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Twice-Weekly Hemodialysis and Clinical Outcomes in the China Dialysis Outcomes and Practice Patterns Study

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Introduction: In China, a quarter of patients are undergoing 2-times weekly hemodialysis. Using data from the China Dialysis Outcomes and Practice Patterns Study (DOPPS), we tested the hypothesis that whereas survival and hospitalizations would be similar in the presence of residual kidney function (RKF), patients *without* RKF would fare worse on 2-times weekly hemodialysis.

Methods: In our cohort derived from 15 units randomly selected from each of 3 major cities (total N = 45), we generated a propensity score for the probability of dialysis frequency assignment, estimated a survival function by propensity score quintiles, and averaged stratum-specific survival functions to generate mean survival time. We used the proportional rates model to assess hospitalizations. We stratified all analyses by RKF, as reported by patients (urine output <1 vs. ≥1 cup/day).

Results: Among 1265 patients, 123 and 133 were undergoing 2-times weekly hemodialysis with and without evidence of RKF. Over 2.5 years, adjusted mean survival times were similar for 2- versus 3-times weekly dialysis groups: 2.20 versus 2.23 and 2.20 versus 2.15 for patients with and without RKF ($P = 0.65$). Hazard ratios for hospitalization rates were similar for 2- versus 3-times weekly groups, with (1.15, 95% confidence interval = 0.66−2.00) and without (1.10, 95% confidence interval 0.68−1.79]) RKF. The normalized protein catabolic rate was lower and intradialytic weight gain was not substantially higher in the 2- versus 3-times weekly dialysis group, suggesting greater restriction of dietary sodium and protein.

Conclusion: In our study of patients in China's major cities, we could not detect differences in survival and hospitalization for those undergoing 2- versus 3-times weekly dialysis, regardless of RKF. Our findings indicate the need for pragmatic studies regarding less frequent dialysis with associated nutritional management.

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The use of 2-times weekly hemodialysis, although rare in high-income countries, is widely practiced in low- and middle-income countries with growing hemodialysis populations. Many nephrologists consider this practice suboptimal due to the theoretically poorer volume, electrolyte, and time average urea concentration control[1,2]; a prescription of <3-times weekly hemodialysis was not considered in the original studies that set dialysis adequacy standards.[3,4]

Two observational studies of patients undergoing 2-times weekly versus more frequent hemodialysis reported similar survival,[5,6] and among patients just starting dialysis, 2 studies additionally suggested better preservation of residual kidney function (RKF).[7,8] The most recent U.S. National Kidney Foundation/Kidney Disease Outcome Quality Initiative guidelines imply that 2-times weekly hemodialysis may be acceptable in

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patients with substantial residual function as long as they meet a weekly standardized Kt/V target of 2.0 or above.[9]

In China, nearly a quarter of patients on hemodialysis are undergoing 2-times weekly frequency of hemodialysis.[6,10] Data from the pilot China Dialysis Outcomes and Practice Patterns Study (DOPPS) indicate that both favorable clinical characteristics (e.g., absence of diabetes and coronary artery disease) as well as economic constraints (e.g., insurance and employment status) correlate with the decision to pursue less frequent dialysis.[10] Notably, a majority, but not all, of the patients undertaking 2-times weekly hemodialysis report presence of residual function.

Using longitudinal data from the China DOPPS, we evaluated survival and hospitalizations on 2- versus 3-times weekly hemodialysis. Given the theoretical advantage of RKF in mitigating putatively poorer solute clearance and volume control with use of less frequent hemodialysis,[11,12] we tested the hypothesis that survival and hospitalizations on 2-times weekly hemodialysis would be similar to those for 3-times weekly hemodialysis in the presence of RKF, but that patients *without* RKF would fare worse on 2-times weekly hemodialysis.

METHODS

Patients and Data Collection

The DOPPS is an international prospective cohort study of prevalent adult patients on hemodialysis.[13] Due to feasibility considerations and availability of registry information, the China DOPPS has been limited to representative data from the metropolitan areas in the 3 largest cities in China (Beijing, Guangzhou, and Shanghai). In each metropolitan area, we randomly selected 15 hemodialysis facilities (N = 45) from a comprehensive roster of hemodialysis units in the 3 cities. The study coordinators abstracted dialysis prescription, laboratory values, and medications at study enrollment and yearly thereafter. We also collected hospitalizations and reasons for departure from the study (including death, transplant, dialysis modality change, facility transfer, etc.) for the duration of the study. We restricted this analysis to data from China DOPPS phase 5 (2012−2015).

Of the 1427 patients with available medical questionnaire data, 87 patients were excluded from the current analysis because they were missing either urine output or frequency assignment data, or received 4-times weekly or more frequent hemodialysis. We also excluded patients in facilities without at least 1 reported death and 1 reported hospitalization (n = 75 patients), yielding an overall analytic cohort of 1265 patients. RKF in the China DOPPS is self-reported and is defined as the presence of urine output of ≥1 cup (≥200 ml) per day. Since patients with end-stage kidney disease are unable to produce concentrated urine (i.e., they are isosthenuric), we assumed that a volume of < 200 ml/day could not contribute to substantial RKF.

Statistical Analysis

We used means and SDs, or proportions as appropriate to characterize the demographics, comorbidities, and laboratory values of participants. We calculated weekly standardized dialysis Kt/V and nPCR[14,15] (Supplementary Table S1). We stratified all analyses by presence of RKF. Our primary outcomes of interest were all-cause mortality and recurrent hospitalizations, and the primary predictor of interest was 2- versus 3-times weekly hemodialysis. To contrast the 2- versus 3-times weekly hemodialysis groups for all-cause mortality, we compared survival curves in a flexible, nonparametric manner. Because nonparametric methods do not easily lend themselves to covariate adjustment, we accounted for covariate imbalance using propensity score stratification.

We first extracted all variables that had an association ($P < 0.10$) with dialysis frequency prescription in the univariable logistic regression model (Supplementary Table S2). We then estimated the propensity score using a multivariable logistic regression model that also included age and sex. We stratified patients into quintiles of propensity score.

To confirm the balance of all covariates listed in Table 1 between the 2 frequency groups after propensity score stratification, we used linear (for continuous covariates) and logistic (for binary covariates) regressions. In each regression model, the covariate of interest was the dependent variable, and independent variables included propensity score quintiles and interaction terms between propensity score quintiles and dialysis frequency. Significance of these interaction terms would provide evidence of imbalance, so we tested whether interaction terms from regression models were non-zero.

We generated survival functions by first estimating a survival function in each propensity score quintile for each dialysis frequency group. To mitigate survival bias from our cohort of prevalent patients, we adjusted for dialysis vintage in the survival model and estimated survival curves at vintage = 0. We then averaged the stratum-specific survival functions to generate the overall survival function for each dialysis frequency. We compared the area under each curve, which corresponds to the average years lived within the total 2.5 years of follow-up. To test the null hypothesis that the difference in mean survival times is equal to 0 in