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Is It Time to Reconsider How We Initiate Maintenance Dialysis?

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Indications for the initiation of kidney replacement therapy are heterogeneous and have evolved over the years since dialysis was provided as a maintenance therapy >50 years ago. The earlier indications, such as significant fluid overload, and substantially altered biochemical measures of critical hyperkalemia or metabolic acidosis, are now replaced by more subjective criteria or simply an estimated glomerular filtration rate less than a specific threshold, usually ≤10 ml/min per 1.73 m^2.[1] Despite the evolving criteria for the decision to start maintenance dialysis, the dialysis prescription at the time of initiation has been very concrete and unchanged, at least for the last several decades. For example, most maintenance hemodialysis (MHD) patients will initiate renal replacement therapy with a thrice-weekly hemodialysis (HD) regimen aimed at minimal single-pool Kt/V of 1.2.[2] Although incremental peritoneal dialysis has been described since the early 90s, its implementation has been sporadic. There are now multiple reports indicating the importance and preference of a more patient friendly and gradual initiation of maintenance dialysis in patients with advanced kidney disease.[3] In addition, in countries where there are significant number of patients with financial constraints, initiation of MHD with 2 session per week schedule is common although this approach heavily relies on physician decision more than having an established approach.[4] In a paper published in this issue of *KI Reports*, Torreggiani *et al.*[5] report their findings regarding incremental HD (iHD) where the approach was standardized to provide sufficient dialytic clearance of uremic solutes and appropriate volume control coupled with escalation of dose frequency as needed determined by clinical assessment.

What Did the Study Reveal?

This was an observational study conducted in a large HD unit in a French Hospital, where iHD was applied as the standard of HD care since 2017. All HD incident patients in 2017 to 2021 were included and stratified into the following 3 groups according to HD start: iHD, where patients received 1 to 2 sessions/wk; decremental HD, when the patients started with 3 sessions/wk and either later reduced to a less frequent basis; and standard HD (sHD), where patients were maintained on 3 sessions/wk. The results were compared with data of all incident MHD patients at the same unit 2 years before the standardization of the incremental program (2015–2017) and started HD 3 times a week. The investigators also compared the outcomes with a propensity score-matched cohort from the French Renal Epidemiology and Information Network registry. The primary outcome of this study was mortality for all comparisons. The investigators also assessed morbidity and costs associated with different initiation groups as exploratory outcomes.

Because the study reflected actual clinical care, the choice of when and how to start HD was based on laboratory evaluation and clinical condition, such as fluid status, presence or absence of uremic symptoms, and blood pressure control. Same criteria were used to decide whether to increase dialysis frequency or not. Of 158 patients who were initiated on HD during 2017 to 2021, 91 (57.6%) started with an iHD schedule, 14 (8.9%) started with sHD and decreased the number of sessions, and 53 (33.5%) started and continued with sHD prescription. One year after iHD start, approximately half of the patients were still on an iHD schedule and approximately 35% were still on a once- or twice-weekly schedule at 2 years. When comparing these cohorts, it was found that patients who started and continued with

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sHD had a lower estimated glomerular filtration rate at start versus patients on iHD and decremental HD. Patients who started iHD had more often follow-up in the predialysis care unit, were more likely to have had a planned dialysis start, and were less frequently hospitalized when initiating on MHD compared with sHD. Initial HD prescriptions were not associated with survival differences in 2017 to 2021 period. During the period 2017 to 2021, no differences were found on the number of hospitalizations ($P = 0.24$) after the start of dialysis. The iHD-decremental HD policy allowed a 16% cost saving, even accounting for supplemental biochemical tests.

When comparing the iHD cohort to patients who started HD between 2015 and 2017, it was found that patients initiating dialysis in the earlier years had less comorbidities and were more likely to begin MHD during hospitalization (86.8% vs. 73.2%, $P = 0.017$) compared with those starting HD between 2017 and 2021. No mortality differences were found between cohorts. After propensity score matching with patients selected from the French Renal Epidemiology and Information Network registry, no differences in survival were observed comparing all patients who started HD at the study center versus other centers in the region.

The results here reported could be compared with the data found by other authors; for example, Vilar *et al.*[6] performed a multicenter feasibility randomized controlled trial in United Kingdom and evaluated the benefits of iHD against sHD. The patients on this study received either high-flux HD or hemodiafiltration with a minimum adequacy target of 2.0 standard Kt/V_{TOTAL} and the HD dose was adjusted because the residual kidney function was lost maintaining a minimum standard Kt/V of 2.0 in contrast of this study where they adjusted the HD dose using clinical and laboratory data. In the study of Vilar *et al.*,[6] the residual kidney function was measured monthly using urea clearance as distinct from that of Torregiani where they used β2-microglobulin level for the evaluation of residual kidney function. Their results reveal that 92% of iHD patients had a urea clearance of $\geq$2 ml/min per 1.73 m^2 at 6 months, with less serious adverse events (incidence rate ratio 0.47, CI: 0.27–0.81). No differences in mortality were found.[6]

Why Is the Study Important and What Are the Future Implications?

This study highlights some important aspects of incremental dialysis. First, it is feasible to offer this strategy as an option to patients considering initiation of renal replacement therapy. Furthermore, in this select cohort and controlled environment, iHD does not result in an obvious increase on mortality or major abnormalities in electrolyte concentrations. This study also highlights the importance of the predialysis care because this was an important determinant for choice of iHD by patients. However, these observations should be considered with caution because this was an observational study with a small number of patients and need to be studied in other populations to confirm its safety and generalizability. Whether standardizing the incremental through protocols for widespread implementation remains as another important clinical question that must be studied further. Finally, additional research is needed to resolve some questions, such as whether residual kidney function be preserved for a long time with iHD, what are the circumstances that would compare iHD to incremental peritoneal dialysis and if incremental dialysis (HD or peritoneal dialysis) were implemented in developing countries, and what would be the impact on mortality, morbidity, and health care systems?

DISCLOSURE

TAI is a consultant to Fresenius Kidney Care. DAM declared no competing interests.

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