Treatment frequency and mortality among incident hemodialysis patients in the United States comparing incremental with standard and more frequent dialysis

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Most patients with end-stage renal disease in the United States are initiated on thrice-weekly hemodialysis (HD) regimens. However, an incremental approach to HD may provide several patient benefits. We tested whether initiation of incremental HD does or does not compromise survival compared with a conventional HD regimen. The survival of 434 incremental, 50,162 conventional, and 160 frequent HD patients were compared using Cox regression analysis after matching for demographic and comorbid factors in a longitudinal national cohort of adult incident HD patients enrolled between January 2007 and December 2011. Sensitivity analysis included adjustment for residual kidney function. After adjustment for residual kidney function, all-cause mortality was not significantly different in the incremental compared with conventional HD group (hazard ratio 0.88, 95% confidence interval 0.72–1.08), but was higher in the frequent compared with the conventional HD group (hazard ratio, 1.56, 95% confidence interval 1.21–2.03). The comorbidity burden modified the association of treatment frequency and mortality, with higher comorbidity associated with higher mortality in the incremental HD group (hazard ratio, 1.77, 95% confidence interval 1.20–2.62) for a Charlson Comorbidity Index of ≥5. Thus, among incident HD patients with low or moderate comorbid disease, survival was similar for patients initiated on an incremental or conventional HD regimen. Clinical trials are needed to examine the safety and effectiveness of incremental HD and the selected patient populations who may benefit from an incremental approach to HDs initiation.

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In the United States, there are >450,000 prevalent patients with end-stage renal disease treated with maintenance dialysis, with ~114,800 patients who newly initiated hemodialysis (HD) as of 2012.[1] Most HD patients are conventionally prescribed a standard thrice-weekly schedule with little individualization of the initial HD regimen.[2–4] Dialysis patients have a 6 to 8 times higher mortality risk than age-matched Medicare patients in the general population,[1] with the highest risk observed during the first 6 months after HD initiation.[5] Many potential risk factors may explain this early high mortality, such as a lack of predialysis nephrology care, a lack of permanent vascular accesses, and preexisting cardiovascular disease or other coexisting medical illnesses.[6] However, the impact of an abrupt transition to a "full-dose" thrice-weekly HD regimen versus a gradual transition by incrementally increasing the HD prescription over several months on mortality risk has not been examined in controlled trials. Randomized, controlled trials of a higher dialysis dose or frequency have shown inconsistent results[7–12] and may accelerate residual kidney function (RKF) decline.[13]

An incremental approach to HD initiation may offer many potential benefits to patients, including better preservation of an arteriovenous fistula, reduced cost, and preservation of RKF. Less frequent (i.e., twice weekly) HD has been associated with greater preservation of RKF after initiation of HD,[14–16] and higher RKF is associated with better patient survival in both PD and HD patients.[17,18] Preservation of RKF may play a key role in the potential association of less frequent HD and survival. This may be of particular importance among incident HD patients because many patients have substantial RKF when transitioning to end-stage renal disease.[16]

We examined a 5-year nationally representative cohort of incident HD patients to determine the outcome of mortality with a conventional HD treatment regimen compared with incremental or frequent HD regimen. We hypothesized that initiation of HD with an incremental approach does not compromise survival compared with a conventional HD regimen.

RESULTS

Baseline patient characteristics of entire and matched cohorts

The final entire study cohort comprised of 87,718 patients from 1737 facilities including 682 incremental (twice weekly or less) HD patients from 444 facilities and 201 frequent (≥4 times weekly) HD patients from 158 facilities (Supplementary Table S1). Compared with the conventional HD patients, the incremental HD patients tended to be older and non-Hispanic white and to have less comorbid burden, whereas the frequent HD patients tended to be younger, male, and non-Hispanic white and to have higher likelihood of having a central venous catheter and a higher comorbid burden (standardized difference >0.1). The final matched cohort included 434 incremental HD patients, 50,162 conventional HD patients, and 160 frequent HD patients (Table 1). Even after matching based on age, sex, race, ethnicity, Charlson

Table 1 | Baseline characteristics by treatment regimen in the matched cohort of 50,756 incident HD patients

Variable	Conventional HD, % n = 50,162	Frequent HD, % n = 160	Std. Diff.	Incremental HD, % n = 434	Std. Diff.
Charlson Comorbidity Index	3 (IQR, 2–4)	3 (IQR, 3–4)	0.03	3 (IQR, 3–4)	0.01
2 (renal disease only)	24	24	0	24	0
3–4	62	62	0	62	0
5	7	7	0	7	0
6	6	6	0	6	0
≥7	1	1	0	1	0
Age (yr)	63 ± 13	62 ± 14	0.06	64 ± 13	0.04
Male (%)	65	65	0	65	0
Race (%)					
Non-Hispanic white	58	58	0	58	0
Non-Hispanic black	29	29	0	29	0
Others	12	12	0	11	0.02
Medicare as primary insurance (%)	54	53	0.03	49	0.10
Central venous catheter use (%)	84	84	0	84	0
Primary disease (%)					
Diabetic nephropathy	49	46	0.06	43	0.11
Hypertensive nephrosclerosis	28	21	0.17	29	0.01
Glomerulonephritis	8	14	0.17	11	0.09
Polycystic kidney disease	1	1	0.05	3	0.11
Others	13	19	0.15	14	0.03
Comorbidities (%)					
Cardiovascular disease	28	36	0.18	31	0.06
Fluid overload	6	64	>0.9	7	0.03
Body mass index (kg/m^2)	26.8 (IQR, 23.1–31.9)	30.6 (IQR, 24.6–37.6)	0.38	26.3 (IQR, 22.8– 30.5)	0.17
Postdialysis body weight (kg)	77 (IQR, 65–92)	91 (IQR, 70–116)	0.36	77 (IQR, 64–91)	0.15
Weekly %IDWG	7.7 ± 3.5	9.5 ± 3.8	0.50	5.8 ± 3.2	0.54
Single-pool Kt/V	1.38 ± 0.30	1.27 ± 0.34	0.37	1.36 ± 0.33	0.09
Renal CL_{urea} (ml/min per 1.73 m^2)	3.1 (IQR, 1.8–4.8)	1.9 (IQR, 1.3–3.2)	0.48	5.4 (IQR, 3.1–.3)	0.88
Laboratory variables					
Hemoglobin (g/dl)	11.3 ± 1.2	10.6 ± 1.1	0.58	11.0 ± 1.2	0.24
Albumin (mg/dl)	3.54 ± 0.45	3.47 ± 0.44	0.18	3.56 ± 0.52	0.04
Creatinine (mg/dl)	5.9 ± 2.3	5.7 ± 2.6	0.07	4.4 ± 2.0	0.68
Calcium (mg/dl)	9.1 ± 0.6	9.0 ± 0.4	0.14	9.1 ± 0.5	0.01
Phosphorus (mg/dl)	5.0 ± 1.2	4.8 ± 1.3	0.12	4.3 ± 1.0	0.62
Intact PTH (pg/ml)	321 (IQR, 205–492)	275 (IQR, 187–443)	0.20	253 (IQR, 321–427)	0.24
Iron saturation (%)	23 ± 9	19 ± 7	0.49	23 ± 10	0.05
Ferritin (pg/nl)	270 (IQR, 158– 460)	256 (IQR, 138–418)	0.10	287 (IQR, 270– 511)	0.11
Bicarbonate (mmol/l)	23.7 ± 2.8	24.1 ± 2.7	0.13	24.3 ± 3.2	0.19

CL_{urea}, urea clearance; HD, hemodialysis; %IDWG, percentage of interdialytic weight gain; IQR, interquartile range; PTH, parathyroid hormone; Std. Diff., standardized difference.

Values are expressed as mean ± SD, median (IQR), or percentage, as appropriate. Data are based on weighted match according to age, sex, race, central venous catheter as vascular access, and the Charlson Comorbidity Index.

Data on laboratory tests were extracted during the first 91 days of dialysis, and those except for ferritin and iPTH were further restricted to the initial thrice-weekly HD period before starting infrequent or frequent HD.

Standardized differences were calculated against the conventional HD group; 0.8, 0.5, and 0.2 were considered large, medium, and small differences, and ≥0.1 was defined as meaningful imbalance.

The frequency of missing data was <2% for most laboratory tests, except for iron saturation (3%), creatinine (6%), and renal CL_{urea} (62%).

Conversion factors for units: albumin and hemoglobin in g/dl to g/l, 10; creatinine in mg/dl to mmol/l, 88.4; calcium in mg/dl to mmol/l, 0.2495; phosphorus in mg/dl to mmol/l, 0.3229. No conversion was necessary for ferritin in ng/ml and mg/l.