Mortality in the Elderly on Dialysis: Is This the Right Debate?

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In his recent book, Gawande (1) states, “Medicine’s focus is narrow. Medical professionals concentrate on repair of health, not sustenance of the soul . . . For more than half a century, we have treated the trials of sickness, aging and mortality as medical concerns . . . That experiment has failed” (1). Bargman (2), in 2007, wrote, “Not every decision in life is, nor should be, made with the sole intention of prolonging survival . . . patients should not be pushed to one modality or the other to press them into the statistical longest-survival mold, which may not even exist, but they should have the freedom to make their own choice” (2). However, studies comparing survival statistics with ever more complex analyses continue to be published. In this issue of CJASN, Han et al. (3) have published an analysis from the Korean registry with an accompanying meta-analysis focusing on the survival of older patients on hemodialysis (HD) and peritoneal dialysis (PD). In such a multimorbid cohort burdened with other geriatric syndromes, mortality outcomes on dialysis are generally poor and will depend on many factors other than dialysis modality. For example, the median survival on dialysis in the United Kingdom is just over 2 years for those ≥75 years (4).

Han et al. (3) have analyzed survival data from a large Korean cohort of older patients on dialysis (2390 patients on PD and 10,675 patients on HD), with a mean follow-up period of 1.8 ± 1.3 years. Mortality rates were significantly higher in the patients on PD (hazard ratio [HR], 1.20, 95% confidence interval [95% CI], 1.13–1.28; P<0.001) compared with those on HD. Han et al. (3) are to be commended for their subsequent meta-analysis of 15 studies (631,421 patients; index study included) in an attempt to address the inevitable bias of modality selection in individual studies. This also showed that mortality rates were higher in patients on PD (pooled HR, 1.10; 95% CI, 1.01 to 1.20). The difference in outcomes was more prominent in patients with diabetes and a dialysis vintage of >1 year. Nevertheless, there are important limitations to highlight. There is substantial heterogeneity in the studies included in the meta-analysis (I^2 statistic = 94.3%). Also, because the included studies are observational and mostly from registry databases, it is possible that important confounders may not have been adjusted for, limiting the validity of the study outcomes.

The outstanding confounder is frailty. In recent times, frailty has gained recognition as a concept, leading to a paradigm shift in the evaluation of morbidity and mortality outcomes for older patients with ESRD. Frailty is a state of impaired homeostasis with loss of physiologic reserve and a consequent impaired response to trivial events. This construct can now be incorporated into clinical practice and has been shown to be associated with increased hospitalization, admission to nursing homes, and mortality (5,6). More importantly, frailty outperforms comorbidity burden as a predictor of mortality. Alfaadhel et al. (7) have recently evaluated frailty in a cohort of 390 patients on dialysis (301 on HD and 89 on PD) using the Canadian Study of Health and Aging Clinical Frailty Scale (8). Mortality outcomes were collected over a median follow-up of 1.7 years (interquartile range =0.9–2.8 years). The degree of frailty was associated with a higher risk of mortality (HR, 1.22; 95% CI, 1.04 to 1.43), even after adjusting for age, comorbidity, and dialysis modality. Similar findings were reported by McAdams-DeMarco et al. (9) in a cohort of 149 patients on HD. Patient selection practices for dialysis vary widely across countries. Older patients considered too frail for HD have been known to be initiated on PD in transition to end of life care. Because frailty was not assessed in the analysis by Han et al. (3), it is unclear how adjusting for it would have influenced outcomes in their study. In France, where frail older patients are preferentially offered PD (assisted), data for 1615 patients ≥75 years old from the French Peritoneal Dialysis Registry (RDPLF) have shown that the median survival for those requiring nurse assistance (80% of cohort) is 24 months (10), which is very similar to that for all comers (90% of whom would be on HD) in the United Kingdom renal registry data (4).

The debate needs to shift to other equally important outcomes, such as quality of life (QoL) and personal preferences about having dialysis at home or in hospital—or no dialysis. As discussed recently by Vandecasteele and Kurella Tamura (11), dialysis for this age group is a “final destination” (11). Patients, when they are aware of a short prognosis, are more likely to focus on supportive treatment than life extension (12). Using a discrete choice study design, Morton et al. (13) have shown that patients are willing to forgo up to 7 months of life expectancy on dialysis to reduce hospital visits and up to 15 months to be able to travel.
Nephrologists are also willing to forgo up to 12 months of patient survival to avoid significant decline in QoL (14). French data from the RDPLF show that older patients on assisted PD prefer to die on PD rather than transfer to HD (15). Indeed, this phenomenon may contribute to the perceived shorter survival of highly comorbid patients with diabetes, because some may elect for supportive care and stop PD when no longer able to carry out the treatment rather than transfer to HD.

It is more difficult to collect QoL data than survival, and therefore, it is not surprising that there are fewer studies evaluating QoL in older patients on dialysis compared with those with survival outcomes. The North Thames Dialysis Study evaluated QoL using the Short Form (36) Health Survey (SF36) and Kidney Disease Quality of Life Questionnaire (KDQOL) in 174 patients ages 70 years old and older. It found no differences in QoL outcomes between modalities at 6 and 12 months, respectively, but did find higher KDQOL scores in the PD group at baseline (16). The Broadening Options for Long-Term Dialysis in the Elderly Study evaluated QoL in 140 patients on dialysis ages ≥65 years and found no differences in QoL outcomes between matched patients on PD and HD, except for significantly less illness intrusion in the PD cohort (17). In our own ongoing Frail Elderly Patients on Dialysis Study (an observational study comparing QoL in older patients on HD with those on assisted PD), the baseline analysis of 251 patients ages ≥60 years showed that treatment satisfaction was significantly higher in the PD group, with no other differences in QoL outcomes (O. Iyasere and E.A. Brown, unpublished data). These observational studies have their limitations but would suggest PD is at least non-inferior to HD in terms of QoL for older patients.

The question of dialysis versus conservative kidney management (CKM) is probably more pertinent for many older patients approaching ESRD. Chandna et al. (18) reported a substantial deficit in median survival in patients on CKM compared with those on dialysis (21.2 versus 67.1 months; $P<0.001$). However, in those >75 years old, the difference in survival was no longer significant after adjusting for age, comorbidity, and diabetes. Da Silva-Gane et al. (19), in a study of 170 patients, compared survival and QoL outcomes between patients on CKM and those opting for dialysis. After adjusting for covariates, the median survival for patients on CKM was 13 months shorter than that of patients on HD. However, 10 of those months represented days on which dialysis took place. QoL was maintained during the 3-year follow-up period in patients on CKM and patients on HD, except for life satisfaction, which declined after starting dialysis in the HD group. Similar outcomes have been reported in other observational studies (20).

How do these studies influence clinical decision-making in older patients with ESRD? It remains unclear whether one dialysis modality confers a substantial advantage over the other in terms of survival or indeed, measured QoL. We need an individualized approach with unbiased information about dialytic and nondialytic therapies, with informed patient choice being paramount. This should not be restricted to mortality risk and lifestyle preferences. Addressing frailty as part of a comprehensive assessment should be integrated into the decision-making process. The effect of dialysis modality on age-related syndromes, such as dementia, should also be considered. A recently published retrospective analysis of 121,623 patients on incident dialysis suggests that the risk of incident dementia is lower with PD compared with HD (HR, 0.46; 95% CI, 0.41 to 0.53) (21). There also seems to be a higher risk of subdural hematomas in patients on HD compared with those on PD (HR, 1.62; 95% CI, 1.17 to 2.33) (22). This is particularly important for a population at high risk of falls.

Because randomized clinical trials are not feasible, we need well designed multicenter observational studies comparing QoL outcomes in patients on CKM with those on different dialysis modalities. The challenge will be standardizing the inclusion criteria for patients on CKM, because clinical practice in conservative kidney care varies widely. Clinical studies evaluating the effect of frailty assessments on nephrology practice patterns are also needed. We think that this is where the true debate lies.

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References


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