Renal Replacement Therapy

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Glycated hemoglobin and glycated albumin in patients with diabetes undergoing hemodiafiltration

Yukie Kitajima[1*], Shunichiro Urabe[2], Takashi Hosono[2], Satoshi Yoshikawa[3], Yuzuru Sato[3] and Toru Hyodo[2]

Abstract

Background: Online hemodiafiltration (OHDF), which results in high albumin leakage, is now widely used in Japan for dialysis, since the national insurance system began reimbursing its costs in 2012. Glycated albumin (GA) levels are affected by albumin leakage into effluent dialysate fluid. Therefore, GA levels in patients requiring diabetes-related dialysis undergoing OHDF require monitoring. However, there have been no previous reports on glycemic control indicators of patients with diabetes undergoing OHDF. We aimed to develop a glycemic control index for patients requiring diabetes-related dialysis undergoing OHDF.

Methods: This study comprised 133 diabetic patients undergoing OHDF. We examined the correlation between GA and glycated hemoglobin (HbA1c) levels. We analyzed effluent dialysate fluid samples from 41 patients classified into 3 groups, namely, group A, non-protein-leaking OHDF ($n = 20$); group B, protein-leaking OHDF ($n = 14$); and group C, highly efficient protein-leaking OHDF ($n = 7$). We examined the association between GA and HbA1c levels in each group and among patients.

Results: A significant positive correlation was observed between GA and HbA1c levels ($r = 0.562$, $p < 0.0001$). There was no significant correlation between pre-dialysis blood glucose levels and HbA1c or GA levels as observed on regular blood tests performed under non-fasting conditions. Patients were classified into 2 groups based on their mean albumin levels (3.4 g/dL cutoff). The correlation between HbA1c and GA levels was found to be weaker in the 51 patients with mean albumin levels < 3.4 g/dL ($r = 0.399$, $p = 0.0037$) than in the 82 patients with mean albumin levels ≥ 3.4 g/dL ($r = 0.674$, $p < 0.0001$). When the hemodiafilter performance was assessed, no correlation was observed between HbA1c and GA levels in group C patients.

Conclusions: GA levels may be underestimated in patients undergoing OHDF because of the effect of albumin leakage into the effluent dialysate fluid. If a stable hemoglobin value can be maintained during OHDF therapy, then GA and HbA1c levels should be used as a glycemic control index for patients requiring diabetes-related dialysis, considering the dialysis treatment method and protein permeability of the dialyzers and hemodiafilters.

Keywords: HbA1c, Glycated albumin, Hemodialysis filtration

* Correspondence: y-kitajima@thcu.ac.jp
[1]Department of Medical Nutrition, Tokyo Healthcare University, 3-11-3 Setagaya, Setagaya-ku, Tokyo 154-8568, Japan
Full list of author information is available at the end of the article

Background

Several factors can affect glycated hemoglobin (HbA1c) levels in patients on dialysis, such as the lifespan of erythrocytes and the use of erythropoiesis-stimulating agents (ESAs). Moreover, some case reports have shown that diurnal variations in blood glucose levels are underestimated [1–3]. Measurement of glycated albumin (GA) has been reported to be useful for patients undergoing hemodialysis (HD), as erythrocyte lifespan has been found not to affect GA levels [4]. Therefore, the use of GA as an indicator of glycemic control in diabetic patients undergoing dialysis has been recommended [5]. However, relative to hypoalbuminemia, GA levels have been reported to be underestimated, and albumin metabolism has been found to affect GA levels [5].

The main procedures for blood purification include HD and hemodiafiltration (HDF). After the online HDF (OHDF) was approved for coverage under the medical insurance system in Japan (2012), the number of patients undergoing OHDF increased approximately four-fold compared to the records in 2009 [6]. Although OHDF removes intermediate-molecular weight proteins more efficiently than HD, albumin leakage into the effluent dialysate fluid is common. Given that GA levels are affected by albumin metabolism and leakage, modalities for GA evaluation in patients undergoing OHDF may differ from the current standards. However, there have been no previous reports on glycemic control indicators of patients with diabetes undergoing OHDF.

In this study, we investigated the efficacy of using HbA1c and GA levels to evaluate glycemic control in patients requiring diabetes-related dialysis undergoing OHDF.

Methods

Participants

This study included 133 patients with diabetes undergoing OHDF at 2 participating institutions. We collected effluent dialysate fluid samples from 41 of the 133 patients with diabetes undergoing OHDF at a single institution. Patients with acute diseases, inflammatory conditions, hemoglobin level < 8.0 g/dL, liver dysfunction, or a history of blood transfusion were excluded. All patients underwent pre-dilution OHDF. Dialysis time, blood flow rate, dialysate flow rate, and replacement fluid volumes are shown in Tables 1 and 2. Information on diabetes medications prescribed to the patients is shown in Tables 3 and 4.

Measurements

HbA1c and GA levels, as well as other laboratory test results, were obtained from blood samples collected before the start of the first dialysis session each week. We investigated the correlation between HbA1c and GA levels in patients undergoing OHDF based on their mean albumin levels (3.4 g/dL cutoff).

In addition, based on a target value for low molecular weight protein removal in relation to complications as proposed by Sakurai [7], we classified the 41 patients from whom we had collected effluent dialysate fluid samples into 3 groups. According to Sakurai's study, the α1-microglobulin (α1-MG) removal rate corresponds to a reduction in uremic symptoms and albumin loss. A 20% α1-MG removal rate is equal to 2 g of albumin loss, and a 35% α1-MG removal rate is equal to 6 g of albumin loss. Therefore, we categorized patients in whom albumin leakage was <

Table 1 Characteristics of the study patients

Variable	
Number of patients (M/F)	133 (81/52)
Age (years)	68.7 ± 13.3
Dialysis history (months)	78.3 ± 67.1
Dialysis time (h)	3.7 ± 1.0
Blood flow rate (mL/min)	204.7 ± 29.6
Dialysate flow rate (mL/min)	531.8 ± 46.8
Replacement fluid volume (L)	45.0 ± 14.8
Dry weight (kg)	56.2 ± 14.1
Albumin (g/dL)	3.4 ± 0.4
UN (mg/dL)	60.6 ± 14.8
Hb (g/dL)	10.6 ± 1.0
Ht (%)	32.5 ± 3.2
Pre-dialysis blood glucose (mg/dL)	138.4 ± 45.4
HbA1c (%)	6.0 ± 0.9
GA (%)	20.4 ± 4.7
Fe (μg/dL)	59.7 ± 23.1
TIBC (μg/dL)	206.3 ± 46.1
TSAT (%)	30.0 ± 12.4
Ferritin (ng/dL)	261.0 ± 187.6
ESAs	
Darbepoetin alfa (μg /week) (number)	21.1 ± 17.4(98)
epoetin beta (U/week) (number)	3187.5 ± 1060.7(2)
epoetin beta pegol (μg /week) (number)	22.7 ± 9.8(11)
ERI (each ESA dose/kg/g/dL/week)	
Darbepoetin alfa (number)	0.04 ± 0.04(98)
Epoetin beta (number)	5.2 ± 1.5(2)
Epoetin beta pegol (number)	0.04 ± 0.02(11)
Iron (intravenous administration)	
Saccharated ferric oxide (mg/week) (number)	44.2 ± 29.0(45)
Iron-based phosphate binder (oral administration)	
Sucroferric oxyhydroxide (mg/week) (number)	8361.1 ± 5233.8(9)
Ferric citrate hydrate (mg/week) (number)	11940.3 ± 6267.9(22)

TSAT(%) = [serum Fe (μg/dL)/TIBC (μg/dL)] × 100. The levels are presented as mean ± standard deviation

Table 2 Group characteristics based on target levels for low-molecular-weight protein removal according to complications

	Group A Non-protein-leaking OHDF	Group B Protein-leaking OHDF	Group C Highly efficient protein-leaking OHDF	*p* value
Classification of albumin leakage	≤ 2.0 g	2.1 g ≥, < 6.0	6.0 g ≥	–
Albumin leakage (g)	0.85 ± 0.60	3.45 ± 1.08	7.64 ± 1.36	–
Number of patients (M/F)	20 (15/5)	14 (12/2)	7(7/0)	–
Age (years)	75.0 ± 7.7	61.1 ± 8.8	57.6 ± 7.0	< 0.0001
Dialysis history (months)	67.7 ± 35.5	71.4 ± 52.0	96.0 ± 67.4	0.7176
Dialysis time (h)	4.0 ± 0.3	3.9 ± 0.3	4.1 ± 0.2	0.7720
Blood flow rate (mL/min)	221.1 ± 25.4	262.9 ± 21.6	257.1 ± 18.9	0.0011
Dialysate flow rate (mL/min)	600	600	600	–
Replacement amount volume (L)	59.5 ± 14.9	58.4 ± 10.1	65.7 ± 9.6	0.4695
Dry weight (kg)	53.7 ± 9.3	70.4 ± 13.9	76.3 ± 10.9	< 0.0001
Albumin (g/dL)	3.3 ± 0.4	3.5 ± 0.3	3.3 ± 0.2	0.2272
UN (mg/dL)	60.5 ± 17.2	57.2 ± 11.0	59.0 ± 14.5	0.7829
Hb (g/dL)	10.2 ± 0.7	10.8 ± 1.6	10.7 ± 0.8	0.2394
Ht (%)	30.4 ± 2.4	32.7 ± 4.3	32.2 ± 2.6	0.0799
Pre-dialysis blood glucose (mg/dL)	131.1 ± 37.8	119.7 ± 48.6	133.8 ± 35.7	0.5783
HbA1c (%)	6.0 ± 0.9	6.4 ± 0.9	6.3 ± 0.9	0.3197
GA (%)	19.5 ± 2.6	18.4 ± 3.7	17.5 ± 4.5	0.2172
Fe (μg/dL)	45.9 ± 27.6	59.7 ± 28.2	74.0 ± 53.2	0.3077
TIBC (μg/dL)	211.3 ± 55.5	244.6 ± 49.8	243.7 ± 66.2	0.2961
TSAT (%)	22.2 ± 12.5	24.8 ± 11.5	35.5 ± 30.3	0.6347
Ferritin (ng/dL)	201.3 ± 183.4	206.2 ± 283.8	225.4 ± 206.6	0.9274
ESAs				
Darbepoetin alfa (μg/week) (number)	21.3 ± 23.8 (11)	20.4 ± 5.9 (3)	3.8 ± 3.5 (2)	–
Epoetin beta (U/week) (number)	2437.5 (1)	3937.5 (1)	–	–
Epoetin beta pegol (μg/week) (number)	23.8 ± 12.0 (5)	18.8 ± 4.4 (5)	37.5 (1)	–
ERI (each ESA dose/kg/g/dL/week)				
Darbepoetin alfa	0.012 ± 0.011	0.008 ± 0.003	0.002 ± 0.001	–
Epoetin beta	4.2	6.3	–	–
Epoetin beta pegol	0.049 ± 0.025	0.030 ± 0.008	0.043	–
Iron (intravenous administration) (mg/week)				
Saccharated ferric oxide (number)	65.0 ± 59.2 (4)	50.0 ± 42.4 (2)	–	–
Iron-based phosphate binder (oral administration) (mg/week)				
Sucroferric oxyhydroxide (number)	7000.0 ± 3031.1 (3)	12250.0 ± 8019.5 (3)	615.0 ± 1237.4 (2)	–
Ferric citrate hydrate (number)	10500.0 (2)	22750 ± 6062.3 (3)	15750 (2)	–

Mean age, blood flow rate, and dry weight were all significantly different among the 3 groups. TSAT(%) = [serum Fe (μg/dL)/TIBC (μg/dL)] × 100. Levels are presented as mean ± standard deviation

2.0 g as non-protein-leaking OHDF patients (group A), patients with albumin leakage of between 2.1 g and 5.9 g as protein-leaking OHDF patients (group B), and patients with albumin leakage of ≥ 6.0 g as highly efficient protein-leaking OHDF patients (group C). Sakurai reported collecting effluent dialysate fluid samples using previously reported partial pooling methods [8]. We then investigated the correlation between GA and HbA1c levels in groups A, B, and C.

Statistical analysis Data are expressed as mean ± standard deviation. The Kruskal-Wallis test was used for comparison among the 3 groups. Correlation coefficients were calculated using simple regression analysis. The statistically significant difference between the two slopes from each group was analyzed by the *Z* test for two correlation coefficients. Statistical analyses were performed using Stat View 4.5 for Windows (SAS Institute, Cary,

Table 3 Information on diabetes medications for the 133 study patients

Variable	Number
Insulin users	32
Dipeptidyl peptidase-4 inhibitor	17
α-glucosidase inhibitor	7
Glucagon-like peptide-1 receptor agonist	2
Glinide	1
Sulfonylurea	0
Non-insulin users	62
Dipeptidyl peptidase-4 inhibitor	55
α-Glucosidase inhibitor	19
Glucagon-like peptide-1 receptor agonist	2
Glinide	6
Sulfonylurea	1
Unused diabetes medications	39

Including multiple users of diabetes medications

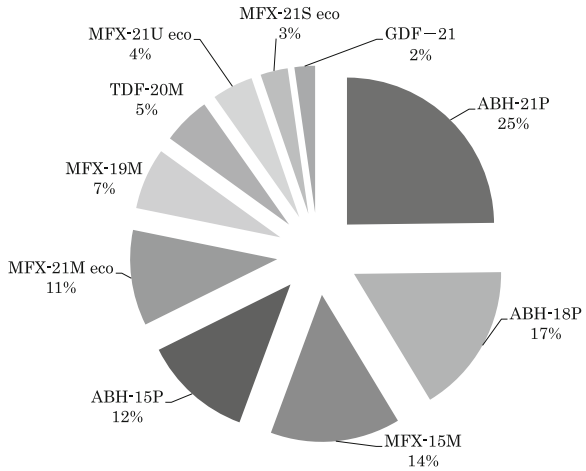

Fig. 1 Hemodiafilters used by participants in the OHDF group. The hemodiafilter ratios were as follows: ABH-21P, 25%; ABH-18P, 17%; MFX-15M, 14%; ABH-15P, 12%; MFX-21M eco, 11%; and one of another five different types of hemodiafilters, 21%

NC). For all analyses, $p < 0.05$ was considered statistically significant.

Results

In the OHDF patient groups, ABH-21P, ABH-18P, MFX-15 M, ABH-15P, and MFX-21 Meco hemodiafilters and one of another five different types of hemodiafilters were used in 25%, 17%, 14%, 12%, 11%, and 21% of patients, respectively (Fig. 1). All patients underwent pre-dilution OHDF. Table 5 shows the changes in hemoglobin (Hb) and hematocrit (Ht) levels 3 months before and after patient data were collected and analyzed. Given that there were no significant changes in Hb and Ht levels, and that acceptable levels were observed, we considered that these parameters had no effect on HbA1c levels. In addition, anemia-related indicator doses of ESAs and iron-containing agents are shown in Table 1.

There was a significant positive correlation between HbA1c and GA levels ($r = 0.562$, $R^2 = 0.316$, $p < 0.0001$) (Fig. 2). There was no significant correlation between pre-dialysis blood glucose levels and HbA1c or GA levels. We further categorized the patients based on mean albumin (3.4 g/dL cutoff) levels, and we examined the correlation between HbA1c and GA levels. The

Table 4 Information on diabetes medications for the 41 study patients in the 3 groups

	Group A Non-protein-leaking OHDF	Group B Protein-leaking OHDF	Group C Highly efficient protein-leaking OHDF
Number of patients	20	14	7
Insulin users (number)	3	5	2
Dipeptidyl peptidase-4 inhibitor (number)	1	3	2
α-Glucosidase inhibitor (number)	0	0	1
Glucagon-like peptide-1 receptor agonist (number)	1	1	0
Glinide (number)	0	1	2
Sulfonylurea (number)	0	0	0
Non-insulin users (number)	14	7	2
Dipeptidyl peptidase-4 inhibitor (number)	13	6	2
α-Glucosidase inhibitor (number)	5	1	1
Glucagon like peptide-1 receptor agonist (number)	1	1	0
Glinide (number)	0	3	0
Sulfonylurea (number)	1	0	0
Unused diabetes medications (number)	3	2	3

Including multiple users of diabetes medications

Table 5 Changes in hemoglobin and hematocrit levels in 133 patients

	Months						
	− 3	− 2	− 1	0	+ 1	+ 2	+ 3
Hb (g/dL)	10.8 ± 0.9	10.7 ± 1.1	10.7 ± 0.12	10.7 ± 0.9	10.8 ± 0.8	10.8 ± 0.8	10.8 ± 0.8
Ht (%)	32.8 ± 2.8	32.7 ± 3.5	32.8 ± 3.8	32.6 ± 3.0	32.8 ± 2.6	32.6 ± 2.9	32.7 ± 0.7

There were no significant changes in hemoglobin, and hematocrit levels in the 3 months before and after patient data were collected and analyzed. 0, baseline (March 2016)

correlation between HbA1c and GA levels was weaker in 51 patients with mean albumin levels < 3.4 g/dL (r = 0.399, R^2 = 0.160, p = 0.0037) than in the 82 patients with mean albumin levels ≥ 3.4 g/dL (r = 0.674, R^2 = 0.454, p < 0.0001) (Fig. 3). There was a significant difference in the correlation coefficients of the two groups (p = 0.0292).

Table 2 shows the results according to the hemodiafilter performance. Similar to the correlation between HbA1c and GA levels in 133 patients, HbA1c and GA levels in 41 patients showed a significantly positive correlation (r = 0.519, R^2 = 0.270, p = 0.0005) (Fig. 4). However, when assessed according to the hemodiafilter performance, a significant positive correlation was observed between HbA1c and GA levels in groups A and B, but no correlation was found in group C (Fig. 5).

Discussion

Inaba, et al. [4] reported a significant positive correlation between HbA1c and GA levels in their HD group (r = 0.777, p < 0.001). Their study involved 538 HD patients with type 2 diabetes. Patient characteristics and other variables in their study were different from those in ours. Therefore, their results may not be comparable to those found in the current study. However, the correlation of our study was weaker (r = 0.562, R^2 = 0.316, p < 0.0001) (Fig. 2), suggesting that GA measurements may be underestimated for patients requiring diabetes-related dialysis undergoing OHDF. Anemia-related indicators and iron agent doses are shown in Table 1. Anemia appeared to be well managed in the study patients across the 2 institutions involved in this study, and Hb and Ht levels during the 3 months before and after patient data collection did not show any significant changes (Table 5). Therefore, we considered that HbA1c levels were not affected by Hb and Ht levels in this study. There was no significant correlation between pre-dialysis blood glucose levels and HbA1c or GA levels. Patients' blood data were obtained from the results of regular blood tests. Blood samples were collected before dialysis under non-fasting conditions. However, the pre-dialysis blood glucose status appeared to be constant according to a patient's dietary habits. Pre-dialysis blood glucose levels (plasma glucose levels) did not significantly differ among the 3 groups. Additionally, the patients did not show evidence of either a hyper- or hypoglycemic status (Table 2).

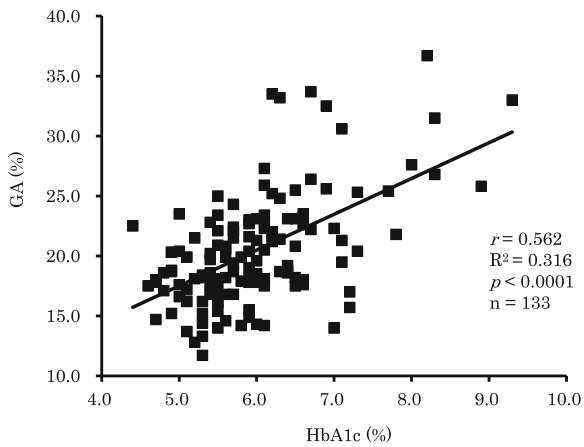

Fig. 2 Correlation of glycated hemoglobin A1c (HbA1c) and glycated albumin (GA) in the OHDF group. There was a significant positive correlation (r = 0.562, R^2 = 0.316, p < 0.0001) between the HbA1c and GA levels

In the OHDF groups, the correlations between HbA1c and GA levels were weaker for patients with mean albumin levels < 3.4 g/dL than for those with mean albumin levels ≥ 3.4 g/dL. This finding suggests that GA measurements in patients undergoing diabetes-related dialysis with low albumin levels who underwent OHDF may have been underestimated (Fig. 3). While no firm conclusions can be drawn concerning the tolerable amount of albumin leakage in a single dialysis session, previous studies have reported high levels of albumin leakage [9, 10]. Obviously, albumin leakage occurs secondary to dialysis. Although a full discussion of the causes of hypoalbuminemia is needed, the half-life of albumin for patients undergoing dialysis has been reported to range from 9 to 15.5 days, which is shorter than the half-life for healthy individuals, which normally has a range of, 17 to 23 days [11, 12]. In patients with nephrotic syndrome, large amounts of albumin leakage into the urine have been reported, and patients have been reported to consequently have low GA levels due to the shortening of the biological half-life of albumin [5]. Therefore, it is possible that GA levels may be underestimated due to OHDF-induced albumin leakage as the associated biokinetics of the procedure may easily lead to low GA levels.

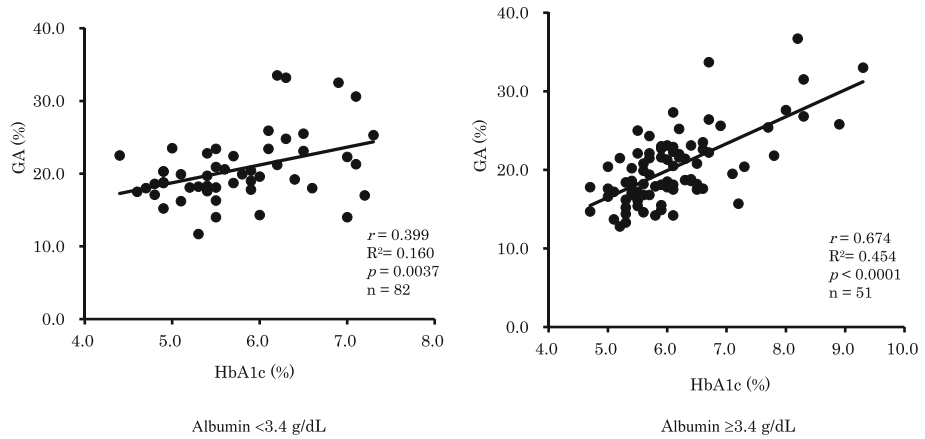

Fig. 3 Correlation of HbA1c and GA levels according to Albumin in the OHDF. The correlation between HbA1c and GA levels was weaker in 51 participants with albumin levels < 3.4 g/dL (r = 0.399, R^2 = 0.160, p = 0.0037) than in 82 participants with albumin levels ≥ 3.4 g/dL (r = 0.674, R^2 = 0.454, p < 0.0001). There was a significant difference in the correlation coefficients between the two groups (p = 0.0292)

Association between poor glycemic control indicated by HbA1c levels and survival in end-stage renal disease has previously been reported [13–15]. Glycemic control has been shown to have a major effect on the survival prognosis of patients with diabetic nephropathy, who account for 38.4% of all chronic dialysis patients [16], and current guidelines recommend using GA as an indicator of glycemic control in patients undergoing diabetes-related dialysis [5]. However, as shown in this study, OHDF results in albumin leakage, hence the evaluation of GA may not be accurate. When assessed in relation to the hemodiafilter performance, group A was found to comprise many elderly patients with diabetes who needed to maintain blood pressure levels within an appropriate range during blood purification therapy, a large proportion of whom had low serum albumin levels. As OHDF treatment is used to maintain blood pressure levels despite low albumin levels, we selected a hemofiltration membrane that leaked a minimal amount of protein. For patients in group B, our objective was to obtain β 2-microglobulin (β2-MG) levels that were as low as possible; therefore, OHDF treatment was used even if there were no dialysis complications, such as carpal tunnel syndrome. Patients in group B had higher serum albumin levels and better nutritional statuses than those in group A. Group C targeted patients with a long-term prognosis of at least 20 years, with the objective of preventing long-term complications from dialysis-related amyloidosis. As a result, this group included patients who were younger and had better initial nutritional statuses than patients in groups A and B. Group C also included patients with restless leg syndrome, with a target elimination rate of α1-MG set at ≥ 40% [17]. Average albumin leakage was high, at 7.64 ± 1.36 g.

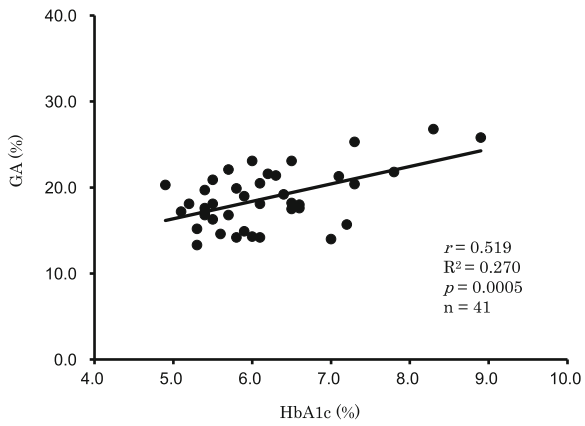

Fig. 4 Correlation of HbA1c and GA in 41 OHDF patients from whom effluent dialysis fluid had been collected for analysis. There was a significant positive correlation between the HbA1c and GA levels (r = 0.519, R^2 = 0.270, p = 0.0005)

The advantages of OHDF over HD (the more conventional blood purification method) are as follows: (i) OHDF stabilizes the circulation dynamics and there is no need to remove low molecular weight proteins proactively, and (ii) OHDF is beneficial in treating dialysis-related amyloidosis, pruritus, and restless leg syndrome; however, proactive removal of low molecular weight proteins (β2-MG and α1-MG) is required in this case. Albumin is also largely removed when treating dialysis-related amyloidosis, pruritus, and restless leg syndrome using OHDF [7]. Furthermore, there was no significant correlation between pre-dialysis blood glucose levels and HbA1c or GA levels in each group as shown in the regular blood test results, which had been performed under non-fasting conditions. In our study, only group C did not show a correlation between HbA1c and GA levels.

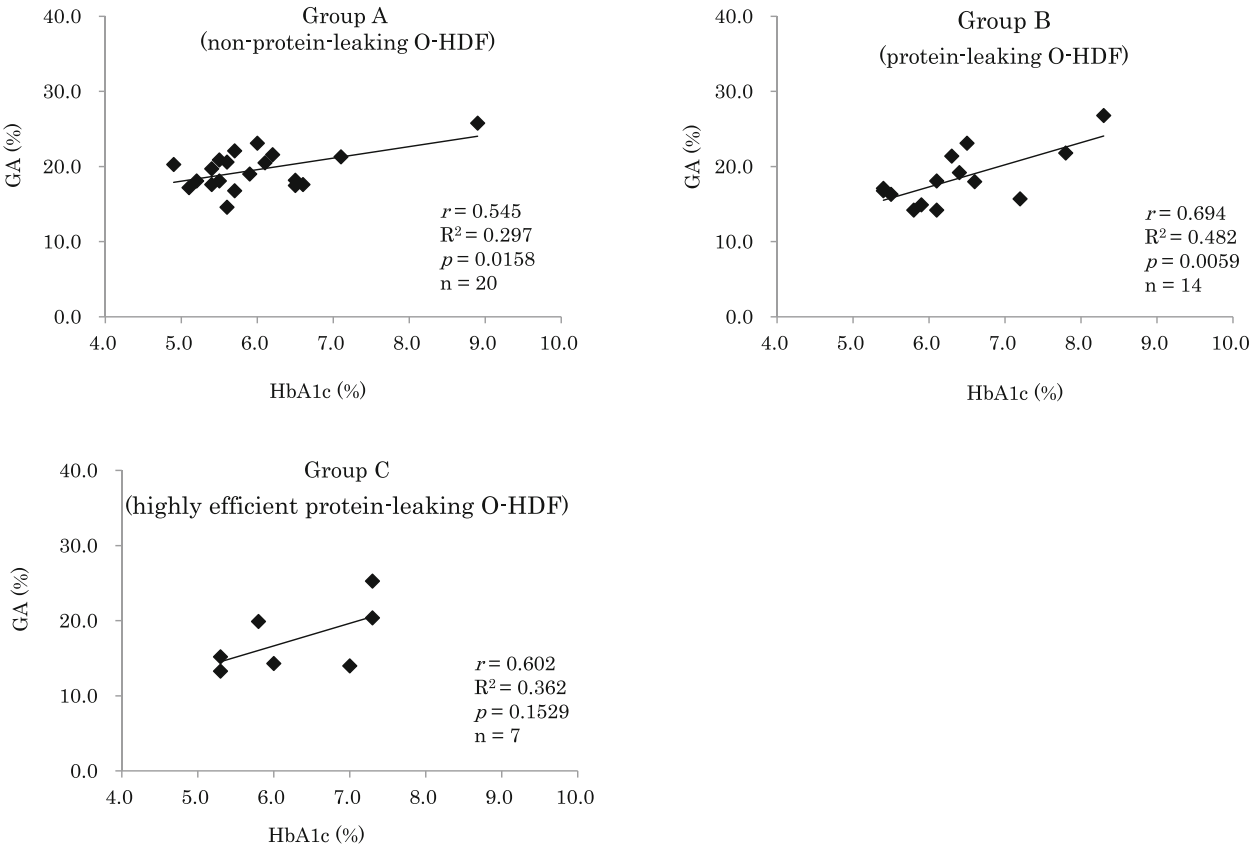

Fig. 5 The patients were divided into 3 groups based on the target value for low molecular weight protein removal. A significant positive correlation was observed between HbA1c and GA levels in groups A (non-protein-leaking OHDF) and B (protein-leaking OHDF), whereas no correlation was found in group C (highly efficient protein-leaking OHDF)

We consider that this was because of the extremely high albumin leakage in group C, at 7.64 ± 1.36 g, which was likely affected by GA metabolism. We observed positive correlations between HbA1c and GA levels in groups A and B, where albumin leakage was < 6 g, and we consider that positive correlations are likely to be present when albumin leakage is low. Therefore, it is possible that the blood glucose index of patients requiring diabetes-related dialysis undergoing OHDF had an effect on the hemodiafilter type and nutritional status of the patients.

The limitation of this study was the relatively low number of patients for whom data regarding dialysate drainage analysis was available. Unfortunately, we were unable to collect dialysate drainage samples from all patients who underwent dialysis because it is difficult to do so in our daily routine.

In summary, we used a range of indicators to evaluate patients in aspects not limited to glycemic control. Different evaluation methods based on the dialysis method are necessary in the future. Our results showed that the use of GA levels only is insufficient for evaluating glycemic control in patients requiring diabetes-related dialysis undergoing OHDF. As such, additional modalities for glycemic control evaluation are warranted in these patients.

Conclusion

It may be necessary to evaluate glycemic control in patients requiring diabetes-related dialysis by combining several glycemic control indicators, such as GA, HbA1c, and pre-dialysis blood glucose levels when considering the appropriate procedure for dialysis.

Abbreviations

ERI: Erythropoiesis resistance index; ESAs: Erythropoiesis-stimulating agents; GA: Glycated albumin; Hb: Hemoglobin; HbA1c: Glycated hemoglobin; HD: Hemodialysis; Ht: Hematocrit; OHDF: Online hemodiafiltration; TIBC: Total iron-binding capacity; TSAT: Transferrin saturation; UN: Urea nitrogen; α1-MG: α1-Microglobulin; β2-MG: β2-Microglobulin

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Authors' contributions

YK and TH were involved in the study design and in writing the manuscript. YK, SU, TH, and SH participated in the study procedure implementation and data collection. TH and YS kindly reviewed and revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets analyzed during this study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
This study was approved by the Ethical Committee of Tokyo Healthcare University (approval number: 26-27). All participants were provided with the opportunity to decline to participate in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of Medical Nutrition, Tokyo Healthcare University, 3-11-3 Setagaya, Setagaya-ku, Tokyo 154-8568, Japan. [2]Eijin Clinic, 4-5-25 Higashishindo, Hiratsuka, Kanagawa 254-0018, Japan. [3]Sato Junkanki Hospital, 4-10-25 Asoda-cho, Matsuyama, Ehime 790-0952, Japan.

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References

1. Ansari A, Thomas S, Goldsmith D. Assessing glycemic control in patients with diabetes and end-stage renal failure. Am J Kidney Dis. 2003;41:523–31.
2. Joy MS, Cefalu WT, Hogan SL, Nachman PH. Long-term glycemic control measurements in diabetic patients receiving hemodialysis. Am J Kidney Dis. 2002;39:297–307.
3. Nakao T, Matsumoto H, Okada T, Han M, Hidaka H, Yoshino M, et al. Influence of erythropoietin treatment on hemoglobin A1c levels in patients with chronic renal failure on hemodialysis. Intern Med. 1998;37:826–30.
4. Inaba M, Okuno S, Kumeda Y, Yamada S, Imanishi Y, Tabata T, et al. CKD Expert Research Group: glycated albumin is a better glycemic indicator than glycated hemoglobin levels in hemodialysis patients with diabetes: effect of anemia and erythropoietin injection. J Am Soc Nephrol. 2007;18:896–903.
5. Nakao T, Inaba M, Abe M, Kaizu K, Shima K, Babazono T, et al. Japanese Society for Dialysis Therapy: best practice for diabetic patients on hemodialysis 2012. Ther Apher Dial. 2015;19(Suppl 1):40–66.
6. Masakane I, Taniguchi M, Nakai S, Tsuchida K, Wada A, Ogata S, et al. and on behalf of Japanese Society for Dialysis Therapy Renal Data Registry Committee. Annual Dialysis Data Report 2016, JSDT Renal Data Registry. Ren Replace Ther. 2018;4:24–9.
7. Sakurai K. Biomarkers for evaluation of clinical outcomes of hemodiafiltration. Blood Purif. 2013;35(suppl 1):64–8.
8. Yamashita A, Yoshimoto T, Yoshimoto K, Shiraishi K, Sakai T, Sakai K. Methodological consideration on measurement of removed solute amount (in Japanese). J Jpn Soc Dial Ther. 1982;15:803–7.
9. Morigami T, Tanaka K, Sakaguchi T, Otsuki H, Yoshimoto H, Tabuchi A, et al. The effect of a decrease in colloidal osmotic pressure due to albumin leakage on in vivo fluid dynamics (in Japanese). J Jap Soc Technol Hemopurification. 2010;18:60–5.
10. Kim S-T. Characteristics of protein removal in hemodiafiltration. Contrib Nephrol. 1994;108:23–37.
11. Bischel M, Sabin N, Homola B, Barbour BH. Albumin turnover in chronically hemodialyzed patients. Trans Am Soc Artif Intem Organs. 1969;15:298–301.
12. Bianchi R, Mariani G, Toni MG, Carmassi F. The metabolism of human serum albumin in renal failure on conservative and dialysis therapy. Am J Clin Nutr. 1978;31:1615–26.
13. Oomichi T, Emoto M, Tabata T, Morioka T, Tsujimoto Y, Tahara H, et al. Impact of glycemic control on survival of diabetic patients on chronic regular hemodialysis: a 7-year observational study. Diabetes Care. 2006;29:1496–500.
14. Kalantar-Zadeh K, Kopple JD, Regidor DL, Jing J, Shinaberger CS, Aronovitz J, et al. A1c and survival in maintenance hemodialysis patients. Diabetes Care. 2007;30:1049–55.
15. Hashimoto Y, Fukuhara S, Akiba T, Akizawa T, Asano Y, Saito A, et al. Diabetes, glycemic control and mortality risk in patients on hemodialysis: the Japan Dialysis Outcomes and Practice Pattern Study. Diabetologia. 2007;50:1170–7.
16. Committee of Renal Data Registry, Japanese Society for Dialysis Therapy. An overview of regular dialysis treatment in Japan as of Dec. 31, 2015. 2016. https://docs.jsdt.or.jp/overview/pdf2016/2015all.pdf. Accessed 01 Dec 2018.
17. Yamashita AC, Sakurai K. Clinical effect of pre-dilution hemodiafiltration based on the permeation of the hemodiafilter. Contrib Nephrol. 2015;185:1–7.

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