beneficial effect of increased treatment time on IDH is more than might be anticipated because of the logarithmic relationship between UFR and IDH: A small increase in time yields a proportionately greater decrease in IDH.12 In addition, the reduction in UFR by itself may reduce mortality risk.13

We write decreasing dietary sodium rather than focus on interdialytic fluid intake to emphasize two points. First, dietary sodium drives fluid intake and weight gain in most patients. Ignoring fluid restriction and concentrating on sodium intake more effectively reduces weight gain than does restricting both—illogical, but perhaps patients just give up from all their dietary restrictions.14 The second reason for emphasizing dietary sodium is that weight gain as a result of primary fluid intake, recognized by predialysis hyponatremia, is far easier to remove without IDH than a similar isonatric fluid load because diffusive sodium gain supports extracellular volume.15

Finally, increasing dry weight is really the default action taken to treat IDH. We may not order it, but patients override us with their low BP. The increased weight expands interstitial volume; the larger this space is, the faster it can be mobilized to replace ultrafiltration-induced declines in plasma volume.16,17 Unfortunately, volume expansion is undesirable and adversely affects mortality.18

The list of adverse consequences from IDH keeps growing. VAT is but one more reason to be concerned about what IDH does to our patients. We can dance around the edges of the problem but it is going to take a change in our traditional thrice-weekly HD regimen to fix it.

DISCLOSURES

None.

REFERENCES


The Achilles Heel of Mortality Risk by Dialysis Modality is Selection Bias

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Since the introduction of ambulatory peritoneal dialysis (PD) in the late 1970s, several investigators have attempted to compare the risk of death between patients treated with PD and those treated with hemodialysis (HD). Clearly, the ideal study design to examine this question would be a ran-
domized clinical trial; however, such a study has not been feasible because of several significant logistic issues. To date, most investigators examining this problem have analyzed data from observational studies—either large administrative datasets or smaller but more comprehensive prospective cohort studies. Over the years, these observational studies have yielded conflicting results, likely due to several inherent limitations of their study design. Some of these limitations include survival bias (particularly in cohorts of prevalent dialysis patients), short (≤2 yr) follow-up, and limited information on comorbidities and process of care, particularly in administrative data.

Selection bias may be one of the most significant limiting factors imposed by observational studies, as it can be introduced through several routes, for example, physician or patient treatment preferences; underlying comorbid conditions of patients, which may favor a particular treatment (usually HD); and timing of referral to a nephrologist. In fact, early referral to a nephrologist associates with improved survival of dialysis patients and earlier placement of arteriovenous fistula, which circumvents the use of central venous catheters that associate with worse outcomes in HD patients.

In this issue of JASN, Quinn et al. compare the risk of death between patients treated on PD and HD by analyzing linked provincial administrative health data from Ontario, Canada. Patients were included in the study cohort if they were eligible for the Ontario Health Insurance Plan for at least 2 yr before start of dialysis and had at least one dialysis billing claim between July 1998 and March 2006. For their primary analyses, the authors restricted their cohort to patients with known chronic kidney disease and with a documented nephrologist visit more than 4 mo before initiation of outpatient dialysis. The following steps, restricting the cohort to patients with ideal predialysis care and without uncontrolled comorbid illness that might precipitate an early or emergent dialysis start, were taken to reduce the risk of selection bias. Baseline comorbidities were identified using the Johns Hopkins University Adjusted Clinical Groups Case-Mix System algorithm, a well-validated risk adjustment model. This elective outpatient cohort included 6573 incident dialysis patients, of whom approximately 31% initiated PD and more than 85% had predialysis care for more than 12 mo (median of nine predialysis visits in overall cohort and in both PD and HD subgroups).

Despite these attempts to limit selection bias, compared with HD patients, PD patients were more likely to have disorders of lipid metabolism but significantly less likely to have cardiomyopathy, cancer, osteoporosis, chronic liver disease, or diabetes mellitus. After 24 mo of follow-up, in the unadjusted analysis, the risk of death was significantly lower in PD patients compared with HD patients; however, after adjustment for demographics, comorbidities, history of hospitalization, and number of hospitalization days in the year preceding dialysis initiation, there was no longer a difference in the risk of death between patients treated by PD and HD. Furthermore, the mortality risk did not change over time and results remained robust even after censoring for kidney transplantation in subsequent sensitivity analyses.

To demonstrate the impact of selection bias in the comparison of mortality risk in patients treated with PD versus HD, Quinn et al. conducted more secondary analyses. The authors constructed two other cohorts, an all outpatient dialysis cohort, which included all patients initiating dialysis as an outpatient, and a 90-d cohort, which included only patients alive at 90 d after dialysis initiation. In both of these cohorts, the authors described a significant interaction between diabetes and dialysis modality, with patients with diabetes having a higher risk of death on PD compared with patients without diabetes. Furthermore, the risk of death increased over time in patients with diabetes and also in patients treated on PD, violating the proportional hazards assumption. In the all outpatient dialysis cohort, among patients without diabetes, the risk of death was lower on PD versus HD over the entire follow-up, whereas in patients with diabetes, this lower risk of death on PD compared with HD extended for less than 2 yr. In the 90-d cohort, among patients without diabetes mellitus, this risk of death remained lower in patients treated with PD compared with HD during the 2 yr of follow-up; on the other hand, among patients with diabetes mellitus, this risk remained higher on PD compared with HD throughout the follow-up time. Overall, these secondary analyses reveal results comparable to previous studies using similar cohort definitions.

Different methods have been used by other authors to address this important issue of selection bias, such as stratification of patients by treatment propensity score, restriction of study cohort to patients awaiting renal transplantation, and stratification of HD patients by planned and unplanned HD starts. Recently, Perl et al. confirmed, in a Canadian cohort of incident dialysis patients, that initial type of HD vascular access was an important effect modifier of the relationship between dialysis modality and the risk of death. The authors determined that the detrimental consequences of central venous catheters at initiation of HD largely explained the early lower mortality risk previously attributed to PD. In their study, Quinn et al. were unequivocably able to expose the impact of selection bias in the differential mortality risk between PD and HD patients by using three different methodological approaches. In restricting their primary cohort to patients with predialysis care and elective outpatient initiation of dialysis, the authors minimized the differences between PD and HD patients, making their comparisons more equitable.

Notwithstanding these findings, some note of caution is important. As with all observational studies, the current study is subject to residual confounding and does not prove causation between dialysis modality and the risk of death. These findings may not necessarily be generalizable, as the process of care might be different in other countries, such as the United States, and high-risk minority populations such as African Americans might not have been well represented. While an integrative care approach to modality selection with PD first is not always necessary, in practice, a timely transfer from PD to HD remains advisable in the event of PD technique failure, which is common. Finally, beyond mortality risk, other
important factors such as patient satisfaction and quality of life must be considered in the choice of dialysis treatment. Studies have shown that PD patients have more satisfaction with their overall care compared with HD patients, and that quality of life is better in some domains for PD patients and better in other domains for HD patients. Since there is no conclusive evidence that either PD or HD provide any specific survival advantage, patients should be informed about the above specific tradeoffs and actively participate as early as possible in the decision-making process regarding their choice of dialysis modality.

DISCLOSURES

None.

REFERENCES


Circulating Anti-PLA2R Autoantibodies to Monitor Immunological Activity in Membranous Nephropathy

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Experimental and human data converge to indicate that deposition along the glomerular basement membrane of immunoglobulin...