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NEPHROLOGY – ORIGINAL PAPER

Nutritional status after conversion from conventional to in-centre nocturnal hemodialysis

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Abstract
Introduction Recipients of conventional hemodialysis (CHD; 3–4 h/session, 3 times/week) experience volume expansion and nutritional impairment which may contribute to high mortality. Prolongation of sessions with in-centre nocturnal hemodialysis (INHD; 7–8 h/session, 3 times/week) may improve clinical outcomes by enhancement of ultrafiltration and uremic toxin removal.
Materials and methods In this prospective cohort study, 56 adult patients who were receiving maintenance CHD for at least 90 days were assigned to CHD (patients who remained in CHD) and INHD (patients who switched to INHD) groups. Both groups were followed for 1 year divided into four 13-week quarters; post-dialysis weight and interdialytic weight gain (IDWG) were captured in each quarter. Repeated measures analysis of variance was used to calculate group main effect, time main effect or time–group interaction effect.
Results Conversion to INHD was associated with a mean (95% confidence interval) change in IDWG of 0.5 (0.08, 1.2) kg as compared to −0.3 (−0.9, 0.1) kg in the CHD group ($p < 0.01$). In the INHD group, post-dialysis weight (% of baseline pre-dialysis weight) decreased after conversion, reaching a nadir during the first 3 months (0.7%) and subsequently it gradually increased and returned to its baseline at the end of follow-up. A similar temporal trend was seen for serum creatinine but not serum N-terminal pro-brain natriuretic peptide (NT-proBNP) which is a marker of extracellular volume. The changes in serum albumin, prealbumin and hs-CRP were not different between the two groups.
Conclusions Conversion to INHD was associated with greater IDWG and relatively stable body mass. We speculate that this gain in weight reflects an increase in lean body mass following the change in dialysis modality, which can be concluded from the parallel increase in serum creatinine and the lack of increase in NT-proBNP.

Keywords Nutrition · Hemodialysis · In-centre nocturnal dialysis · Interdialysis weight gain · Serum creatinine · Body mass index

Introduction

The life expectancy of maintenance hemodialysis (HD) patients is severely reduced as compared with the general population [1]. Malnutrition and inflammation may be important mediators [2–4]. Inflammation and nutritional status in dialysis patients can be evaluated by the circulating levels of inflammatory and nutritional biomarkers. C-reactive protein (CRP), as a marker of inflammation, and the nutritional markers, albumin and prealbumin, have been shown to be robust predictors of cardiovascular events and mortality [5–9].

The receipt of conventional hemodialysis (CHD), typically characterized by 3 sessions per week and 3–4 h/session, is associated with progressive nutritional impairment

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that is characterized by low caloric intake which deteriorates further over time [10]. In the HEMO trial, the dietary intake of the participants who were all on CHD was far below the requirements that would be needed to maintain equilibrated nitrogen balance [11]. The inadequate removal of solutes that accumulate in advanced kidney failure which cannot be fully compensated by CHD may explain this phenomenon of uremia-related anorexia [12]. Furthermore, restrictions on dietary sodium, potassium and phosphate may lead to a relatively unpalatable diet and reduced caloric intake [13, 14]. Dialysis intensification, as achieved either through increased frequency and/or prolongation of dialysis sessions, can be organized in a variety of schedules and settings [15]. Many studies have suggested that prolonged dialysis sessions may improve clinical outcomes [16, 17]. In-centre nocturnal hemodialysis (INHD), delivered three times per week, for 7–8 h per session in a dialysis facility, presents a unique opportunity to overcome dialysis intensification challenges without the barriers associated with self-care [18].

It is conceivable that conversion to INHD improves nutritional status by decreasing the burden of uremic toxins that might predispose to wasting and poor appetite. Enhanced clearance of sodium, potassium and phosphate might also permit the relaxation of dietary restrictions and the consumption of a more appetizing diet.

Most completed studies evaluating nutritional status with nocturnal dialysis lacked an appropriate control group and have short a duration of follow-up [19–22]. We conducted a two-center prospective cohort study that evaluated the change in nutrition–inflammation markers after conversion from CHD to INHD. Our goal was to compare weight and nutritional markers over a 1-year follow-up period and their association with conversion from CHD to INHD, as compared with remaining on CHD. We hypothesized that inflammation and nutritional status would improve in the INHD group as compared with the CHD group.

Materials and methods

Participants

Patients between the ages of 18 and 75 on media at St. Michael's Hospital (Toronto, Canada) and St. Paul's Hospital (Vancouver, Canada) were eligible for participation. As there are no consensus recommendations for INHD, the primary reasons for recommending conversion to INHD included refractory hyperphosphatemia, intradialytic hypotension on CHD limiting volume removal, labile blood pressure on CHD, patient preference and preservation of employment opportunities. The patient and treating nephrologist made the decision to convert to INHD jointly. Exclusion criteria were serious comorbidity with life expectancy <1 year, planned kidney transplant from a live donor in the coming year and confirmed pregnancy. We recruited a control group comprising individuals who met the eligibility criteria as described but who elected to remain on CHD with no anticipated conversion to INHD. In this stub-study, we only included patients who remained on the initial therapy for the entire duration of follow-up and in whom complete blood work data were available. The research ethics board at each site approved the study, and all study participants provided written informed consent.

Treatments

INHD was administered three times per week for a planned duration of 7–8 h per session. Blood flow was 300 mL/min and dialysate flow 500 mL/min. Dialysis machines (Phoenix, Gambro, Richmond Hill, ON at St. Michael's Hospital and Dialog + ®, B. Braun, Bethlehem, PA at St. Paul's Hospital) and dialyzers (Xenium 210, Baxter Healthcare Corp., McGraw Park, IL at St. Michael's Hospital and Rexeed 21S, Asahi, Memphis, TN at St. Paul's Hospital) were not changed following INHD conversion. All patients in the CHD arm continued on their previous dialysis prescription. In both groups, prescription adjustments were made based on clinical assessments and biochemical and hematologic indices obtained on routine laboratory testing. Dietitians monitored the patients' progress and scheduled routine periodic follow-up visits during the study period in both groups as necessary. Each patient was followed for 52 weeks. The 52-week follow-up period was preceded by a 12-week "baseline period" during which all patients were on CHD.

Outcomes

In this substudy, pre-specified primary outcomes were post-dialysis weight (% of 1st pre-dialysis wt), interdialytic weight gain (IDWG) defined as the amount of fluid (kg) gained between sessions, BMI and serum creatinine (as a surrogate marker of muscle mass) and the temporal trends of these parameters from baseline until the end of follow-up. Additional outcomes included serum nutritional and inflammatory markers including albumin, prealbumin, cholesterol and high-sensitivity C-reactive protein (hs-CRP).

Measurements

The 52-week follow-up period was divided into four 13-week quarters (q1–q4); data were captured and averaged for the final three dialysis sessions of each of the four 13-week quarters. At the conclusion of 52 weeks of observation, a 12-week "end-of-study" period commenced

during which the same data recorded in the baseline and follow-up period were captured. A blood draw (plasma isolated and frozen at −80 °C) was collected at baseline and during the end of study period. The following elements were analyzed: serum hemoglobin (Coulter STKS machine—Beckman Coulter, Inc, Fullerton, Calif), serum albumin (quantitative calorimetric method—Beckman Coulter Albumin Reagent kit, Beckman Instruments Inc), prealbumin (nephelometric method—Beckman Coulter Immunochemistry Systems), hs-CRP (turbidimetric latex agglutination method—Beckman Coulter CRP kit), intact PTH (chemiluminescence method—DPC, Diagnostic Product Corporation, Los Angeles, CA, USA), total cholesterol, creatinine, potassium, calcium, phosphorus (calorimetric method—Beckman Cx-7 autoanalyzer, Beckman Instruments Inc) and N-terminal pro-brain natriuretic peptide [NT-proBNP] (proBNP assay for the Elecsys 2010).

Dialysis session data (dialysis session duration, blood flow, dialysate composition), systolic and diastolic blood pressure (recorded pre-dialysis, after initiation of therapy, nadir and end of dialysis), ultrafiltration volume, *Kt*/*V* and IDWG were also recorded.

The evolution of post-dialysis body weight over time was calculated according to the following formula [23]:

$$\frac{\text{Average of post-dialysis body weights at each quartile}}{\text{predialysis body weights at baseline}} \times 100\%.$$

The relative IDWG (RIDWG) was calculated as IDWG divided by the respective post-dialysis weight.

BMI (post-dialysis weight in kilograms divided by height in meter squared) was calculated; *Kt*/*V* (single pool) was calculated by using urea kinetic modeling (UKM) formula representing simplified UKM equations, which is as follows [24, 25]:

$$Kt/V = -\ln(R - 0.008 \times t) + [(4 - 3.5 \times R) \times \text{UF}/W]$$

where R is the ratio of post-dialysis to pre-dialysis serum urea, t is time of dialysis in hours, UF is the amount of ultrafiltration (in liters) and W is post-dialysis weight (in kilograms).

Statistical analysis

Continuous variables were summarized using means and standard deviations (SD), and categorical variables were summarized using frequencies and proportions. Descriptive summaries of changes in treatment-related variables are provided for the cohort with non-missing values at baseline, at months 3, 6, 9, 12 and after the end of study.

An "on treatment" (per-protocol) analysis was performed using repeated measures analysis of variance. Data were analyzed from baseline to 52 weeks to determine whether there were significant between-group main effect (CHD and INHD), time main effect (regardless of group assignment) or interaction effects between groups over time.

The effects of treatment assignment on the outcomes which were measured only two times (baseline and end of study) were assessed by comparisons between two groups of adjusted mean changes from baseline to the average level after 1 year using independent sample t test. In all comparisons, we also adjusted for case-mix variables including age, gender, race/ethnicity, diabetes history and dialysis vintage. We plotted the correlation between the changes of some variables. Spearman correlation was used when the variable was not normally distributed.

Statistical analyses were carried out with Stata statistical software version 11.0 (Stata Corporation, www.stata.com).

Results

Baseline characteristics

We enrolled 37 patients who converted from CHD to INHD between July 2008 and June 2011 [26], of whom 35 were eligible for this substudy (32 at St. Michael's Hospital and 3 at St. Paul's Hospital). We identified an additional 30 patients who were eligible for INHD, but chose to remain on CHD and agreed to serve as controls, of whom 29 (26 at St. Michael's Hospital and 3 at St. Paul's Hospital) were eligible for this substudy. All 64 patients underwent the baseline measurements. Among patients who converted to INHD, 3 returned to CHD, 1 received a kidney transplant and 1 died during the 1-year follow-up period. In the CHD group, 2 individuals converted to INHD and 1 underwent transplantation. Therefore, in total 56 patients remained in their initial assigned group and completed all baseline, follow-up and end of study biochemical, clinical and nutritional assessments and are the subjects of this substudy.

Individuals who converted to INHD were more likely to have diabetes, had a higher BMI and lower serum prealbumin levels, as compared to individuals who remained on CHD (Table 1). Tunneled central venous catheters were the predominant vascular access among patients who converted to INHD (53.5%), whereas arteriovenous fistulae were utilized in the majority (58.8%) of patients who remained on CHD. The treatment characteristics of patients are described in Table 2. Patients who converted to INHD received a mean of 7.1 ± 0.4 h/session as compared to 3.7 ± 0.5 h/session in the CHD group ($p < 0.001$). Mean ultrafiltration per session was higher among INHD recipients (3393 ± 1015 vs 2552 ± 763 ml, $p = 0.011$).

Table 1 Patient characteristics at study entry

	Nocturnal ($n = 30$)	Conventional ($n = 26$)	p value
Age (years)	56.3 ± 9.0	53.0 ± 11.8	0.28
Male sex, *n* (%)	14 (46.7)	7 (41.1)	0.72
Ethnicity			0.27
Caucasian, *n* (%)	11 (37.9)	3 (11.7)	
African Canadian, *n* (%)	6 (20.7)	8 (29.4)	
Pacific Islander, *n* (%)	5 (17.2)	6 (23.5)	
East Indian, *n* (%)	3 (10.3)	3 (11.8)	
Asian, *n* (%)	4 (13.8)	3 (11.8)	
Latin American, *n* (%)	0 (0.0)	2 (5.9)	
Dialysis vintage (months)[†]	20 (8–56)	43 (17–79)	0.12
Diabetes mellitus, *n* (%)	19 (63.3)	5 (29.4)	0.03
Coronary artery disease, *n* (%)	5 (17.2)	1 (5.9)	0.27
Cause of ESRD			
Diabetes mellitus, *n* (%)	16 (53.3)	6 (23.1)	0.27
Hypertension/ischemic, *n* (%)	1 (3.3)	0 (0.0)	
Glomerulonephritis, *n* (%)	8 (26.7)	14 (53.8)	
Polycystic kidney disease, *n* (%)	1 (3.3)	1 (3.8)	
Other, *n* (%)	4 (13.3)	5 (19.2)	
Vascular access in use			
Arteriovenous fistula (%)	43.3	58.8	0.21
Arteriovenous graft (%)	3.3	11.8	
Tunneled catheter (%)	53.3	29.4	
Nutritional parameters			
BMI (kg/m^2)	28.4 ± 5.7	24.5 ± 4.5	<0.01
Serum albumin (g/l)	38.13 ± 2.70	40.35 ± 3.89	0.02
Serum prealbumin (g/ml)	0.30 ± 0.06	0.36 ± 0.08	<0.01
Serum cholesterol (mmol/l)	3.92 ± 0.83	4.48 ± 1.69	0.13
Serum creatinine (μmol/l)	856 ± 345	882 ± 329	0.72
Post-dialysis weight (kg)	80.4 ± 21.2	72.5 ± 18.9	0.12
Serum calcium (mmol/l)	2.16 ± 0.20	2.14 ± 0.2	0.71
Serum phosphorus (mmol/l[†])	1.69 (1.47–2.17)	1.60 (1.38–1.92)	0.12
Serum PTH[†]	39.2 (21.5–51.6)	50.9 (27.3–80.0)	0.15
Serum potassium (mg/dl)	4.71 ± 0.77	4.59 ± 0.57	0.53
Serum Hgb (g/l)	113.3 ± 11.3	110.2 ± 13.2	0.32
TSAT %[†]	0.20 (0.16–0.26)	0.22 (0.16–0.29)	0.47

Continuous variables displayed as means (SD); categorical variables expressed as number (%). Serum albumin, prealbumin and cholesterol at baseline and end of study were available for 17 patients from the CHD group

TSAT transferrin saturation

[†] Median (interquartile range) variables expressed as number (%)

Nutritional parameters over time

In the INHD group, post-dialysis weight (expressed as % of baseline pre-dialysis weight) decreased after conversion to INHD, reaching a nadir during first 3 months (0.7%); this was followed by a gradual return to the baseline weight by the end of study follow-up (Table 3; Fig. 1a, b). Between 3 and 12 months, mean body weight increased by 0.6% in INHD group.

Among patients who converted to INHD, pre-dialysis serum creatinine decreased initially, reached a nadir 3 months after conversion and then gradually increased (Fig. 2). To check if the increase in post-dialysis weight was attributable to an increase in extracellular volume,

Table 2 Characteristics of study treatments

	INHD ($n = 30$)	Conventional ($n = 26$)	p value
Mean session duration (h)	7.1 ± 0.4	3.7 ± 0.5	<0.001
Mean ultrafiltration per session (ml)	3393 ± 1015	2552 ± 763	0.01
Maximum blood flow (ml/min)	272 ± 9.9	355 ± 33.1	<0.01
Lowest dialysate sodium (mmol/l)	138.2 ± 2.1	138.1 ± 2.0	0.77
Dialysate potassium (mmol/L)	2.0 ± 0.6	1.8 ± 0.4	0.12
Dialysate calcium (mmol/L)	1.3 ± 0.1	1.3 ± 0.1	0.34

we examined the correlation between change of serum NT-proBNP and post-dialysis weight from baseline to the end of follow-up in the INHD group and did not find a significant relationship (Spearman correlation coefficient = −0.08, $p = 0.67$). On the other hand, the change in post-dialysis weight from baseline to end of follow-up showed a significant correlation with the change in serum creatinine (Spearman correlation coefficient = 0.40, $p < 0.05$) in the INHD group suggesting that muscle mass may have accounted for the rise in weight. Such a correlation was not observed in the CHD group.

Table 4 shows the nutrition–inflammation and cardiac parameters at baseline and at the end of follow-up in both arms. The change in albumin and prealbumin from baseline to 12 months did not differ significantly between treatment arms. However, total serum cholesterol concentration increased significantly in the INHD group in comparison with CHD group (0.26 ± 0.08 vs. −0.25 ± 0.08 mmol/l, $p < 0.05$). There were no intragroup differences in the prevalence of statin use at the beginning and at the end of study. (McNemar's $p = 0.09$ and 0.32 for INHD and CHD groups, respectively). There was no association between INHD conversion and hs-CRP concentration.

Discussions

As compared with CHD, conversion to INHD was associated with greater intedialytic weight gain and relatively stable body mass. Though serum creatinine concentration declined as expected after the introduction of INHD, its subsequent rise suggested a gain in muscle mass in patients who converted to INHD. Cholesterol concentration rose after commencement of INHD, but other conventional markers of nutrition, such as albumin and prealbumin, and the inflammatory marker hs-CRP were not significantly impacted by conversion to INHD.

Table 3 Nutritional parameters in 30 INHD and 26 CHD patients during follow-up (from baseline to 12 months)

Variable	Arm	Observed data (mean ± SD)						Change from baseline	p value		
		Baseline	Q1	Q2	Q3	Q4	End of study		Difference p^*	Repeated measure p^{**}	Repeated measure p^{***}
Post-dialysis weight (% of 1st pre-dialysis wt)	CHD	96.30 ± 1.10	95.69 ± 3.96	95.53 ± 4.21	95.91 ± 4.08	95.51 ± 4.11	95.90 ± 4.08	−0.19 ± 3.82	0.94	0.97	0.70
	INHD	96.69 ± 0.90	96.11 ± 3.13	96.39 ± 3.67	96.44 ± 4.47	96.59 ± 5.15	96.59 ± 5.56	−0.09 ± 5.56			
Interdialysis weight gain (kg)	CHD	2.5 ± 0.8	2.2 ± 1.3	2.2 ± 1.1	2.6 ± 1.1	2.3 ± 1.0	2.3 ± 1.0	−0.2 ± 0.5	<0.01	<0.01	<0.01
	INHD	2.6 ± 1.0	3.3 ± 1.5	3.4 ± 1.4	3.1 ± 1.3	3.3 ± 1.2	3.1 ± 1.1	0.5 ± 0.8			
RIDWG (%)	CHD	3.7 ± 1.1	3.3 ± 1.8	3.2 ± 1.6	3.7 ± 1.4	3.4 ± 1.3	3.5 ± 1.3	−0.3 ± 0.8	0.08	<0.01	<0.01
	INHD	3.4 ± 1.0	4.1 ± 1.5	4.2 ± 1.4	3.9 ± 1.2	4.2 ± 1.3	3.9 ± 1.0	0.5 ± 0.9			
BMI (kg/m^2)	CHD	24.5 ± 4.5	24.5 ± 4.6	24.7 ± 4.6	24.8 ± 4.5	24.3 ± 4.3	24.4 ± 4.7	−0.1 ± 0.9	0.006	0.46	0.46
	INHD	28.4 ± 5.7	28.3 ± 5.7	28.5 ± 5.9	28.8 ± 5.9	28.8 ± 5.8	28.6 ± 5.8	0.2 ± 1.6			
Serum creatinine (μmol/l)	CHD	871 ± 329	860 ± 325	865 ± 318	888 ± 334	867 ± 342	853 ± 337	−3.9 ± 194	0.17	0.23	0.23
	INHD	884 ± 345	792 ± 231	797 ± 229	828 ± 248	830 ± 199	830 ± 196	−54 ± 216			

Q1–Q4 quartile 1–quartile 4 shows four 13-week quarters

* p for difference of the mean group changes

** p for interaction effects (groups × time), *** p for interaction effects after adjustment for case-mix (age, gender, race/ethnicity, diabetes and dialysis vintage)

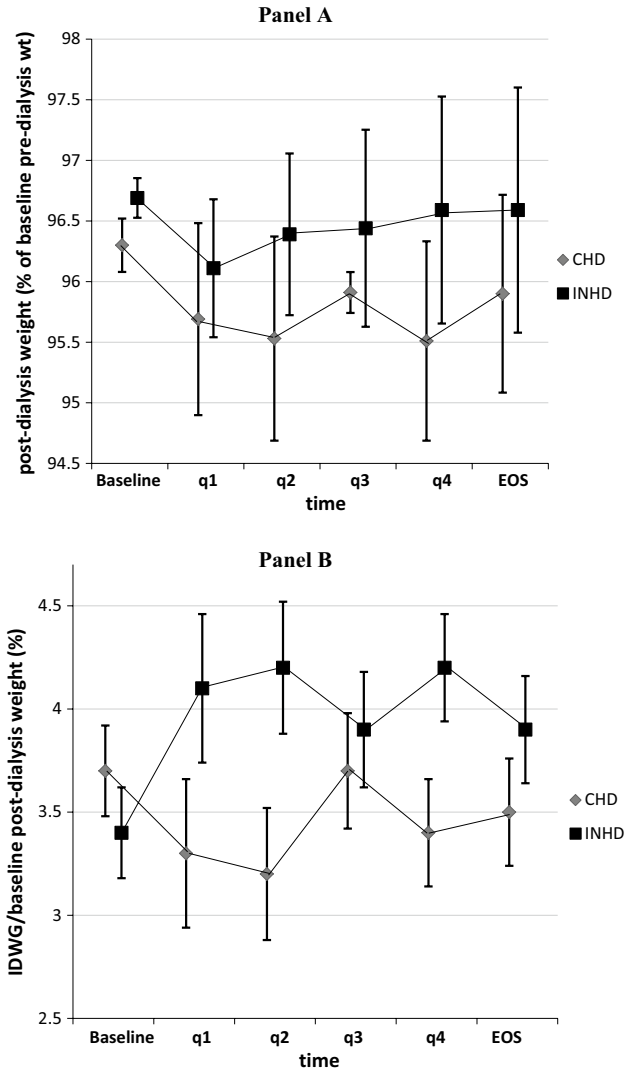

Fig. 1 Temporal changes in weight in CHD ($n = 26$) and INHD ($n = 30$) groups. Data are mean ± standard error. One-year follow-up period was divided into four 13-week quarters (*q1–q4*); post-dialysis weight and interdialytic weight gain (IDWG) were captured and averaged for the final three dialysis sessions of each of the four 13-week quarters. EOS end of study

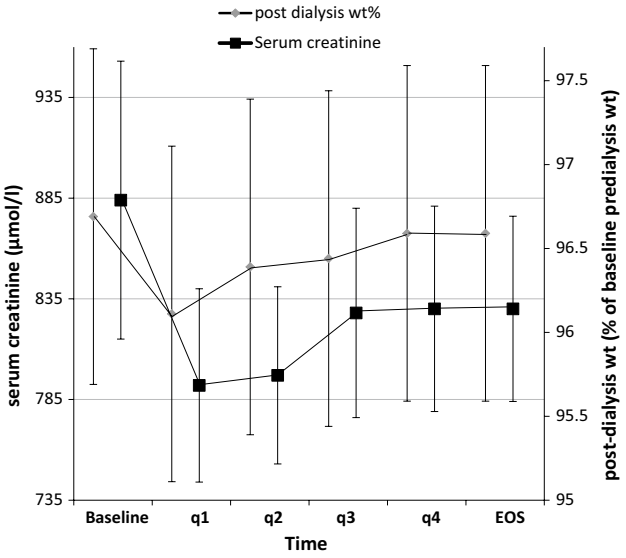

Fig. 2 Temporal change in post-dialysis weight and serum creatinine in INHD group during 1-year follow-up ($n = 30$). Data are mean ± standard error. One-year follow-up period was divided into four 13-week quarters (*q1–q4*); post-dialysis weight and serum creatinine were captured and averaged for the final three dialysis sessions of each of the four 13-week quarters. *EOS* end of study

We believe that the ability to safely consume more solute and fluid interdialytically, presumably because of the ability of INHD to safely remove more fluid/session due to a lower ultrafiltration rate, is of critical significance to dialysis recipients whose diets are often restricted on CHD regimens. This suggests that CHD recipients whose high IDWG creates challenging CHD sessions (due to intradialytic hypotension, for example) may be excellent candidates for INHD where a higher IDWG is better tolerated.

In a large-cohort study, Chang et al. [27] reported a decline in post-dialysis weight which reached a nadir at the 5th month in incident HD patients. Larger weight loss during the first 12 months was associated with higher death risk, whereas weight gain was associated with greater survival. The pattern of weight change in our study was different than theirs as our study was among the prevalent HD patients. Body weight can reflect both fluid volume and nutritional status separately or in tandem. The evolution of body weight in HD is the net result of two opposing processes: the control of the extracellular fluid volume and increase in muscle and fat as a result of anabolism induced by HD treatment. We speculate that the initial decline in weight among our patients who converted to INHD was probably the result of a trend toward extracellular volume normalization. With extended duration dialysis, controlling extracellular volume became easier due to lower ultrafiltration rate (8.73 vs. 6.73 ml/kg/h in INHD and CHD, respectively). After a drop at the beginning of follow-up, we observed a gradual weight gain. We speculate that this gain in weight does not reflect a "rebound" increase in extracellular volume, but it might reflect a gain in dry weight especially lean body mass following the change in dialysis modality, which can be concluded from the parallel increase in serum creatinine and the lack of increase in NT-proBNP. Indeed, a protective role has been described for high serum creatinine concentrations in dialysis patients [28]. When residual kidney function and dialysis dose are stable, the serum creatinine concentration may be used as a surrogate of muscle mass in dialysis patients [29–32]. The

Table 4 Nutrition–inflammation and cardiac biomarkers at baseline and at the end of follow-up

	INHD ($n = 30$)	Conventional ($n = 17$)	p	p Adjusted for case-mix*
Albumin (g/l)				
Baseline	38.1 ± 2.7	40.4 ± 3.9	0.02	0.18
One year	39.1 ± 3.1	40.3 ± 3.3	0.22	0.98
Difference	1.0 ± 3.2	−0.1 ± 3.9	0.17	0.20
Prealbumin (g/ml)				
Baseline	0.30 ± 0.06	0.36 ± 0.08	<0.001	0.03
One year	0.31 ± 0.08	0.36 ± 0.08	0.04	0.27
Difference	0.01 ± 0.08	−0.002 ± 0.08	0.29	0.36
Cholesterol (mmol/l)				
Baseline	3.92 ± 0.83	4.48 ± 1.69	0.13	0.42
One year	4.17 ± 1.09	4.23 ± 1.20	0.87	0.76
Difference	0.26 ± 0.08	−0.25 ± 0.08	0.03	0.16
hs-CRP (mg/l)**				
Baseline	7.75 (2.6, 15.3)	5.3 (2.7, 20.7)	0.75	0.80
One year	6.4 (2.1, 12.4)	5.4 (2.0, 9.6)	0.26	0.50
Difference	0.3 (−2.9, 6.0)	−1.4 (−13.3, 2.5)	0.08	0.39
Statin use (%)				
Baseline	57	53	0.80	
One year	67	59	0.59	
McNemar's p	0.09	0.32		
NT-proBNP (ng/L)**				
Baseline	2430 (1570, 7396)	1566 (948, 2466)	0.04	0.03
One year	1626 (938, 5496)	1667 (1053, 2770)	0.44	0.47
Difference	−627 (−5136, 1510)	76 (−344, 1046)	0.08	0.15
Troponin I (μg/L)**				
Baseline	0.025 (0.013, 0.036)	0.012 (0.004, 0.023)	0.11	0.25
1 year	0.021 (0.013, 0.031)	0.015 (0.005, 0.022)	0.15	0.27
Difference	−0.001 (−0.007, 0.005)	0.001 (−0.003, 0.005)	0.27	0.73

Baseline and end of study nutrition–inflammation markers were available for 17 patients in the CHD group

* Case-mix variables included age, gender, race/ethnicity, diabetes history and dialysis vintage

** Data expressed as median and interquartile range due to skewness

initial sharp drop in serum creatinine is probably due to its higher clearance with INHD, and its subsequent gradual increase, with a stable dialysis prescription, suggests a gradual gain in muscle mass possibly due to a better appetite and so a better nutritional status. In the INHD group, we did not see a significant correlation between weight gain and change in serum NT-proBNP which is a marker of extracellular volume status [33]. Although weight increased, serum NT-proBNP decreased in the INHD group (Table 4). This suggests that the observed weight gain was not mediated by extracellular volume expansion.

In our study, similar to the study of Ipema et al. [34], serum cholesterol increased in the INHD group and decreased in the CHD group. Hypercholesterolemia as well as increased body weight seem to be protective features that are associated with a better survival among dialysis patients [35]. The increase in serum cholesterol in the INHD group, which was observed despite comparable patterns in the use of statins over time, may be a further indicator of better appetite and improved dietary intake.

In our study, serum albumin increased in the INHD group from baseline to the end of study, but this change was not significantly different compared with CHD group. Eriguchi et al. also reported a gradual rise in serum albumin in HD patients over 18-month follow-up period, but their population consisted of incident hemodialysis patients [36]. The lack of effect of intensified dialysis on serum albumin concentration was similarly shown in the frequent hemodialysis network trials [37]. Noting that prealbumin is a more sensitive indicator of nutritional status [38, 39], we elected to measure this marker as well. However, we found

no significant changes in serum prealbumin with INHD as compared to CHD.

In contrast to the study of Demirci et al.[20] which reported a decrease in serum hs-CRP, we did not observe a significant decrease in serum hs-CRP in INHD group after 1 year. Though we hypothesized that longer HD would mitigate the inflammatory state attributed to dialysis, it has been shown that the HD procedure could induce a net protein catabolic state at the whole-body level [40]. More dialysis may induce higher protein catabolism and heighten the inflammatory process. These might explain the lack of a significant rise in serum albumin and prealbumin and the failure to decrease inflammatory markers (serum hs-CRP) irrespective of actual nutritional status.

The strengths of our study include the use of serial quarterly measures of nutritional parameters and comparisons to a control group comprising patients who remained on CHD. This is also the first study to measure the association between INHD conversion and prealbumin, a sensitive marker of nutritional status [38]. We also conducted analyses that adjusted for important confounders such as age, race, gender and dialysis vintage.

However, there are important limitations to consider. First, our study was limited by a small sample size, lack of randomization and lack of dietary records from participants. Second, unequal frequency of the follow-up nutrition counseling by the dietitians between the two groups is another limitation. However, the less access to dietitian in the INHD group might even lead to underestimation of the effect of INHD. Third, patients were enrolled from only two centers in Canada, which may limit the generalizability of the results, but our inclusion and exclusion criteria were broad, and control patients were representative of the general HD population with no medical contraindications to INHD conversion. Third, we did not directly measure fat and muscle mass and we used serum creatinine and body weight as surrogates. Finally, though the impact of INHD on nutritional and inflammatory parameters was modest, it is possible that greater dialysis intensification (e.g., as delivered by nightly home nocturnal dialysis) would have been associated with benefit. Unfortunately, we did not include such patients in our cohort.

In conclusion, conversion to INHD was associated with greater intedialytic weight gain and relatively stable body mass, which supports the notion that INHD permits more liberal dietary intake. It was also associated with an initial decline followed by a significant increase in serum creatinine concentration which, in the face of stable dialytic clearance, might suggest increased muscle mass. Though cholesterol concentration rose in patients who commenced INHD, there was no evidence that conversion to INHD suppressed inflammation or had a salutary effect on other nutritional markers.

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