolemia is relegated to a lower priority, unless florid features of congestive heart failure or symptoms of volume overload or treatment-resistant hypertension are present.

Results presented at the Boston ESRD Conference in 2009, published in this journal (8), noted the abysmal improvements in outcomes for our incident and prevalent patients and concluded with a very short but poignant list of observations and tentative opinion-based recommendations. First, morbidity and mortality have not improved significantly in dialytic RRT in over 20 years, despite all that we think we are doing correctly, following the traditional guidelines and performance measures. The conclusion of the conference was that the measures we are using are not enough, and are even wrong. How we claim success is simply wrong! If only we would continue what we are doing but now begin to stress other clinical practices, the preponderance of evidence suggests that patients will live longer and avoid unnecessary hospitalizations, even in the first few weeks, months, or year after the start of dialytic RRT.

We seem to be awaiting the next demonstration project, the next prolonged and expensive trial or study before acting. We seem to be saying that proposals for charting a new path of care are not sufficiently “evidence-based” and not yet worthy of serious consideration rather than dispas-sionately examining the preponderance of studies and evidence throughout the literature and taking some action to alleviate an obvious deficiency in the quality of our care, not yet addressed by the plethora of clinical guidelines and clinical performance measures.

The solution seems simple: we must get rid of indwelling vascular catheters, using assertive and aggressive means within the first few weeks of care, and cease over-reliance on Kt/V as an exclusive measure of adequacy. While still using Kt/V to maintain quantification of dialysis dose for solute removal, the new outcome must be to improve and preserve the anatomy and function of the left ventricle, first through determining whether it is compromised, then through assertive restriction of sodium (not water, sodium) by lowering the dialysate sodium, avoiding sodium modeling, and aggressive dietary counseling about avoiding salt (it is illogical to unceasingly counsel patients about not drinking water when we load them with sodium); attaining euolemia the first of the week by increasing dialysis time or performing an extra dialysis or changing modality; and not exceeding ultrafiltration rates of 12 ml/h per kg to avoid “cardiac stunning.” We must acknowledge that our
perception of “dry weight” belongs in museums and historical papyrus. We must also add nutritional supplements for incident patients. This plan is a “one-two-three” punch to the abysmal outcomes that our incident patients face when beginning their RRT journey under our care.

The authors of the referenced paper show us the nature and magnitude of the problem. We are now aware, and the solutions are at hand. De Gourmont said that “Simple ideas lie within the reach only of complex minds.” We have a reasonable and relatively simple path on how to correct the problem in the first 120 days of care. How many hospitalizations, how much cost, and how many deaths must be endured before we start?

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Disclosures

None.

References


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