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Risk of cardiovascular disease in patients on thrice-weekly versus twice-weekly hemodialysis

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Thrice-weekly HD has been considered to be a standard RRT for ESRD patients [1]. Nevertheless, twice-weekly HD remains prevalent in the developing countries, and also could be found in some developed countries [2,3]. Thus far, there were scarce data regarding the clinical outcomes, especially cardiovascular disease (CVD), in twice-weekly HD patients in the developing world. CVD is a major cause of morbidity and mortality in ESRD patients [4]. However, risk of CVD in thrice-weekly HD compared to twice-weekly HD remained uncertain. HD patients have a distinct complication, i.e., intradialytic hypotension (IDH), which is the most common complication for HD and is strongly associated with many adverse clinical events [5–8]. Of note, IDH failed to be enrolled into CVD events in previous studies. In the present study, we considered IDH to be a CVD event. Therefore, the purpose of this work was to evaluate risk of CVD in patients on thrice-weekly vs. twice-weekly HD.

Incident and prevalent patients were enrolled from a single HD center of the Second Affiliated Hospital of Nanchang University between January 1, 2013 and January 31, 2014. Enrollment included patients aged ≥18 years who had received HD for more than 3 months, except those who had undergone peritoneal dialysis (PD) previously, malignant disease or refused to give written consent.

This work was a prospective study. Eligible patients were divided into two groups according to nephrologists' recommendation and patients' choice: thrice-weekly group and twice-weekly group. Baseline characteristics, including age, sex, HD vintage, diabetes, pre-existing CVD, hypertension as well as etiology of renal disease were recorded at the initiation of entry of this study. Time-dependent parameters included dry weight, uric output, hemoglobin, serum uric acid, calcium, phosphate, intact parathormone (iPTH), albumin cholesterol and single pool Kt/v (spKt/v).

The primary endpoint was the occurrence of CVD. All patients were followed up until death, transfer to PD therapy, kidney transplantation, transfer of care from our center, or censoring on January 31, 2014. The study protocol was approved by the Ethics Committee of the Second Affiliated Hospital of Nanchang University. All patients provided informed consent before study entry.

Diagram flow was shown in Fig. 1. In this study, 40 (30.1%) were in the thrice-weekly group and 103 (69.9%) in the twice-weekly group. The baseline characteristics in the thrice-weekly DH group and twice-weekly HD group were generally well balanced (Table 1). During the follow-up, 41 patients (28.7%) developed CVD events, including 20 (50.0%) in the thrice-weekly group and 21 (20.4%) in the twice-weekly group (Table 2). CVD incidence was significantly higher in the thrice-weekly group compared to the twice-weekly group [odds ratio (OR) 3.91, 95% confidence index (CI) 1.78–8.55, $p < 0.001$]. Patients with thrice-weekly HD had significantly higher IDH incidence compared to those on twice-weekly HD (OR 2.63, 95% CI 1.16–4.69, $p = 0.033$). Notably, CVD incidence (excluded IDH) remained remarkably higher in patients with thrice-weekly HD compared with their counterparts (OR 2.70, 95% CI 1.11–5.72, $p = 0.043$).

Multivariate analysis showed that older age [hazard ratio (HR) 1.05, 95% CI 1.02–1.08, $p = 0.004$], diabetes (HR 2.13, 95% CI 1.06–4.26, $p = 0.034$), higher phosphate (HR 1.38, 95% CI 1.17–2.84, $p = 0.001$) and thrice-weekly HD (with twice-weekly HD as reference, HR 2.52, 95% CI 1.34–4.73, $p = 0.004$) were independently associated with increased risk of CVD in the study patients (Table 3). On multivariate analysis, older age (HR 1.05, 95% CI 1.01–1.09, $p = 0.045$), diabetes (HR 3.05, 95% CI 1.47–7.75, $p = 0.011$), higher phosphate (HR 1.36, 95% CI 1.09–1.81, $p = 0.003$) and cholesterol (HR 1.20, 95% CI 1.05–3.18, $p = 0.011$) were independent risk factors for

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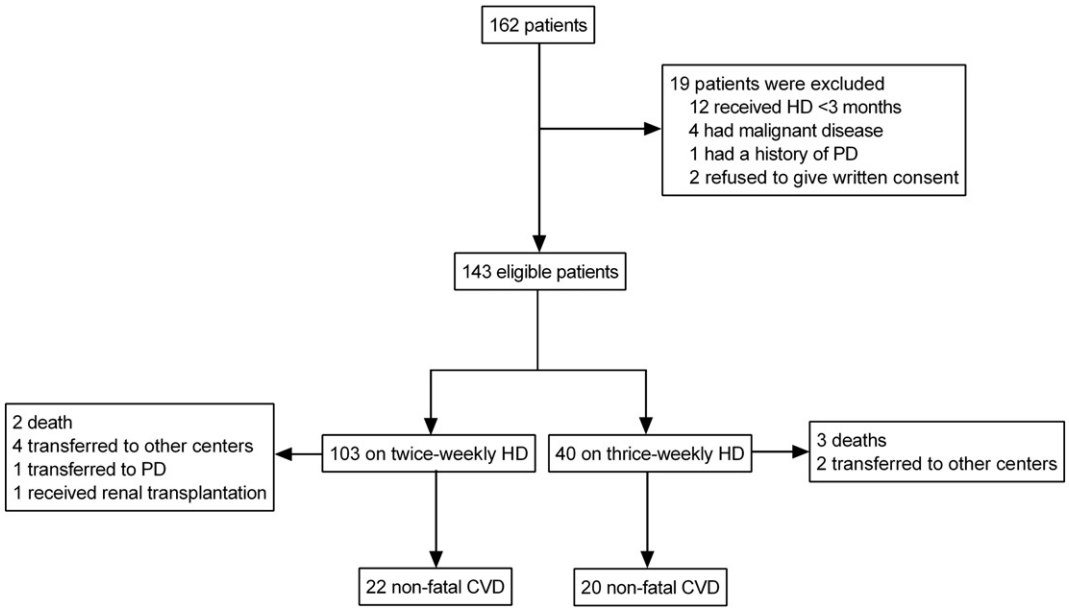

Fig. 1. Flow diagram.HD, hemodialysis; PD, peritoneal dialysis; CVD, cardiovascular disease.

Table 1
Baseline data of total HD patients.

	Total patients (n = 143)	Thrice-weekly group (n = 40)	Twice-weekly group (n = 103)	*p* value
Age (years)	61.7 ± 15.1	61.1 ± 13.9	62.0 ± 15.6	0.737
Male (%)	96 (67.1)	27 (67.5)	69 (67.0)	0.954
HD vintage (months)	12.0 (6.2–23.2)	18.3 (8.2–26.5)	11.0 (6.0–19.5)	0.061
Dry weight (kg)	57.8 ± 10.2	57.7 ± 12.0	57.9 ± 9.4	0.937
Urine output (mL/24 h)	400.0 (0.0–800.0)	200.0 (0.0–400.0)	500.0 (400.0–1000.0)	<0.001
Diabetes (%)	51 (35.7)	19 (47.5)	32 (31.1)	0.066
Pre-existing CVD (%)	32 (22.4)	7 (17.5)	25 (24.3)	0.383
Hypertension (%)	119 (83.2)	36 (90.0)	83 (80.6)	0.176
Etiology of renal disease (%)				
Chronic glomerulonephritis (%)	51 (35.7)	11 (27.5)	40 (38.8)	0.204
Diabetic nephropathy (%)	47 (32.9)	18 (45.0)	29 (28.2)	0.054
Hypertensive nephrosclerosis (%)	25 (17.5)	5 (12.5)	20 (19.4)	0.382
Other/unknown (%)	20 (14.0)	6 (15.0)	14 (13.6)	0.828
Lab measurements				
Hemoglobin (g/L)	89.1 ± 18.1	89.7 ± 17.2	88.9 ± 18.4	0.800
Serum uric acid (μmol/L)	456.5 ± 120.9	446.2 ± 97.7	460.5 ± 129.0	0.526
Calcium (mmol/L)	2.1 ± 0.2	2.1 ± 0.2	2.0 ± 0.2	0.066
Phosphate (mmol/L)	1.8 ± 0.5	2.0 ± 0.6	1.8 ± 0.5	0.003
iPTH (pg/mL)	200.1 (125.3–349.5)	250.5 (134.3–364.3)	176.9 (124.8–344.4)	0.221
Serum albumin (g/L)	35.7 ± 4.3	35.3 ± 4.9	35.8 ± 4.0	0.557
Serum cholesterol (mmol/L)	3.9 ± 1.0	4.0 ± 1.1	3.9 ± 0.9	0.638
spKt/v	1.3 ± 0.3	1.3 ± 0.4	1.2 ± 0.4	0.273

HD, hemodialysis; CVD, cardiovascular disease; iPTH, intact parathormone; spKt/v, single pool Kt/v.

Table 2
CVD events in the study population.

	Total patients (n = 143)	Thrice-weekly group (n = 40)	Twice-weekly group (n = 103)
IDH (n, %)	24 (16.8)	11 (27.5)	13 (12.6)*
Myocardial infarction (n, %)	3 (2.1)	3 (7.5)	0 (0.0)
Heart failure (n, %)	3 (2.1)	2 (5.0)	1 (0.9)
Stroke (n, %)	4 (2.8)	3 (7.5)	1 (0.9)
Others (n, %)	7 (4.9)	1 (2.5)	6 (5.8)

CVD, cardiovascular disease; IDH, intradialytic hypotension. Thrice-weekly HD vs. twice-weekly HD.
* $p < 0.05$.

Table 3
Hazard ratio of CVD in the study population using multivariate analysis[a].

	Total patients (n = 143)		
	HR	95% CI	*p* value
Age (per 1 year increase)	1.05	1.02–1.08	0.004
Diabetes (yes/no)	2.13	1.06–4.26	0.034
Phosphate (per 1 mmol/L increase)	1.38	1.17–2.84	0.001
Thrice-weekly HD[b]	2.52	1.34–4.73	0.004

CVD, cardiovascular disease; HD, hemodialysis; HR, hazard ratio; CI, confidence index.
[a] Factors, which had a difference in relative risk of events by >10% (<0.90 or >1.1) in the univariate analysis, were included in the multivariate analysis.
[b] Reference group is twice-weekly HD.