Significant Fluctuations in Total Complement Hemolytic Activity as a Nutritional Parameter After Transition from Hemodialysis to Online Hemodiafiltration

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Objective: Online hemodiafiltration (OLHDF) therapy has clinical benefits in patients requiring blood purification; however, it may lead to essential serum protein elimination. Previous studies suggest that total complement hemolytic activity (CH50) is related to nutritional status. This study aimed to evaluate the association of CH50 fluctuations and nutritional status after transition from hemodialysis (HD) to OLHDF.

Methods: Serum samples from 20 patients were analyzed during transition from HD to OLHDF therapy and at 3 and 9 months after the transition. Nutritional status was assessed by the Geriatric Nutritional Risk Index (GNRI). Subgroup analysis was performed according to CH50 increase or decrease.

Results: Variability rate of CH50 was positively correlated with that of serum albumin (Alb) and other serum nutritional indicators at 9 months ($p < 0.05$). In patients with a decrease in CH50 at 9 months, serum Alb and other serum nutritional indicators also reduced ($p < 0.05$). GNRI at 9 months was lower in the CH50-decrease than in the CH50-increase group ($p < 0.05$).

Conclusions: Significant CH50 fluctuations were found to be as a nutritional parameter after transition from HD to OLHDF.

Key words: online hemodiafiltration (OLHDF), total complement hemolytic activity (CH50), complement, nutritional status, Geriatric Nutritional Risk Index (GNRI)

Authors contributions

D.H. conceived the study, participated in the study design, carried out data interpretation, performed the statistical analysis, drafted the manuscript, and critically revised the article for important intellectual content. I.O., K.T., and H.T. conceived the study, participated in the design of the study, and contributed to data interpretations and drafting of the manuscript. K.S. and M.N. were responsible for the collection of blood samples and assembly of

clinical data. H.R., Y.T., and Y.S. conceived and participated in the design of the study and critically revised the manuscript. The final version of the manuscript was approved by all authors.

Introduction

Levels of serum complement components, such as C3 and C4, often fluctuate within the normal range, and baseline levels differ per individual¹⁾. The complement system is not only required for immune response mechanisms but also vital for

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other physiological processes^{2) 3)}. Moreover, the complement system is closely linked to nutritional and metabolic status^{4) 5)}. In undernourished individuals, serum C3 levels are generally low, and nutritional rehabilitation is associated with reversion of serum C3 to the normal range^{6) 7)}. However, fluctuations in serum complement components have not gained adequate attention in clinical practice.

To optimize renal replacement therapy for patients with end-stage renal disease (ESRD), hemodiafiltration (HDF) has been performed as an alternative to hemodialysis (HD)^{8) 9)}. In conventional HD, diffusion is the main clearance mechanism. Consequently, uremic toxins of low molecular weight are efficiently eliminated, whereas those of mid-to-high molecular weight are not¹⁰⁾. Retention of uremic toxins was correlated with morbidity and mortality in ESRD patients^{11) 12)}. To facilitate the elimination of high-molecular-weight uremic toxins, online HDF (OLHDF) has been implemented. Although dialysis fluid purification by OLHDF has several clinical benefits^{13) 14)}, serum proteins, such as albumin (Alb), that can bind to uremic toxins may also be eliminated^{15) 16)}. Removal of Alb, which has a half-life of about 14 days, was observed to some extent in a previous study¹⁷⁾. Furthermore, studies suggest that protein wasting is related to morbidity and mortality in patients receiving maintenance HD^{18) 19)}. Thus, frequent nutritional status monitoring is essential for the treatment of ESRD patients and all dialysis patients^{20) 21)}. Moreover, biological markers of protein wasting and nutritional status in patients with ESRD are also significant.

Total complement hemolytic activity (CH50) analysis enables the assessment of the overall functioning of the complement system. CH50 represents early turnover proteins and can be a clinical marker for nutritional and metabolic states²⁾. Only a few studies investigated the association of CH50 fluctuation and nutritional status after transition from HD to OLHDF; thus, this study aimed to evaluate the relationship between CH50 fluctuations and nutritional status in patients requiring blood purification for ESRD after transition from HD to OLHDF.

Materials and Methods

1. Data collection

This study enrolled 20 ESRD outpatients who were transitioned from HD to OLHDF for blood purification therapy at Nerima Sakuradai Clinic (Tokyo, Japan) in April 2012. Study procedures were performed in accordance with the Declaration of Helsinki and the protocol was approved by the Nerima Sakuradai Clinic ethics committee (No. 1). Written informed consent was obtained from all participants prior to inclusion. Blood samples were obtained from each patient during and at 3 and 9 months after the transition from HD to OLHDF therapy. Serum parameters were analyzed, including CH50, urea nitrogen (UN), creatinine (Cre), Alb, uric acid (UA), sodium (Na), potassium (K), chloride (Cl), calcium (Ca), phosphorus (P), total cholesterol (T-chol), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin (Hb), and hematocrit (Hct). Other clinical data, including systolic blood pressure (SBP), diastolic blood pressure (DBP), dry weight (DW), Kt/V (an index of hemodialysis treatment adequacy), and patient's background characteristics, were also collected. All patients were treated with the same type of OLHDF device (TR-3000M; TORAY, Tokyo, Japan), with post-dilution three times a week. The parameter settings for OLHDF were the same for all patients, except for the hemodiafilter size, session time, and Q_B (ml/min), which represents the blood flow rate for blood purification. The patients were not on intermittent total parenteral nutrition in the duration.

2. Nutritional status indicator

The Geriatric Nutritional Risk Index (GNRI) is a useful tool for nutritional status assessment in ESRD patients^{22) 23)}, which was developed as a simple method requiring only three objective parameters: body weight, height, and serum Alb. Here, the nutritional status of all patients was determined using the GNRI, calculated as follows: $GNRI = 14.89 \times \text{serum Alb (g/dl)} + 41.7 \times \{\text{DW (kg)} / \text{ideal body weight (IBW) (kg)}\}$. In the case of $DW > IBW$, $DW/IBW = 1$. $GNRI < 91$ indicates an at-risk nutritional status.

3. Statistical analysis

All statistical analyses were performed with GraphPad Prism 6J software for Windows, version 6.01 (San Diego, CA, USA). For comparisons of clinical data, t-tests and one-way analysis of variance were employed, with Bonferroni correction for multiple comparisons. A two-sided p-value <0.05 was considered to denote statistical significance. Data are expressed as mean $\pm$ standard deviation (SD), except for age (median).

Results

1. Patient characteristics and dialysis conditions before and after transition to OLHDF

Patient characteristics, including age, sex, primary disease related to ESRD, and dialysis conditions before and after transition to OLHDF, are shown in Table-1. The study population comprised 11 females and 9 males. The median age was 74.5 years, the mean duration between initiation of HD and transition to OLHDF was 4.0 years, and primary renal diseases included chronic glomerular nephritis, diabetic nephropathy, and nephrosclerosis.

Table-1 Patient characteristics and HD conditions before and after transition to OLHDF

Pt No.	Age (y)	Sex	Primary disease	Duration with HD (y)	transition period				9 months after the transition			
					Hemo-diafilter	Time (h)	Replacement fluid (L/h)	Q _B (ml/min)	Hemo-diafilter	Time (h)	Replacement fluid (L/h)	Q _B (ml/min)
1	78	F	CGN	4	MFX-15	3.5	4	150	MFX-15	3.5	4	150
2	68	M	DMN	2	MFX-15	3	4	180	MFX-15	3	4	180
3	81	F	Unknown	0.5	MFX-15	3	4	150	MFX-21	3	4	150
4	77	M	Renal cancer	1	MFX-15	3	4	150	MFX-15	3	4	150
5	61	M	Ureter cancer	0.5	MFX-15	3	4	200	MFX-21	3	4	200
6	75	F	DMN	7	MFX-15	3.5	4	180	MFX-21	3.5	4	180
7	42	F	CGN	11	MFX-15	4	4	220	MFX-21	4	4	200
8	64	M	LMBS	6	MFX-15	3.5	4	200	MFX-21	3.5	4	200
9	72	F	CGN	3	MFX-15	3.5	4	180	MFX-15	3.5	4	180
10	58	F	CGN	6	MFX-15	3	4	200	MFX-21	3	4	200
11	77	F	Renal sclerosis	3	MFX-11	3.5	4	150	MFX-11	3.5	4	150
12	90	M	Renal sclerosis	0.5	MFX-15	3	4	210	MFX-15	3	4	210
13	70	F	DMN	7	MFX-11	3.5	4	180	MFX-11	3.5	4	180
14	72	F	Low heart function	1	MFX-15	4	4	180	MFX-15	4	4	180
15	87	M	Renal sclerosis	4	MFX-15	3	4	180	MFX-15	3	4	180
16	81	M	CGN	4	MFX-15	3	4	180	MFX-15	3	4	180
17	74	F	CGN	8	MFX-15	3.5	4	180	MFX-21	3.5	4	180
18	75	M	CGN+DMN	4	MFX-11	3.5	4	180	MFX-11	3.5	4	180
19	58	F	PCK	6	MFX-15	3.5	4	200	MFX-15	3.5	4	200
20	79	M	DMN	0.5	MFX-15	3	4	180	MFX-15	3	4	180

Abbreviations: Pt No.: patient number, CH50: total complement hemolytic activity, M: male, F: female, HD: hemodialysis, OLHDF: online hemodiafiltration, CGN: chronic glomerulonephritis, DMN: diabetic nephropathy, LMBS: Laurence-Moon-Biedl syndrome, PCK: polycystic kidney, MFX[®]: maxiflux[®]

Duration with HD (y) represents HD treatment duration until the transition to OLHDF. Time (h) represents the continuous time length of each OLHDF session. Replacement fluid (L/h) represents the quantity of supplementary liquid per hour during OLHDF. Q_B (ml/min) represents blood flow rate during OLHDF. The hemodiafilter size of MFX-11 is 1.1 m², MFX-15 is 1.5 m², and MFX-21 is 2.1 m².

None of the patients received intravenous nutrition during the 9-month study period. With regard to OLHDF conditions, the hemodiafilter size was increased throughout the study period in 7 patients, each session was 3 to 4 h, and Q_B was set at 150 to 220 ml/min for all patients.

2. Clinical and blood analysis data before and after the transition

Clinical parameters, including DW, Kt/V, SBP, and DBP, and blood analysis data during and 9 months after transition are shown in Table-2. Kt/V improved at 9 months ($p < 0.05$); no significant

changes in DW, SBP, or DBP were observed; and no significant changes in serum parameters throughout the study period, except for a decrease in HDL-C levels ($p < 0.05$), were noted. However, analysis of the relationship between CH50 fluctuations and specific nutritional parameters throughout the study period demonstrated that the variability rate of CH50 was positively correlated with that of Alb ($p < 0.05$, $r = 0.53$), K ($p < 0.05$, $r = 0.45$), T-chol ($p < 0.05$, $r = 0.48$), and HDL-C ($p < 0.05$, $r = 0.51$) (Figure-1). To further evaluate the clinical significance of CH50 fluctuations in relation to nutritional status, patients were divided into two

Table-2 Clinical and blood analysis data before and after the transition

	all			CH50-increase group			CH50-decrease group		
	before	9 months later	p-value	before	9 months later	p-value	before	9 months later	p-value
Age (y)	74.5			70.0			76.0		n.s.
Height (meter)	1.54 $\pm$ 0.08			1.53 $\pm$ 0.08			1.54 $\pm$ 0.08		n.s.
DW (kg)	49.6 $\pm$ 9.75	50.0 $\pm$ 10.4	n.s.	52.2 $\pm$ 10.7	52.9 $\pm$ 11.8	n.s.	47.0 $\pm$ 8.4	47.0 $\pm$ 8.4	n.s.
kt/V	1.31 $\pm$ 0.30	1.39 $\pm$ 0.27	<0.05	1.31 $\pm$ 0.31	1.40 $\pm$ 0.25	n.s.	1.32 $\pm$ 0.30	1.39 $\pm$ 0.31	n.s.
SBP (mmHg)	139.3 $\pm$ 22.0	136.8 $\pm$ 31.8	n.s.	142.1 $\pm$ 17.1	143.1 $\pm$ 31.4	n.s.	136.4 $\pm$ 26.7	130.5 $\pm$ 32.6	n.s.
DBP (mmHg)	73.9 $\pm$ 12.4	69.8 $\pm$ 13.2	n.s.	77.7 $\pm$ 11.0	72.3 $\pm$ 12.4	n.s.	70.1 $\pm$ 13.1	67.2 $\pm$ 14.1	n.s.
CH50 (U/ml)	41.5 $\pm$ 7.6	40.3 $\pm$ 8.6	n.s.	39.3 $\pm$ 7.6	43.5 $\pm$ 7.8	<0.01	43.6 $\pm$ 7.4	37.1 $\pm$ 8.6	<0.01
WBC (/ μ l)	5,445 $\pm$ 1,972	5,705 $\pm$ 3,774	n.s.	5,640 $\pm$ 2,146	6,880 $\pm$ 5,008	n.s.	5,250 $\pm$ 1,875	4,530 $\pm$ 1,386	n.s.
RBC (10^4 / μ l)	334.8 $\pm$ 46.4	333.6 $\pm$ 46.0	n.s.	346.0 $\pm$ 56.6	344.4 $\pm$ 55.7	n.s.	323.6 $\pm$ 32.6	322.8 $\pm$ 33.1	n.s.
Hb (g/dl)	10.6 $\pm$ 1.5	10.6 $\pm$ 1.2	n.s.	10.9 $\pm$ 1.9	10.9 $\pm$ 1.6	n.s.	10.3 $\pm$ 1.0	10.2 $\pm$ 0.6	n.s.
Hct (%)	33.5 $\pm$ 4.1	32.9 $\pm$ 3.5	n.s.	34.3 $\pm$ 5.1	34.0 $\pm$ 4.4	n.s.	32.6 $\pm$ 2.7	31.9 $\pm$ 1.9	n.s.
UN (mg/dl)	61.2 $\pm$ 13.8	56.5 $\pm$ 14.3	n.s.	68.4 $\pm$ 13.4 ^a	63.6 $\pm$ 13.8 ^d	n.s.	53.9 $\pm$ 10.2 ^a	49.3 $\pm$ 11.1 ^d	n.s.
Cre (mg/dl)	9.60 $\pm$ 3.44	9.72 $\pm$ 3.15	n.s.	11.3 $\pm$ 3.2 ^d	11.3 $\pm$ 3.4 ^e	n.s.	7.86 $\pm$ 2.82 ^b	8.19 $\pm$ 2.13 ^e	n.s.
Alb (g/dl)	3.70 $\pm$ 0.34	3.57 $\pm$ 0.42	n.s.	3.79 $\pm$ 0.32	3.79 $\pm$ 0.32 ^f	n.s.	3.60 $\pm$ 0.40	3.34 $\pm$ 0.39 ^f	<0.05
UA (mg/dl)	7.45 $\pm$ 1.08	7.23 $\pm$ 1.23	n.s.	7.83 $\pm$ 1.11	8.04 $\pm$ 0.97 ^g	n.s.	7.06 $\pm$ 0.95	6.41 $\pm$ 0.88 ^g	<0.05
Na (mmol/L)	140.8 $\pm$ 2.6	140.4 $\pm$ 4.6	n.s.	141.4 $\pm$ 3.0	140.2 $\pm$ 5.5	n.s.	140.2 $\pm$ 2.0	140.5 $\pm$ 3.8	n.s.
K (mmol/L)	5.11 $\pm$ 0.69	4.96 $\pm$ 0.60	n.s.	5.34 $\pm$ 0.72	5.26 $\pm$ 0.54 ^h	n.s.	4.88 $\pm$ 0.62	4.63 $\pm$ 1.53 ^h	n.s.
Cl (mmol/L)	106.9 $\pm$ 3.4	107.3 $\pm$ 4.9	n.s.	106.9 $\pm$ 3.6	106.0 $\pm$ 5.4	n.s.	106.8 $\pm$ 3.3	108.6 $\pm$ 4.3	n.s.
Ca (mg/dl)	8.77 $\pm$ 0.76	8.75 $\pm$ 0.55	n.s.	8.81 $\pm$ 0.67	8.83 $\pm$ 0.57	n.s.	8.73 $\pm$ 0.88	8.66 $\pm$ 0.55	n.s.
P (mg/dl)	5.55 $\pm$ 1.24	5.29 $\pm$ 1.21	n.s.	6.06 $\pm$ 1.10	5.43 $\pm$ 1.56	n.s.	5.04 $\pm$ 1.21	5.15 $\pm$ 0.79	n.s.
T-chol (g/dl)	165.4 $\pm$ 31.3	163.9 $\pm$ 31.5	n.s.	179.2 $\pm$ 34.2 ^c	186.9 $\pm$ 26.0 ⁱ	n.s.	151.6 $\pm$ 21.8 ^c	140.9 $\pm$ 15.7 ⁱ	n.s.
HDL-C (g/dl)	51.4 $\pm$ 13.5	48.5 $\pm$ 12.9	<0.05	52.8 $\pm$ 13.7	52.5 $\pm$ 13.3	n.s.	49.9 $\pm$ 13.9	44.5 $\pm$ 11.7	<0.05
LDL-C (g/dl)	93.9 $\pm$ 23.9	88.8 $\pm$ 20.1	n.s.	102.0 $\pm$ 26.5	102.9 $\pm$ 15.2 ^j	n.s.	85.8 $\pm$ 19.0	74.6 $\pm$ 13.3 ^j	n.s.
TG (mg/dl)	104.5 $\pm$ 60.0	115.5 $\pm$ 89.3	n.s.	118.5 $\pm$ 77.1	145.0 $\pm$ 119.3	n.s.	90.4 $\pm$ 34.5	85.9 $\pm$ 25.7	n.s.

Abbreviations: n: number, DW: dry weight for hemodialysis and hemodiafiltration, Kt/V: an index to quantify hemodialysis treatment adequacy, SBP: systolic blood pressure, DBP: diastolic blood pressure, CH50: total complement hemolytic activity, WBC: white blood cell, RBC: red blood cell, Hb: hemoglobin, Hct: hematocrit, UN: serum urinary nitrogen, Cre: serum creatinine, Alb: serum albumin, UA: serum uric acid, Na: sodium, K: potassium, Cl: chloride, Ca: calcium, P: phosphorus, T-chol: total cholesterol, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, TG: triglycerides. All values are expressed as mean $\pm$ SD, except for age (y) (median). Kt/V in all patients significantly increased from the start of transition to 9 months after the transition. No significant change in blood analysis data in all patients between the transition period and 9 months after was noted, except for a decrease in HDL-C level. Alb, UA, and HDL-C levels in the CH50-decrease group significantly declined from the transition period to 9 months after the transition. ^{a-i} $p < 0.05$

Figure-1 The association of the rate of variability between CH50 and nutritional indicators in blood analysis CH50: total complement hemolytic activity, Alb: serum albumin, K: serum potassium, T-chol: total cholesterol, HDL-C: high-density lipoprotein cholesterol, r: correlation coefficient. The variability rate of CH50 in all patients from the start of transition to 9 months after the transition was significantly positively correlated with that of Alb (A), K (B), T-chol (C), and HDL-C (D) (all $p < 0.05$; $r = 0.53$, $r = 0.45$, $r = 0.48$, and $r = 0.51$, respectively). These results suggest that CH50 fluctuations can reflect changes in nutritional status.

Table-3 GNRI for nutritional status assessment in patients treated with OLHDF

		before	9 months later	p-value
GNRI	CH50-increase group	95.1 ± 5.7	95.2 ± 6.0	n.s.
	CH50-decrease group	90.2 ± 9.1	86.3 ± 9.3	n.s.
p-value		n.s.	$p < 0.05$	
GNRI < 91	CH50-increase group	3	3	
Patients (n)	CH50-decrease group	4	6	

Abbreviations: OLHDF: online hemodiafiltration, CH50: total complement hemolytic activity, n: number, GNRI: geriatric nutritional risk index, GNRI < 91: nutritional risk range

In the CH50-increase group, GNRI was not significantly different between the transition period and 9 months after the transition, and three patients had GNRI < 91 in the CH50-increase group at both timepoints. The GNRI in the CH50-decrease group was lower than that in the CH50-increase group at the transition, and GNRI was significantly lower in the CH50-decrease than in the CH50-increase group at 9 months after the transition. Moreover, in the CH50-decrease group, the number of patients with GNRI < 91 increased from four during the transition period to six at 9 months after the transition.

groups according to an increase or decrease in CH50 from 0 to 9 months; each group comprised 10 patients. At the start of transition (0 month), UN, Cre, and T-chol levels were lower in the CH50-decrease than in the CH50-increase group (all $p < 0.05$). At 9 months, Alb, UA, K, and HDL-C, as well as UN, Cre, and T-Chol, levels were significantly lower in the CH50-decrease than in the CH50-increase group (all $p < 0.05$). Moreover, a significant decline in Alb, UA, and HDL-C levels in the CH50-decrease group throughout the study period ($p < 0.05$) was observed.

3. Nutritional status assessment

As shown in Table-3, the nutritional status of all patients was evaluated using the GNRI. Among patients with increased CH50, the GNRI was 95.1 ± 5.7 at the transition period and 95.2 ± 6.0 at 9 months after, and three patients had GNRI < 91 at both timepoints. By contrast, the GNRI in the CH50-decrease group was 90.2 ± 9.1 during the transition, and 86.3 ± 9.3 at 9 months after, which was significantly lower than that in the CH50-increase group ($p < 0.05$). Furthermore, four patients in the CH50-decrease group had GNRI < 91 during the

Figure-2 CH50 fluctuation in the CH50-increase (A) and CH50-decrease (B) groups
CH50: total complement hemolytic activity. The mean CH50 in the CH50-increase group (A) was significantly increased at 3 months after the transition (44.0 ± 10.5 U/ml, $p < 0.05$); no significant change was noted thereafter. The mean CH50 in the CH50-decrease group (B) showed no fluctuation during the first 3 months (44.6 ± 7.4 U/ml) but significantly decreased at 9 months after the transition ($p < 0.05$).

transition, which increased to six patients at 9 months thereafter.

4. CH50 fluctuations in the two groups from the start of transition to 3 months and from 3 to 9 months after transition

CH50 fluctuations in the CH50-increase and CH50-decrease groups from the start of transition to 3 months and from 3 to 9 months after the transition are shown in Figure-2. The mean CH50 in the CH50-increase group significantly elevated at 3 months after the transition (44.0 ± 10.5 U/ml, $p < 0.05$); no significant change occurred thereafter. The mean CH50 in the CH50-decrease group showed no fluctuation during the first 3 months (44.6 ± 7.4 U/ml) but significantly decreased at 9 months after the transition ($p < 0.05$).

Discussion

OLHDF therapy has been reported to be beneficial in a variety of clinical scenarios, including anemia, biocompatibility, hemodynamic instability, dialysis-related hypotension, residual renal function maintenance, and dialysis-related amyloidosis prevention, as well as in increasing survival rates in ESRD patients^{13) 14)}. However, in this study, except for Kt/V elevation, no improvements in clinical characteristics, such as anemia, were observed. Nevertheless, since the study duration and the

number of enrolled patients were limited, which are conceivable limitations, long-term observational studies and more patients are necessary to verify this finding. Moreover, this study identified, through blood analysis, a significant positive correlation between the variability rate of CH50 and that of nutritional indicators, including Alb, K, T-chol, and HDL-C, until 9 months after transition from HD to OLHDF therapy. CH50 fluctuations were reflective of the nutritional status of patients receiving blood purification therapies. Although fluctuations occur within the normal range and the baseline level differs per patient, the changes in CH50 are considered to be clinically significant after transition from HD to OLHDF, as previously described in a general situation¹⁾. Furthermore, subgroup analysis revealed differences between patients with increased and those with decreased CH50 at 9 months after the transition. Patient numbers 1-10 belonged to the CH50-increase group, and patient numbers 11-20 belonged to the CH50-decrease group. At 9 months after the transition, the CH50-increase group had no significant change in nutritional status. Nevertheless, the hemodiafilter size was increased in six of the 10 patients at 9 months. Before the transition from HD to OLHDF therapy, the CH50-decrease group had a smaller hemodiafilter size than the CH50-increase group, and only one patient (No. 17) had an

increased hemodiafilter size at 9 months. The CH50-decrease group had a poorer nutritional status based on blood analysis data, including significant decreases in Alb, UA, and HDL-C at 9 months after the transition.

GNRI, which is generally used in elderly people, is also a clinically useful marker for nutritional status assessment in HD patients²⁴⁾. At 9 months after the transition, the GNRI in the CH50-decrease group was significantly lower than that in the CH50-increase group and the number of patients with an at-risk nutritional status was higher in the CH50-decrease group. Given that protein wasting is related to morbidity and mortality in patients receiving maintenance HD treatment, these results are clinically significant.

The decline in serum Alb levels could be a consequence of direct leakage from the hemodiafilter and/or poor nutrient intake resulting in albumin synthesis reduction due to systemic inflammatory responses and infection^{25) 26)}. Based on this study's findings, transition from HD to OLHDF might be inappropriate for patients with poor nutritional status. Thus, transitioning to OLHDF therapy should be considered in the context of individual nutritional status. Particularly, patients with low UN, Cre, and T-chol levels or low GNRI during transition possibly have inadequate nutritional status to adapt to OLHDF.

In this study, CH50 fluctuations were significantly positively correlated with nutritional status at 9 months after transition from HD to OLHDF in patients receiving blood purification therapy. Fluctuations in CH50 over the 9-month follow-up period were of interest in both the CH50-increase and CH50-decrease groups. The timing of significant changes in mean CH50 was different between the two groups, with an increase from 0 to 3 months in the CH50-increase group and a decrease from 3 to 9 months in the CH50-decrease group. However, the reason for these results is unclear. It is possible that the balance between CH50 in the liver and body metabolism is affected by nutritional status. As a limitation, we should take some factors into consideration which can affect their CH50 levels such as inflammation diseases, collagen diseases, or infection diseases. However, those patients hadn't had any diseases which could strongly affect their CH50 levels except their primary diseases shown in

Table-1. Further studies about complement component fluctuations are needed; long-term observational studies and enrollment of more patients are also necessary to improve the clinical use of CH50 as a nutritional parameter. As a conclusion, significant CH50 fluctuations were observed as a nutritional parameter after transition from HD to OLHDF.

List of abbreviations

HDF: hemodiafiltration
 ESRD: end-stage renal disease
 HD: hemodialysis
 OLHDF: online hemodiafiltration
 Alb: serum albumin
 CH50: total complement hemolytic activity
 UN: serum urea nitrogen
 Cre: serum creatinine
 UA: serum uric acid
 Na: serum sodium
 K: serum potassium
 Cl: serum chloride
 Ca: serum calcium
 P: serum phosphorus
 T-chol: total cholesterol
 HDL-C: high-density lipoprotein cholesterol
 LDL-C: low-density lipoprotein cholesterol
 TG: triglycerides
 WBC: white blood cell
 RBC: red blood cell
 Hb: hemoglobin
 Hct: hematocrit
 SBP: systolic blood pressure
 DBP: diastolic blood pressure
 DW: dry weight
 GNRI: Geriatric Nutritional Risk Index
 IBW: ideal body weight
 SD: standard deviation

Ethics approval and consent to participate

Study procedures were performed in accordance with the Declaration of Helsinki and the protocol was approved by the hospital ethics committee. Informed consent was obtained from all participants prior to inclusion.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no conflict of interest.

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