

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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KEYWORDS: dialysis frequency; dialysis provision in low-resource settings; outcomes on hemodialysis; 2-times weekly hemodialysis

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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

Table 1. Patient characteristics according to urine output and frequency of dialysis

Patient characteristics	Urine output ≥1 cup/day		Urine output <1 cup/day	
	2-Times weekly	3-Times weekly	2-Times weekly	3-Times weekly
Patients, n	123	290	133	719
Demographics				
Age, yr	61.3 (15.6)	58.2 (15.1)	57.7 (15.2)	60.0 (14.7)
Male, %	57%	60%	50%	54%
Time on dialysis, yr	1.70 (1.97)	1.89 (2.44)	3.45 (3.36)	5.38 (4.87)
Time on dialysis <1 yr, %	54%	54%	28%	15%
Insurance coverage <90%	44%	29%	57%	29%
Body mass index, kg/m ²	21.6 (3.0)	22.6 (4.0)	21.0 (3.0)	21.7 (3.7)
Postdialysis weight, kg	58.6 (9.8)	62.0 (12.7)	56.4 (9.9)	59.2 (11.5)
Urine output per day, % ^a				
200–500 ml	35%	60%	—	—
500–1000 ml	48%	29%	—	—
>1000 ml	17%	11%	—	—
Travel time to facility <1 h, %	81%	86%	70%	81%
Facility size (#HEMODIALYSIS pts)	109 (89)	107 (102)	136 (71)	130 (99)
Dialysis prescription				
Standardized dialysis Kt/V	1.38 (0.23)	2.07 (0.27)	1.47 (0.17)	2.12 (0.25)
eKt/V, per session	1.18 (0.35)	1.14 (0.25)	1.30 (0.27)	1.18 (0.25)
Intradialytic weight loss, kg	1.71 (1.11)	2.00 (1.02)	2.61 (1.10)	2.37 (0.83)
Dialysis session length, min	244 (31)	236 (15)	253 (26)	239 (14)
Ultrafiltration rate, ml/h per kg	8.15 (5.55)	8.60 (4.43)	11.8 (4.9)	10.6 (3.7)
Catheter use, %	21%	18%	9%	10%
Comorbidities, %				
Coronary heart disease	17%	29%	17%	31%
Cancer	8%	5%	2%	3%
Other cardiovascular disease	13%	17%	17%	25%
Cerebrovascular disease	7%	15%	17%	17%
Congestive heart failure	19%	26%	25%	24%
Diabetes	15%	38%	21%	27%
GI bleeding	1%	4%	2%	3%
Hypertension	90%	91%	85%	86%
Peripheral arterial disease	6%	12%	5%	10%
Laboratory values				
Hemoglobin, g/dl	10.1 (2.0)	10.4 (1.9)	10.1 (1.8)	10.8 (1.8)
Albumin, g/dl	3.85 (0.57)	3.88 (0.48)	4.00 (0.42)	3.90 (0.45)
Creatinine, mg/dl	9.95 (3.70)	9.54 (3.61)	12.2 (3.9)	10.4 (3.1)
nPCR, g urea nitrogen/kg/d	0.60 (0.18)	0.76 (0.27)	0.66 (0.22)	0.78 (0.26)
Sodium, mEq/l	140 (4)	139 (4)	139 (3)	139 (4)
Potassium, mEq/l	5.07 (0.88)	4.96 (0.85)	5.43 (0.89)	4.97 (0.77)
Bicarbonate, mEq/l	20.1 (4.1)	21.5 (3.7)	20.2 (4.9)	21.9 (3.7)
Patient-reported quality of life				
Physical component summary (PCS) score	40.8 (11.0)	40.3 (9.9)	39.2 (10.2)	38.1 (10.3)
Mental component summary (MCS) score	42.8 (8.8)	42.9 (9.2)	40.8 (10.1)	42.7 (10.3)

GI, gastrointestinal; nPCR, normalized protein catabolic rate.

^aUrine output categories are abstracted from patient charts but are as reported by patients, not measured; therefore, these were not included in the analytical models. Mean values are shown with SDs in parentheses.

the 2- versus 3-times weekly groups, we used bootstrapping with 1000 replicates to calculate the *P* value.

For hospitalizations, we used the proportional rates model to assess the relationship between frequency and recurrent hospitalizations, adjusted for all covariates listed in Table 1 and accounting for facility clustering by using robust sandwich-type covariance estimators.¹⁶ We used the proportional rates model in order to include multiple hospitalizations for each patient and

to account for time between hospitalizations, expressing the effects as rate ratios of hospitalizations comparing 2- versus 3-times weekly dialysis.

Although our nonparametric method for comparing all-cause mortality allowed us to fit a flexible model without relying on the tenuous proportional hazards assumption, we performed sensitivity analyses using the Cox proportional hazards model. We also used the Cox proportional hazards model in sensitivity analyses to

assess the relationship between frequency of dialysis and time to first hospitalization, disregarding all subsequent hospitalizations. We retained the stratification by RKF in these models, accounting for facility clustering and incrementally adjusting for patient demographics, insurance status, comorbidities, intradialytic weight loss, and laboratory values.

Overall, missingness for covariates considered in the modeling was low (e.g., <5% for the majority of covariates; <20% for all covariates). For missing data, we used the Sequential Regression Multiple Imputation Method implemented by IVEware¹⁷ and analyzed using the MIAnalyze procedure in SAS/STAT 9.4. We used SAS 9.4 (SAS Institute, Cary, NC) for all analyses. All presented data incorporate multiple imputation.

RESULTS

Table 1 lists characteristics of patients at enrollment in the China DOPPS study, stratified by RKF and frequency of hemodialysis. In general, patients with evidence of RKF had shorter vintage on dialysis and had less intradialytic weight loss. These patients also had a higher frequency of catheter use and were dialyzing in somewhat smaller facilities.

Comparing patients on 2- versus 3-times weekly dialysis within each RKF category revealed the following differences: (i) a higher frequency of <90% insurance coverage; (ii) lower standardized dialysis Kt/V and shorter weekly treatment time; and (iii) a lower frequency of diabetes and coronary heart disease in the 2-times weekly groups.

Electrolyte values were similar across the groups, except for slightly higher mean potassium values in the 2-times weekly group compared with the 3-times weekly group without RKF. The normalized protein catabolic rate (nPCR) was on average <1 g/kg per day for all 4 groups, but consistently lower in the 2-times weekly than in the 3-times weekly groups. Intradialytic weight loss was similar within RKF categories. Finally quality of life, assessed using the Medical Outcomes Study Short Form-12, demonstrated similar scores on the Physical Component Summary (PCS) score for all 4 groups, but lower scores on the Mental Component Summary (MCS) score for the 2-times weekly hemodialysis group without RKF.

Mortality According to Frequency Prescription

Mortality for all patients in our study was 92 per 1000 patient-years (95% confidence interval [CI] = 80–106). The rate was lower in the group with evidence of RKF when compared with the group without RKF: 80 (95% CI = 56–110) versus 98 (95% CI = 81–118) deaths in 3-times weekly dialysis, and 87 (95% CI = 50–142) versus 90 (95% CI = 55–139) deaths in

2-times weekly dialysis, per 1000 patient-years (Supplementary Table S3). Rate and reasons for departure from the DOPPS were similar in the 2 frequency groups (Supplementary Table S4). Unadjusted survival in the dialysis frequency groups stratified by category of RKF did not differ appreciably (Figure 1).

The propensity score analysis accounting for the characteristics associated with prescription of 2- versus 3-times weekly dialysis and stratified by RKF demonstrated similar survival among the 2 frequency groups (Figure 2). Supplementary Table S2 lists the covariates included in the propensity scores; for both RKF groups, covariates were balanced between 2 frequency assignments after taking into account propensity score quintiles.

After adjusting for the propensity score quintiles and vintage on dialysis, for patients with RKF, area under the survival curves was 2.23 for 3-times versus 2.20 for 2-times weekly dialysis assignment over the 2.5 years of follow-up. For patients without RKF, area under the survival curves was also similar: 2.15 for 3-times versus 2.20 for 2-times dialysis weekly assignment.

The Cox proportional hazards model results, adjusting for patient demographics, category of RKF, vintage on dialysis, insurance status, and

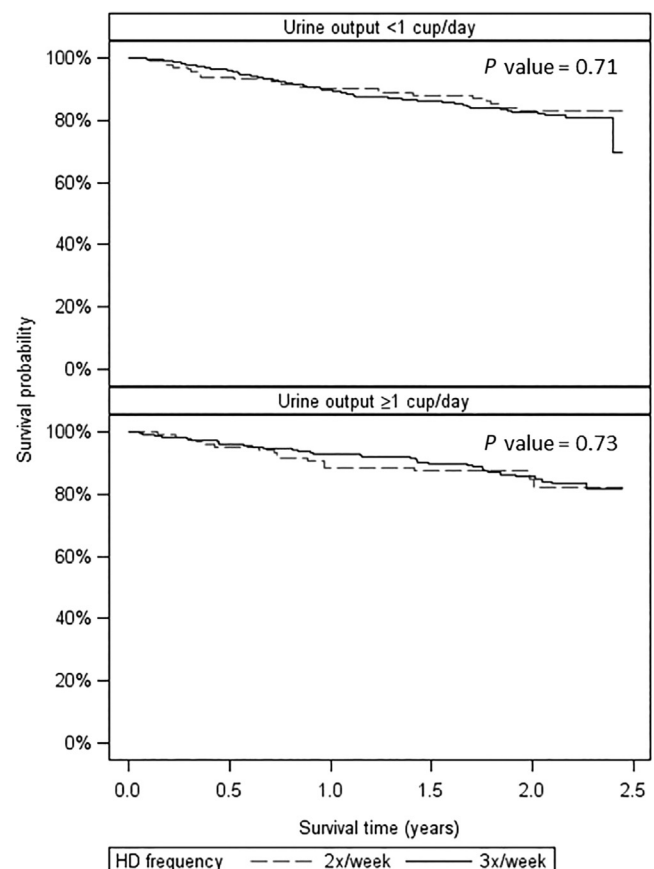


Figure 1. Unadjusted survival curves for 2-times weekly versus 3-times weekly dialysis, by urine output. HD, hemodialysis.

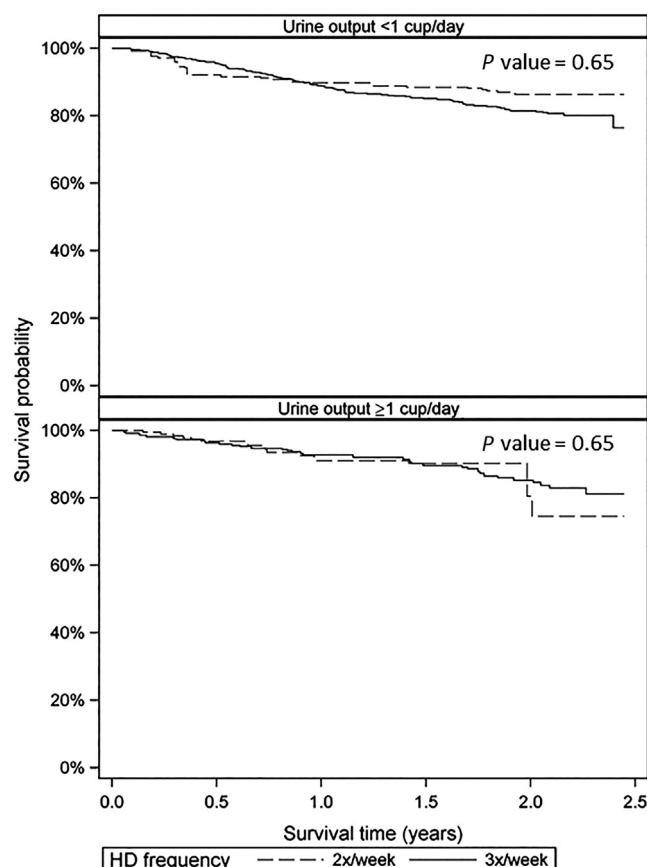


Figure 2. Survival curves adjusted for propensity of dialysis frequency and vintage for 2-times versus 3-times weekly dialysis, by urine output. HD, hemodialysis.

comorbidities, are shown in Table 2. Again we did not find any difference in patient survival according to frequency of dialysis after these adjustments and after stratification by RKF. Few patients ($n = 96$) switched frequency assignment during the follow up period; a majority among these (65%) switched from 2-times weekly to 3-times weekly dialysis. In sensitivity analyses censoring patients who had switched dialysis

Table 2. Hazard ratios for mortality for 2-times weekly versus 3-times weekly dialysis, by urine output

Two-times weekly (vs. 3-times weekly)	Urine output			
	≥1 cup/d (N=413)		<1 cup/d (N=852)	
	HR (95% CI)	P	HR (95% CI)	P
Model 1: unadjusted ^a	1.09 (0.60–1.99)	0.77	0.93 (0.61–1.42)	0.73
Model 2: model 1+patient demographics ^b	0.96 (0.53–1.74)	0.89	1.12 (0.71–1.76)	0.63
Model 3: model 2+ vintage ^c	0.95 (0.53–1.71)	0.87	1.12 (0.72–1.76)	0.61
Model 4: model 3+insurance	0.89 (0.49–1.60)	0.69	1.05 (0.69–1.60)	0.80
Model 5: model 4+comorbidities	1.15 (0.66–2.00)	0.63	1.10 (0.68–1.79)	0.70

CI, confidence interval; HR, hazard ratio.

N = 190 events overall ($n = 53$ in patients with urine output ≥ 1 cup/d; $n = 137$ in patients with urine output < 1 cup/d).

^aAccounting for facility clustering.

^bAge, sex, and body mass index.

^cInteraction P value between twice-weekly dialysis and vintage > 0.08 for overall and by urine output models.

frequency ($n = 41$ [9.9%] for the RKF group and $n = 55$ [6.5%] for the group without RKF), we obtained similar results (not shown) for the relationship between frequency of dialysis and mortality.

Hospitalization and Other Outcomes According to Frequency Prescription

In the group with RKF, hospitalization rate was slightly lower for patients with 3-times weekly dialysis, whereas in the group with RKF, hospitalization rate was substantially lower for patients with 2-times weekly dialysis (Supplementary Table S3). When evaluating causes of hospitalization, we did not see higher heart failure or fluid overloaded hospitalization rates in the 2-times weekly dialysis group (Supplementary Table S5). After adjustment for patient demographics, insurance status, and comorbidities, there was no difference in the number of hospitalizations experienced by patients by dialysis frequency assignment, regardless of RKF (Table 3). Time to first hospitalization (Cox model) was also consistent (Table 4).

DISCUSSION

In our multicity study of prevalent patients on hemodialysis in China's major cities, we found that patients on 2-times weekly dialysis have similar survival and hospitalization compared with patients on 3-times weekly dialysis. We had hypothesized that RKF would be an important modifier of the relationship between frequency prescription and outcomes. However, we found no difference in survival between the 2- and 3-times weekly dialysis groups, even among patients without RKF.

Table 3. Rate ratios for inpatient hospitalizations for 2-times weekly versus 3-times weekly dialysis, by urine output

Two-times weekly (vs. 3-times weekly)	Urine output			
	≥1 cup/d (N=413)		<1 cup/d (N=852)	
	RR (95% CI)	P	RR (95% CI)	P
Model 1: unadjusted ^a	0.72 (0.53–0.97)	0.03	0.70 (0.51–0.97)	0.03
Model 2: model 1+patient demographics ^b	0.67 (0.48–0.94)	0.02	0.75 (0.53–1.06)	0.10
Model 3: model 2+ vintage	0.67 (0.48–0.95)	0.02	0.74 (0.52–1.05)	0.09
Model 4: model 3+insurance	0.67 (0.48–0.94)	0.02	0.74 (0.52–1.05)	0.10
Model 5: model 4+comorbidities	0.72 (0.50–1.02)	0.06	0.79 (0.57–1.09)	0.15
Model 6: model 5+intradialytic weight loss ^c	0.71 (0.50–1.02)	0.06	0.79 (0.57–1.09)	0.16
Model 7: model 6+labs (Hgb, albumin)	0.69 (0.49–0.98)	0.04	0.78 (0.57–1.09)	0.14

CI, confidence interval; labs, laboratory values; RR, risk ratio.

N = 1019 events overall ($n = 308$ in patients with urine output ≥ 1 cup/d; $n = 711$ in patients with urine output < 1 cup/d).

^aAccounting for facility clustering.

^bAge, sex, and body mass index.

^cAverage intradialytic weight loss for the most recent 3 (or 2) sessions before study enrollment.

Table 4. Hazard ratios for first in-patient hospitalization for 2-times versus 3-times weekly dialysis, overall and by urine output

Two-times weekly (vs. 3-times weekly)	Urine output			
	≥1 cup/d (N=413)		<1 cup/d (N=852)	
	HR (95% CI)	P	HR (95% CI)	P
Unadjusted ^a	1.08 (0.74–1.57)	0.71	0.76 (0.47–1.22)	0.26
Adjusted model ^b	1.06 (0.66–1.73)	0.80	0.69 (0.44–1.09)	0.11

CI, confidence interval; HR, hazard ratio.

N = 548 events overall (n = 175 in patients with urine output ≥1 cup/d; n = 373 in patients with urine output <1 cup/d).

^aAccounting for facility clustering.^bAge, sex, body mass index, vintage, insurance, comorbidities, average intradialytic weight loss, and laboratory values (Hgb, albumin).

Our data indicating equivalent survival in the 2- and 3-times weekly dialysis groups *with* evidence of RKF are consistent with a majority of^{5,6}, but not all,¹⁸ observational studies. In an analysis of 1288 patients from the Shanghai Dialysis Registry, Lin *et al.* reported equivalent survival in the 2- versus 3-times weekly dialysis groups,⁶ although the authors did not account for underlying RKF in their analysis. Similarly, when Hanson *et al.*⁵ evaluated outcomes by frequency among more than 15,000 patients in the 1993 Dialysis Morbidity and Mortality Study in the United States, patients on 2-times weekly dialysis did not fare worse than patients on 3-times weekly dialysis.

In the United States, under the assumption that, at the start of dialysis, the presence of RKF protects against complications of less frequent dialysis, the practice of “incremental dialysis” for patients just starting dialysis has been under recent investigation. Obi *et al.* evaluated outcomes in patients starting dialysis at a 2-times weekly hemodialysis for the first 6 weeks.⁸ In an incident cohort of 351 patients (who had survived for 1 year) matched with 8068 patients on ≥3-times weekly hemodialysis, the authors noted that in patients with urea clearance of >3 ml/min per 1.73 m², survival was similar (hazard ratio = 0.99; 95% confidence interval = 0.76–1.28) on the incremental prescription. Furthermore they reported better preservation of markers of RKF with the incremental prescription, presenting support for the argument that the dialysis session itself may accelerate loss of RKF, although the totality of evidence on this issue remains mixed.¹ After evaluating ultrafiltration rates and weekly standardized Kt/V of 410 patients new to dialysis, Chin *et al.* reported that more than one-half of patients with substantial RKF (e.g., >700 ml/d) would be appropriate candidates for incremental 2-times weekly dialysis.¹⁹

But what about patients undergoing less frequent dialysis in the absence of RKF? Even though this practice is common in many resource-constrained countries, our study is 1 of the largest to report data on patients without RKF prescribed 2-times weekly hemodialysis (10% of our total cohort, on dialysis for

an average of 3.5 years). We postulate 3 potential explanations for the counterintuitive finding that this group’s survival and hospitalization rate were similar to those of the 3-times weekly group: (i) residual confounding by indication; (ii) misclassification of true RKF; and (iii) stricter diet restriction among the patients on 2-times weekly hemodialysis. Residual confounding, that is, inability to adjust for all the differences between the groups assigned 2- versus 3-times weekly dialysis, remains a consideration in any observational study. However, we attempted to address this by creating a propensity score that resulted in a more balanced distribution of the measured covariates.

Misclassification of our patient-reported dichotomous RKF variable remains a possibility. We abstracted presence of urine output (yes/no, based on urine output of ≥1 cup or <1 cup [200 ml]/d) from the patient record. Although measured urine collections would have been preferred, 24-hour urine collections are not common in any DOPPS region and even less common in China. A small fraction of patients are asked by their medical team to undertake timed urine collections, and patients with available data are likely to be nonrepresentative, as patients who have negligible urine volumes are rarely asked for timed urine volume measurements. Our recent analyses also demonstrate a strong correlation between patient-reported and measured 24-hour urine collections, and with outcomes including mortality.²⁰

We had anticipated that the 2-times weekly frequency assignment in patients who self-report minimal RKF would lead to higher rate of hospitalizations, as these patients, no matter how healthy, would theoretically run into complications related to the longer interdialytic interval, such as fluid overload and/or electrolyte disturbances. We did not find strong evidence for this, although there was mild hyperkalemia and higher ultrafiltration rates in the group on 2-times weekly dialysis frequency without RKF. Considering the longer interdialytic period, weight gain was not substantially higher in the 2- versus 3-times weekly group without RKF. In terms of protein restriction, although nPCR was low in all patients, patients on 2-times weekly dialysis frequency with and without RKF had lower values than those on the 3-times weekly frequency. This suggests that patients in the 2-times weekly group were self-restricting or more closely following instructions for salt and protein restriction. The implications of this dietary management on markers of nutrition, muscle mass, and functional status, and of the higher ultrafiltration rates on cardiovascular rates, require further study.

Based on our prior comparison of the characteristics of persons undergoing dialysis in China in comparison with the United States, Australia, New Zealand, and Western Europe, patients in China were younger, had a

lower mean body mass index, and had a lower comorbidity burden.¹⁰ This may imply that patients in China therefore can better sustain this lower frequency than patients dialyzing in other regions.¹⁰

Patients on the 2-times weekly frequency without residual function seemed to be facing more economic constraints. Specifically, more of them were traveling for >1 hour to reach the dialysis facility, and more of them lacked insurance coverage to cover >90% of their health costs. Perhaps these constraints partly spurred the lower frequency prescription and partly explain the lower rates of hospitalization, as patients expected to pay partly for hospitalizations may make more efforts to avoid them. It is interesting to note that although physical health-related quality of life did not differ according to dialysis frequency prescription, mental health-related quality of life was lower in this subgroup on 2-times weekly dialysis.

In summary, our study comparing 2- versus 3-times weekly hemodialysis in a prevalent cohort of patients on hemodialysis in China could not detect a clear difference in survival and hospitalization over a 2-year follow-up, even among patients without documented RKF. The patients on 2-times weekly hemodialysis seemed to have been more closely restricting sodium and protein intake, thereby sparing them some of the immediate complications related to less frequent dialysis. However, because our study is observational, it may be subject to residual confounding, despite the detailed data collection and extensive levels of adjustment. Thus, caution must be applied in interpreting these results. We also note that we studied a prevalent cohort in major metropolitan areas, and our findings therefore may not be extrapolated to patients new to dialysis or patients undergoing dialysis in rural areas. However, RKF is known to be substantially higher at initiation of dialysis, so that the impact of dialysis frequency may be expected to be smaller in the early phase of dialysis and thus may be more difficult to detect.

At the same time, given the rising numbers of patients with end-stage renal disease in middle-income countries facing significant resource constraints in financing chronic dialysis therapy, we highlight the need for studies, such as pragmatic clinical trials, with rigorous ascertainment of RKF to determine whether a strategy of less frequent dialysis may be acceptable for subsets of patients who are able to follow strict diet protein and sodium restrictions.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Table S1. Equations for standardized dialysis Kt/V and nPCR.

Table S2. Covariates included in the propensity score model of 2-times weekly dialysis prescription, by residual kidney function, based on univariate association with frequency assignment at $P < 0.1$.

Table S3. Time at risk and numbers of events, by residual kidney function and dialysis frequency.

Table S4. Study departure reasons, by dialysis frequency.

Table S5. Cause of hospitalizations, by residual kidney function and dialysis frequency.

Supplementary material is linked to the online version of the paper at www.kireports.org.

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