

Influence of dry weight reduction on anemia in patients undergoing hemodialysis

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Abstract

Objective: Volume load in patients undergoing hemodialysis correlates with renal anemia, with reductions in volume load significantly improving hemoglobin levels. We performed a prospective controlled study to assess the effect of post-dialysis dry weight reduction, resulting from the gradual enhancement of ultrafiltration, on renal anemia in this patient population.

Methods: Sixty-four patients with renal anemia on maintenance hemodialysis were randomized to an ultrafiltration group, in which dry weight was gradually reduced by slightly increasing the ultrafiltration volume while maintaining routine hemodialysis, and a control group, in which patients underwent conventional dialysis while routine ultrafiltration was maintained. After 28 weeks, post-dialysis weight and levels of hematocrit, hemoglobin, C-reactive protein, serum albumin, serum ferritin, and transferrin saturation were compared.

Results: All parameters were similar at baseline between the two groups and remained unchanged at week 28 in the control group compared with baseline. In contrast, the ultrafiltration group showed a significant reduction in post-dialysis weight and C-reactive protein concentration and a significant increase in hematocrit, hemoglobin, albumin, serum ferritin, and transferrin saturation.

Conclusions: Dry weight reduction resulting from enhanced ultrafiltration may improve renal anemia in patients undergoing hemodialysis.

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Keywords

Hemodialysis, dry weight, renal anemia, enhanced ultrafiltration, post-dialysis, volume load

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Renal anemia is the most common complication in patients with chronic renal failure undergoing maintenance hemodialysis (MHD), with an incidence of over 90% in this patient population. Renal anemia results from the inability of failed kidneys to synthesize erythropoietin. Anemia in patients with chronic renal failure can lead to premature cardiovascular disease and a marked increase in hospital admission and mortality rates. Renal anemia is difficult to treat in patients undergoing hemodialysis, and the treatment success rate remains low.¹ The control of hemoglobin (Hb) level in dialysis patients in China is far from satisfactory. For example, a survey in 2012 found that Hb was not adequately controlled, i.e., ≥ 110 g/L, in 60% of Chinese dialysis patients.² In contrast, 85% of dialysis patients in Switzerland had Hb ≥ 110 g/L,³ and data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) showed that 50.1% of MHD patients in Canada, 60.5% in the United States, 54.9% in France, 61.1% in Germany, 48.1% in the United Kingdom, 51.1% in Italy, 36% in Japan, and 51.1% in Spain had Hb concentrations of 110 to 130 g/L.⁴ Hb control in MHD patients involves multiple factors including patient compliance, rational use of iron and erythropoietin (EPO) preparations, parathyroid hormone level, and infections. Factors such as volume overload can reduce the effectiveness of treatment for renal anemia. Volume load in these patients has been found to correlate with renal anemia, and reductions

in volume load can significantly improve Hb levels.^{5,6} Few studies to date have assessed this relationship, however. This prospective controlled study assessed the effect of post-dialysis dry weight reduction, resulting from the gradual enhancement of ultrafiltration, on renal anemia in patients undergoing MHD.

Patients and methods**Patients**

This study enrolled patients with uremia who underwent regular hemodialysis at our center from March 2011 to October 2011. Patients were included if they had been stable on hemodialysis for over 6 months and had renal anemia, no apparent edema, and stable body weight after 3 months of hemodialysis. Patients were excluded if they had an unstable cardiovascular system, such as history of arrhythmia, ischemic heart disease, or heart failure; history of cerebrovascular disease, tumor, trauma, immune system disease, blood disease, acute/chronic blood loss, or infection; expected survival < 12 months; and expected poor compliance with treatment and follow-up. The study protocol was approved by the ethics committee of Xuanwu Hospital of Capital Medical University (approval no. 2018076). All patients provided written informed consent prior to participation.

Research methods

Grouping and treatment. Weight-matched patients, differing by less than 5.0 kg after dialysis, were randomized into a control group and an ultrafiltration group. Patients in the control group were maintained on the original dialysis protocol, with ultrafiltration applied according to increased body weight during the hemodialysis interphase and according to current dry weight, but without enhanced ultrafiltration. Patients in the ultrafiltration group were treated by slowly and constantly increasing the ultrafiltration volume to gradually reduce post-dialysis weight (PW). Specifically, the ultrafiltration volume was increased during each dialysis session by 0.1 to 0.5 L, based on each patient's tolerance level, with the aim of reducing PW after dialysis. A new dry weight was considered achieved when the patient could no longer tolerate a further 0.1-L increase in ultrafiltration volume. After a period of stability, body weight was further adjusted according to each patient's condition to sustain the body weight adjustment. Dry weight reduction was small and gradual to ensure that each increase in ultrafiltration volume was tolerated by patients and symptoms of discomfort avoided. All patients were carefully monitored during treatment. Ultrafiltration volumes were adjusted if patients experienced dizziness, heart palpitations, sweating, and/or other signs of discomfort to avoid severe complications such as hypotension or muscle spasms during dialysis. Patients were educated before and after the assessments on methods of controlling sodium and water intake and on controlling weight increase.

All patients received oral ferrous succinate tablets (600 mg/d; Jinling Pharmaceutical Co., Ltd., Nanjing, China) and intravenously injected EPO (Chengdu Tiantai Mountain Pharmacy Co., Ltd.,

Sichuan, China) after each dialysis session. EPO dose and target renal anemia goals were adjusted based on the Expert Consensus on the Application of Recombinant Human Erythropoietin in Patients with Renal Anemia (2010 revision).² The target hemoglobin concentration was 110 to 120 g/L, with a maximum level of 130 g/L.

All other dialysis protocols remained unchanged, and utilized a Fresenius 4008S dialysis machine (Fresenius Medical Care, Schweinfurt, Germany) and a Nipro triacetate hollow-fiber dialyzer SUREFLUX-130G (Nipro Corporation, Osaka, Japan). Standard unfractionated heparin was used for anticoagulation during hemodialysis. The calcium and sodium concentrations in the dialysis solution were 1.25 mmol/L and 138 mmol/L, respectively. The dialysate flow rate was 500 mL/minute and the blood flow rate was 200 to 250 mL/minute. All patients were scheduled to undergo 4 hours of dialysis three times per week for 28 consecutive weeks. The sample size calculation was based on $\alpha=0.05$, $\beta=0.10$, $1-\beta=0.10$, and $\delta/\sigma=1$, indicating that a sample size of 23 was required for each group. Allowing for a 20% dropout rate in each group, the final sample size was 28 patients per group.

Assessments. Measurements obtained 1 week before the start of the study were defined as baseline values and those obtained after 28 weeks represented the study endpoints. Serum albumin concentration was measured as an indicator of nutritional status and C-reactive protein (CRP) concentration was measured as an indicator of microinflammation. Changes in Hb, hematocrit (Hct), EPO dose, and PW were recorded, as were changes in CRP, albumin, serum ferritin (SF), transferrin saturation (TSAT), creatinine (Cr), urea, intact parathyroid hormone (iPTH), folic acid, vitamin B₁₂ concentration, and Kt/V.

All parameters were measured in pre-hemodialysis blood samples.

Biochemical parameters including Hb, Hct, albumin, Cr, urea, and SF were measured using an automatic biochemical analyzer (Hitachi, Tokyo, Japan). CRP concentration was determined by scatter turbidimetry (IMMAGE Immunochemistry System; Beckman Coulter, Inc. Brea, CA, USA) and folic acid, vitamin B₁₂, and ferritin concentrations were measured using microparticle chemiluminescent immunoassays (Access Immunoassay System; Beckman Coulter). Serum NT-proBNP was measured using an electro-chemiluminescent immunoassay (Roche, Basel, Switzerland). Total iron-binding capacity was determined using ferrous benzoxazine colorimetry on an automatic biochemical analyzer (Hitachi), and TSAT was subsequently calculated according to the following formula: serum iron/TIBC × 100%. iPTH was measured using an electro-chemiluminescent immunoassay (Roche). Kt/V was calculated using the Daugirdas formula. Weight gain and ultrafiltration rates were average values obtained after three stable dialysis treatments within 1 week.

PW was defined as the mean of three stable PW measurements within one week, with stable PW defined as patient dry weight.

Acute complications. Acute complications, including hypotension and muscle spasms, were monitored throughout the study and compared between the two groups.

Statistical analysis

All statistical analyses were performed using SPSS 11.5 (SPSS Inc., Chicago, IL, US). Continuous data were expressed as mean ± standard deviation (SD) and analyzed using t tests. Categorical data were compared using chi-squared tests.

Values of P < 0.05 were considered statistically significant.

Results

General data

Ninety-two patients underwent preliminary screening to determine whether they met baseline criteria – i.e., no apparent edema at the start of the study in March 2011, with stable dialysis quality, and renal anemia after 3 months of hemodialysis, with hemodialysis remaining stable. Of these 92 patients, 28 were excluded as they did not meet the baseline conditions, including 13 patients with cardiovascular instability, arrhythmia, ischemic heart disease, or heart failure; 3 with tumors; 4 with autoimmune disease; 2 with chronic blood loss; 3 with chronic infection; and 3 without weight matches. Baseline characteristics of the remaining 64 patients are shown in Table 1.

The 64 patients were randomized to the control and ultrafiltration groups, with 32 patients per group. There were no significant differences between these groups in age, sex, duration of dialysis, PW, primary disease, Hb, CRP, albumin, other biochemical parameters, and EPO dose (Table 2).

Treatment

All patients completed the 28 weeks of planned treatment. Oral doses of ferrous succinate remained unchanged during the treatment period. The dose of EPO was adjusted according to change in hemoglobin level. Some patients experienced significant reductions in blood pressure, and blood pressure medications were adjusted accordingly. Other drugs were adjusted according to each patient's condition.

Table 1. Baseline demographic characteristics of hemodialysis patients.

	Enrolled patients (n = 64)
Age (years)	37.0–80.0 (60.33 ± 10.18)
Gender (male/female; %)	29/35 (45.3%/54.7%)
Time on hemodialysis (months)	14.0–73.0 (35.69 ± 14.28)
Cause of ESRD	
Chronic glomerulonephritis	15
Hypertensive renal injury	14
Diabetic nephropathy	24
Drug-induced renal impairment	2
Polycystic kidney	2
Unknown	7
Weight after dialysis (kg)	37.10–88.20 (61.57 ± 13.03)
IDWG (kg)	1.30–4.84 (2.70 ± 0.73)
UFR (mL/minute)	5.40–20.17 (11.29 ± 3.08)
Hb (g/L)	83.14–132.24 (103.41 ± 10.52)
Hct (%)	24.90–39.50 (31.05 ± 3.16)
SF (µg/L)	69.20–439.50 (172.94 ± 77.43)
TSAT (%)	7.25–45.09 (18.10 ± 8.03)
Folic acid (mmol/L)	4.25–20.15 (10.35 ± 4.53)
Vitamin B12 (mmol/L)	212.20–1478.91 (735.91 ± 384.26)
Cr (µmol/L)	589.00–2065.00 (941.81 ± 202.22)
Urea (mmol/L)	16.16–33.67 (23.19 ± 3.69)
iPTH (ng/L)	35.00–678.00 (295.13 ± 133.36)
Kt/V	1.10–1.50 (1.31 ± 0.10)
NT-proBNP (ng/L)	843–3356 (2021.75 ± 734.80)
CRP (mg/L)	3.00–17.20 (9.88 ± 3.17)
ALB (g/L)	30.12–45.23 (36.42 ± 3.56)
SBP (mmHg)	95–174 (137.45 ± 22.73)
DBP (mmHg)	58–100 (75.02 ± 10.43)
EPO (U/kg·W)	50–220 (146.44 ± 38.04)

Data are presented as range (mean ± SD).

ESRD, end-stage renal disease; IDWG, interdialytic weight gain, UFR, ultrafiltration rate; Hb, hemoglobin; Hct, hematocrit; SF, serum ferritin; TSAT, transferrin saturation; Cr, creatinine; iPTH, intact parathyroid hormone; Kt/V; index of urea clearance; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein; ALB, albumin; SBP, systolic blood pressure; DBP, diastolic blood pressure; EPO, erythropoietin.

Change in body weight

PW at baseline was similar between the control and ultrafiltration groups, and remained stable in the control group throughout the study. In the ultrafiltration group, however, PW gradually but significantly decreased, and was 3.07 ± 0.67 kg lower after 28 weeks than at baseline ($P < 0.01$; Tables 2 and 3). There were no

significant between-group differences in the rate of weight gain and ultrafiltration rate from baseline to 28 weeks.

Laboratory parameters

Laboratory parameters did not differ significantly between the two groups at baseline. During the study period, all parameters remained stable in the control group, with

Table 2. Comparison of baseline characteristics between the ultrafiltration and control groups of hemodialysis patients.

	Control group (n = 32)	Ultrafiltration group (n = 32)	P value
Average age \pm SD	60.69 \pm 10.61	59.97 \pm 9.88	0.780
Time on hemodialysis (months)	34.88 \pm 15.63	36.50 \pm 12.99	0.653
Cause of ESRD			0.473
Chronic glomerulonephritis	6	9	–
Hypertensive renal injury	7	7	–
Diabetic nephropathy	14	10	–
Drug-induced renal impairment	2	0	–
Polycystic kidney	1	1	–
Unknown	2	5	–
Weight after dialysis (kg)	62.12 \pm 12.88	61.01 \pm 13.35	0.540
IDWG (kg)	2.77 \pm 0.75	2.63 \pm 0.72	0.458
UFR (mL/minute)	11.62 \pm 3.19	11.96 \pm 2.98	0.398
Hb (g/L)	104.88 \pm 11.03	101.94 \pm 9.94	0.267
Hct (%)	31.49 \pm 3.29	30.61 \pm 3.00	1.127
CRP (mg/L)	9.78 \pm 2.97	9.97 \pm 3.40	0.815
ALB (g/L)	36.66 \pm 3.62	36.19 \pm 3.55	0.603
SF (μ g/L)	177.25 \pm 76.84	168.63 \pm 79.01	0.660
TSAT (%)	18.53 \pm 7.98	17.67 \pm 8.18	0.673
Folic acid (mmol/L)	10.55 \pm 4.73	10.15 \pm 4.39	0.731
VitB12 (mmol/L)	755.50 \pm 408.51	716.31 \pm 363.87	0.687
Cr (μ mol/L)	928.16 \pm 158.68	955.47 \pm 239.87	0.593
Urea (mmol/L)	23.01 \pm 4.03	23.37 \pm 3.37	0.702
iPTH (ng/L)	289.97 \pm 139.22	300.28 \pm 129.25	0.760
Kt/V	1.32 \pm 0.11	1.30 \pm 0.10	0.492
NT-proBNP (ng/L)	2079.60 \pm 737.90	1986.53 \pm 722.10	0.612
SBP (mmHg)	136.84 \pm 24.02	138.06 \pm 21.74	0.832
DBP (mmHg)	74.78 \pm 10.77	74.25 \pm 10.25	0.859
EPO (U/kg-W)	152.03 \pm 37.60	140.84 \pm 38.23	0.242

Data are presented as mean \pm SD.

ESRD, end-stage renal disease; IDWG, interdialytic weight gain; UFR, ultrafiltration rate; Hb, hemoglobin; Hct, hematocrit; SF, serum ferritin; TSAT, transferrin saturation; Cr, creatinine; iPTH, intact parathyroid hormone; Kt/V; index of urea clearance; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein; ALB, albumin; SBP, systolic blood pressure; DBP, diastolic blood pressure; EPO, erythropoietin.

no significant differences observed at 28 weeks compared with baseline. In the ultrafiltration group, however, Hb, Hct, and serum albumin levels were significantly higher at 28 weeks than at baseline ($P < 0.01$ each). In addition, CRP was significantly lower ($P < 0.01$) and SF and TSAT were significantly higher ($P < 0.05$ each) at 28 weeks. In contrast, serum Cr, urea, iPTH, folic acid, vitamin B12 concentrations, and Kt/V

values did not change significantly (Tables 2 and 3).

Drug dosage

Patients in both groups received EPO, and doses remained stable from baseline to 28 weeks in the control group. In the ultrafiltration group, however, EPO dose was significantly lower at 28 weeks than at baseline ($P < 0.01$; Table 4).

Table 3. Changes in variables from baseline to week 28 within each group and between the two groups.

Outcome measure	Control group (n = 32)	P value ^a	Ultrafiltration group (n = 32)	P value ^a	P value ^b
ΔWeight after dialysis (kg)	-0.20 ± 0.6	0.086	-3.07 ± 0.67	0.000	0.000
ΔIDWG (kg)	-0.10 ± 0.32	0.585	-0.11 ± 0.13	0.560	0.455
ΔUFR (mL/minute)	-0.52 ± 1.36	0.517	-0.45 ± 0.53	0.560	0.455
ΔHb (g/L)	0.44 ± 3.74	0.881	13.47 ± 4.66	0.000	0.001
ΔHct (%)	0.13 ± 1.21	0.887	4.03 ± 1.44	0.000	0.001
ΔCRP (mg/L)	-0.28 ± 0.75	0.710	-3.40 ± 1.49	0.000	0.000
ΔALB (g/L)	0.29 ± 0.82	0.750	3.70 ± 1.04	0.000	0.004
ΔSF (μg/L)	-6.37 ± 24.06	0.741	19.93 ± 17.26	0.036	0.042
ΔTSAT (%)	-0.65 ± 2.69	0.751	5.99 ± 4.75	0.017	0.021
ΔFolic acid (mmol/L)	-0.06 ± 0.69	0.958	1.04 ± 1.71	0.364	0.547
ΔVitB12 (mmol/L)	-16.47 ± 111.82	0.871	34.00 ± 57.20	0.716	0.908
ΔCr (μmol/L)	3.34 ± 47.87	0.933	7.94 ± 58.84	0.900	0.559
ΔUrea (mmol/L)	-0.09 ± 0.89	0.929	0.28 ± 1.62	0.751	0.447
ΔiPTH (ng/L)	-3.44 ± 47.97	0.924	-16.66 ± 61.13	0.605	0.933
ΔKt/V	0.01 ± 0.08	0.840	0.01 ± 0.56	0.760	0.579
ΔNT-proBNP (ng/L)	-69.60 ± 895.43	0.700	1443.47 ± 309.50	0.006	0.004
ΔSBP (mmHg)	-1.59 ± 2.03	0.790	-14.03 ± 9.66	0.007	0.034
ΔDBP (mmHg)	-1.25 ± 1.83	0.646	-7.09 ± 4.31	0.007	0.041
ΔEPO (U/kg·W)	-2.63 ± 8.06	0.775	-32.11 ± 17.25	0.000	0.000

IDWG, interdialytic weight gain; UFR, ultrafiltration rate; Hb, hemoglobin; Hct, hematocrit; SF, serum ferritin; TSAT, transferrin saturation; Cr, creatinine; iPTH, intact parathyroid hormone; Kt/V; index of urea clearance; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein; ALB, albumin; SBP, systolic blood pressure; DBP, diastolic blood pressure; EPO, erythropoietin.

Δ, difference in mean score from baseline to week 28.

^aComparison between baseline and week 28 within each group and ^bcomparison between the two groups.

Table 4. Dosages of EPO before and after observation (U/kg·W) ($\bar{x} \pm s$).

Group	Week 0	Week 28	t ₂	P
Control group	152.03 ± 37.60	149.41 ± 35.61	0.287	0.775
Ultrafiltration group	140.84 ± 38.23	108.73 ± 23.18 ^{1,2}	4.063	0.000
t ₁	1.180	5.415		
P	0.242	0.000		

Note: ¹P < 0.01 vs. week 0 in the same group; ²P < 0.01 vs. the control group.

t₁: Comparison between the two groups at the same time point; t₂: comparison between Week 0 and Week 28 in the same group.

Acute complications

Each group of patients completed 2688 dialysis treatments, and no patients dropped out of the study. None of the 64 patients experienced cerebral vascular abnormalities, severe arrhythmia, acute

myocardial ischemia, cardiac arrest, or other serious cardiac or cerebral vascular complications. Rates of hypotension and muscle spasm during dialysis were 3.91% (105/2688) and 5.54% (149/2688), respectively, in the control group and 4.69%

(126/2688) and 6.21% (167/2688), respectively, in the ultrafiltration group. The combined rates of hypotension and muscle spasm in the control and ultrafiltration groups were 9.45% (254/2688) and 10.90% (293/2688), respectively, and the difference between the groups was not statistically significant.

Discussion

The goal of hemodialysis treatment is to achieve adequate dialysis, thus reducing patient mortality. Adequate dialysis requires the thorough removal of solutes and sufficient ultrafiltration to maintain water and electrolyte balance. An important objective of hemodialysis is therefore to remove excess water from the body, thereby reducing dry weight. At present, there is no simple and accurate method for assessing dry weight in clinical settings. Thus, comprehensive evaluation of clinical indicators remains the standard approach, despite being highly dependent on the clinician's experience. As a result, dry weight is frequently overestimated, with a high proportion of patients undergoing MHD remaining in a state of chronic volume overload and not attaining actual dry weight.^{8,9} We have observed similar findings in our clinical, in that a significant number of patients remain in volume overload after dialysis. Attainment of actual dry weight can improve patient cardiovascular status and quality of life.^{10,11}

Volume overload is not only a major risk factor for cardio-cerebrovascular complications in dialysis patients but is also associated with other adverse effects. For example, chronic volume overload is a risk factor for a microinflammatory state, in which the levels of inflammatory factors or markers, such as CRP, interleukin-6 (IL-6), transforming growth factor- β 1, and brain natriuretic peptide, are markedly higher compared with patients that have

no volume overload. Of these markers, CRP has shown relatively high specificity and correlation with hypervolemia, showing a positive correlation with the degree of inflammation but a negative correlation with serum albumin and Hb levels.¹³⁻¹⁷

Chronic volume overload has also been closely associated with malnutrition, which has an estimated incidence of 23% to 76% among patients undergoing MHD in China and 10% to 51% among those in other countries. Nutritional status can directly affect patient quality of life, long-term survival rate, and prognosis, as well as being associated with increased rates of morbidity and mortality. Increased levels of inflammatory cytokines in hypervolemic dialysis patients have also been associated with decreased levels of nutrition indicators such as serum albumin, ferritin, and Hb.¹⁸⁻²⁰

Patients with chronic volume overload also show reduced responsiveness to EPO. The microinflammation and malnutrition induced by chronic overload can reduce iron absorption and utilization, thereby reducing patient responsiveness to EPO. High CRP and low serum albumin levels have been correlated with reduced responsiveness to EPO.²¹⁻²⁴ Thus, although hypervolumic load is a key cause of poor treatment efficacy in patients with renal anemia, it is frequently overlooked in clinical settings.

Volume overload, dialysis membrane bio-incompatibility, microbial contamination of dialysate, vascular access, and/or potential infections are not uncommon in patients undergoing MHD. In particular, disorders in toxin metabolism and cytokine excretion can occur in patients with chronic kidney failure, resulting in the accumulation of advanced glycation end-products and oxidation protein products and leading to a microinflammatory state.³ Reductions in volume load and dry weight can alleviate inflammation, thus improving nutrition

and anemia.²⁵ In the clinical setting, volume load is adjusted primarily by restricting sodium and water intake and through dialysis and ultrafiltration. However, reductions in water and sodium intake require lifestyle changes, which may not be adhered to over long periods of time. Conversely, increasing the frequency or duration of dialysis can increase treatment costs. Increasing ultrafiltration to reduce dry weight may represent a relatively simple strategy, although a potential increase in the incidence of complications following enhanced ultrafiltration may be problematic.

As the extend of volume overload can differ between patients, we adjusted treatment in individual patients based on their weight between dialysis sessions. The ultrafiltration volume was slowly and constantly increased to gradually reduce PW, enabling patients to achieve or approach their "actual dry weight". Patient status was subsequently maintained for several weeks, serum CRP concentration was reduced, and serum albumin and ferritin concentrations as well as TSAT were increased, indicating improvements in both inflammation and nutrition status. Furthermore, Hb concentration was increased, resulting in improvements in anemia and reduced EPO dosage. The improvements in anemia may have been attributable to improvements in microinflammation and nutrition status, increased iron absorption, and/or increased sensitivity to EPO.

Higher ultrafiltration rates may also increase the risk of death and cardiovascular death, with this increased risk primarily related to an increase in weight during the interval between dialysis treatments.²⁶⁻²⁸ Patients were required to strictly control or reduce the amount of weight gain between dialyses. Our enhanced ultrafiltration protocol consists of small, gradual increases in ultrafiltration volume which were dependent on the patient's capacity

to reduce weight after dialysis. During periods of body mass adjustment, increases in the ultrafiltration rate are small and of short duration. However, during periods of body mass stability, rates of ultrafiltration are not altered further.

These gradual increases in ultrafiltration volume also require increased observation and nursing care to enable the timely detection and treatment of patient discomfort. Our study protocol was not associated with an increased incidence of severe cardiovascular disease, hypotension, muscle spasm, or other complications, including patient discomfort after hemodialysis. Other adverse events, including fatigue, dizziness, and low blood pressure, were not quantified. Reductions in patient body mass resulted in a more stable cardiovascular condition and increased tolerance of ultrafiltration. Control of volume load is important in dialysis patients as it reduces microinflammation and blood pressure and improves nutritional status, cardiovascular stability, and drug responsiveness.²⁹⁻³⁴ Although the patients in our study benefited from a reduction in load capacity, the long-term effects of this reduction were not quantified.

This study had some limitations. First, the clinical evaluation methods used were based on clinical signs and symptoms instead of using a body composition monitor (BCM) to assess the volume load of patients. However, we evaluated the levels of serum NT-proBNP in patients. Recent studies have shown that BNP and NT-proBNP levels can better reflect the water load in patients with chronic kidney disease dialysis.^{35,36} Other studies have shown that BNP and NT-proBNP have a good correlation with BCM for assessment of volume load in dialysis patients.^{37,38} Further studies using BCM to assess the volume load are therefore warranted. Second, blood samples were collected prior to dialysis, when the body weight of

participants was significantly higher than that after the final dialysis. Furthermore, the body fluid load was increased and the blood was in a high volume load state prior to dialysis. We adjusted the dry weight so that it approached the “true dry weight”, so that patients would not be in a blood-concentrated state during the interdialytic period.

In summary, enhanced ultrafiltration can significantly reduce PW, allowing patients to achieve or approach actual dry weight. Reduced PW may facilitate improvements in renal anemia. Additional investigations are needed, however, to assess the underlying mechanism, safety, and effectiveness of ultrafiltration.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Ethics and consent statement

The study was approved by the Xuanwu Hospital's Committee on Ethics of Human Experiments. All patients provided written informed consent to participate in this study.

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