Renal Replacement Therapy

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Hemodialysis crossover study using a relative blood volume change-guided ultrafiltration control compared with standard hemodialysis: the BV-UFC study

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Abstract

Background: It has been difficult to sufficiently achieve body-fluid management using blood volume (BV) monitor during hemodialysis (HD) with constant ultrafiltration (UF) rate. Recently, a relative BV change-guided UF control (BV-UFC) system was developed by combining the concepts of an automatic feedback system that could control the UF rate and profile with real- time monitoring of relative changes in BV (*%ΔBV*). However, this system has limited application in the clinical setting. Therefore, in this study, we aimed to perform the crossover study on HD with BV-UFC compared to standard HD in terms of hemodynamic stability during HD.

Methods: Forty-eight patients entered an 8-week crossover period of standard HD or HD with BV-UFC. Prevalence of intradialytic hypotension (IDH) as a primary outcome and changes in blood pressure (BP), differences in *%ΔBV*, and achievement of the target ultrafiltration volume as secondary outcomes were compared. IDH was defined as a reduction in systolic BP ≥20 mmHg from the baseline value at 10 min after HD initiation.

Results: No significant differences were found in the prevalence of IDH, frequency of intervention for symptomatic IDH, and achievement of the target ultrafiltration volume between the groups. The *%ΔBV* was significantly fewer (-12.1 ± 4.8% vs. -14.4 ± 5.2%, p <0.001) in the HD with BV-UFC than that in the standard HD.

Conclusions: HD with BV-UFC did not reduce the prevalence of IDH compared with standard HD. The relief of a relative BV reduction at the end of HD may be beneficial in patients undergoing HD with BV-UFC.

Trial Registration: UMIN, UMIN000024670. Registered on December 1, 2016.

Keywords: Automatic feedback system using blood volume monitoring, Hemodialysis, Blood pressure drop, Relative changes in blood volume, Ultrafiltration

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Introduction

Excessive body- fluid removal has been known to result in intradialytic hypotension (IDH) through the impairment of plasma refilling from the interstitium to the capillary circulation [1]. This event is more likely to occur at the late phase of hemodialysis (HD) [2], mainly due to the development of hemodynamic instability associated with ultrafiltration (UF)- induced blood volume (BV) reduction. Conversely, fluid overload with insufficient fluid removal during HD is associated with hypertension and left ventricular hypertrophy [3, 4]. Both IDH and fluid overload with insufficient intradialytic fluid management were reported to be associated with increased mortality [5, 6]. Therefore, to prevent body- fluid management failure during HD, BV monitoring systems that could evaluate relative changes in BV (*%ΔBV*) during HD have been developed [7–11]. However, it has been difficult to sufficiently achieve body- fluid management using a BV monitor during HD with a constant UF rate [12].

Controlling the UF profile is one of the maneuvers used to maintain hemodynamic stability during HD, in which the UF rate is gradually decreased after starting HD at a high rate, to induce increase in plasma refilling [13–16]. Recently, a relative BV change- guided UF control (BV-UFC) system (Nikkiso, Tokyo, Japan) was developed for HD therapy by combining the concepts of an automatic feedback system that could control the UF rate and profile with real- time monitoring of *%ΔBV* during HD. However, thus far, this system has limited application in the clinical setting of HD therapy. Therefore, in this study, we aimed to perform the crossover study on HD with BV-UFC compared to standard HD in terms of hemodynamic stability, including the prevalence of IDH, as a primary outcome, and changes in blood pressure (BP), differences in *%ΔBV*, and achievement of the target UF volume (UFV) at the end of HD as secondary outcomes.

Materials and methods

Study design

This study was registered at the University Hospital Medical Information Network (study No. UMIN000024670, date of registration: December 1, 2016) in Japanese Primary Registry Network; approved by the institutional review board of Saitama Medical Center, Jichi Medical University, Japan (RINS 16-003); the study was conducted in accordance with the Declaration of Helsinki (2004 Tokyo revision). All patients signed informed consent forms before participation.

We designed a 12-week prospective, crossover, intervention study, which included the first and second HD sessions but excluded the third, to compare HD with BV-UFC and standard HD at a constant UF rate for the management of body- fluid status in patients undergoing HD. In this study, all of the third HD session were performed using standard HD. Prior to this study, we could not judge if the reliability of HD with BV-UFC would be able to reach the dry weight or not to delay the achievement of the target UFV at the end of HD. It would be important to strictly manage the body- fluid status at the third HD session because HD therapy was not performed for 2 days after the third HD session. Therefore, we performed the session using standard HD, which could reliably achieve dry weight at the third HD session in each patient. Patient recruitment was performed from December 1, 2016 to June 30, 2017 and this study was conducted between December 1, 2016 and September 30, 2017 in our medical center and four other hospitals in Japan.

Patients

Patients undergoing HD who met the following criteria were enrolled: (i) age ≥ 18 years; (ii) started HD at least 3 months before the study; (iii) undergoing HD 3 times weekly at 4 h per session; (iv) had a BV reduction induced by UF during HD; and (v) had a serum albumin level ≥ 3.0 g/dL before study enrollment. The exclusion criteria were as follows: cardiovascular disease with hemodynamic instability including congestive heart failure, myocardial infarction, and unstable angina pectoris; severe cerebrovascular disease; cognitive impairment; use of antihypotensive medication during HD; and existence of vascular access recirculation.

Definitions

During HD, BP was measured using an electronic sphygmomanometer at several timepoints, as follows: HD initiation, initiation of BV monitoring (10 min after HD initiation; BP baseline), and hourly during HD. IDH was defined as a reduction in systolic BP ≥20 mmHg from the baseline value [17–19]. The interventions for symptomatic IDH, which is accompanied with nausea, dizziness, and cramps, included prompt change of the dialysis bed (Trendelenburg position), oxygen inhalation, and infusion of saline.

Monitoring of %ΔBV values during HD

Relative BV reduction during HD, measured using a BV monitor mounted on the dialysis equipment (DCS-100NX; Nikkiso, Tokyo, Japan), was evaluated as *%ΔBV* from 10 min after HD initiation to the end of HD in each patient, as previously described [11].

Run-in period

The setting of dry weight in each faculty was performed using some kinds of dry weight setting methods, including physical findings, hemodynamic status during HD, cardiothoracic ratio measured by chest X-ray, measurement

of inferior vena cava diameter, and the degree in *%ΔBV* reduction. To adequately reach the dry weight in HD with BV-UFC, the increase in UF rate in the second part of HD compared with the constant UF rate and values of *%ΔBV* at the end of the automatic UF rate- adjustment period with BV-UFC were determined within a 4-week run-in period in each enrolled patient and were not changed throughout crossover study period (Fig. 1).

Crossover study period

During this period, UF was performed under standard HD or HD with BV-UFC (Fig.1). Data collection was performed in the first and second HD sessions for each therapy in a cross-over manner. The third HD session was performed using standard HD to successfully achieve the target body weight at the end of HD and was excluded from the analysis. During an 8-week period, each participant was crossed over between standard HD and HD with BV-UFC as the first and second HD sessions without any change in dry weight.

UF rate setting during HD with the BV-UFC system

HD with the BV-UFC system was divided into four parts according to changes in the UF rate during the HD session (Fig. 2). First, from HD initiation to 10 min, the UF rate was set as a constant (constant UF rate period), and calculated as body weight gain (kg)/4 h, similar to that in standard HD. Second, the UF rate was set as 1.2-1.5 times higher than that in the first part for the next 60 min of HD (higher UF rate period). Third, the UF rate was automatically adjusted to match the *%ΔBV*, which was set to values ranging from -3% to -6% at the end of this part, for the next 150 min (automatic UF rate-adjustment period). *%ΔBV* was set to decrease curvilinearly during this part in this study. That is, the degree in *%ΔBV* reduction was set to reach 50% in the first quarter, 80% in the second quarter and 95% in the third quarter of the automatic UF rate-adjustment period. Finally, the UF rate was automatically determined as a constant rate to reach the dry weight at the end of HD (automatic constant UF rate period) in response to the residual body-fluid excess at the end of the third part. The changes in the UF rate in standard HD and HD with BV-UFC are shown in Fig. 2. In HD with BV-UFC, the UF rates in the second part were 1.35 ± 0.06 times (0.95 ± 0.27 L/h) higher than those in the first part, indicating a significant increase (UF rate in the first part: 0.72 ± 0.21 L/h, p <0.001). However, compared with those in the first part, the UF rates were significantly suppressed from 140 min after HD initiation to the end of HD (p <0.001). To confirm precision of the sample mean in the UF rate during HD, the standard error of the mean was calculated. In standard HD, the standard error in the UF rate was 0.01 L/h throughout the HD session, and in HD with BV-UFC, ranged from 0.01 L/h to 0.02 L/h, which were considered small values in each group.

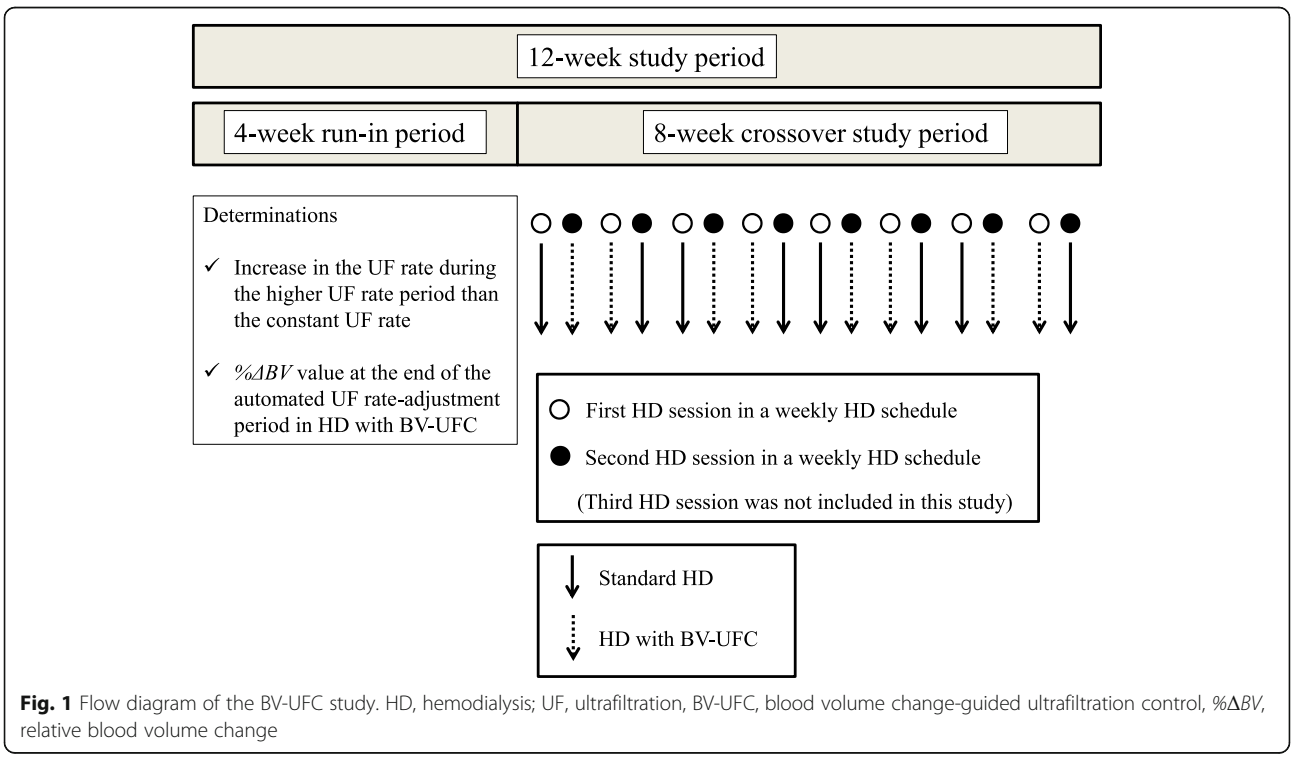

Fig. 1 Flow diagram of the BV-UFC study. HD, hemodialysis; UF, ultrafiltration, BV-UFC, blood volume change-guided ultrafiltration control, *%ΔBV*, relative blood volume change

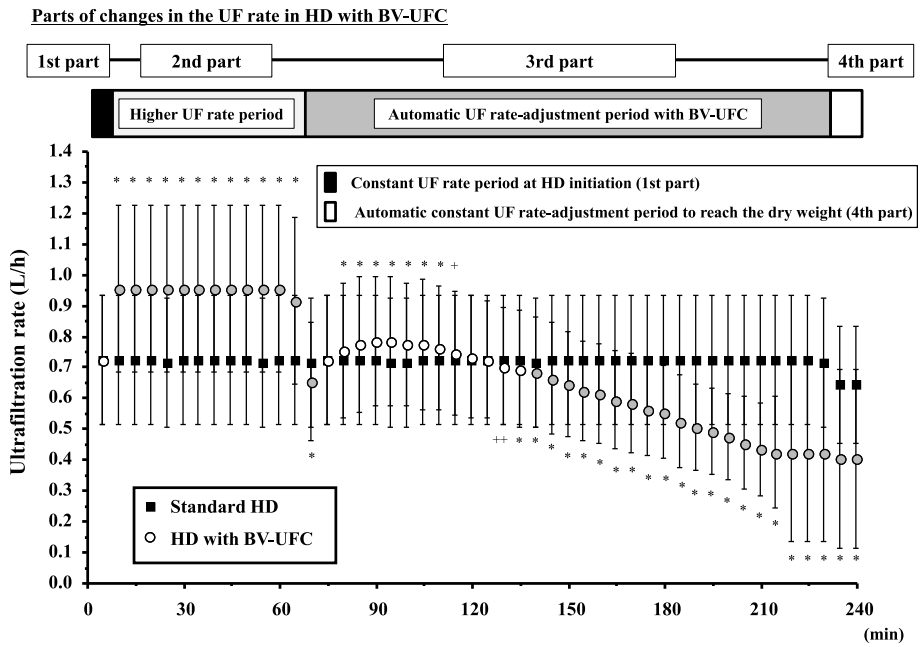

Fig. 2 Changes in ultrafiltration rate in HD with BV-UFC in comparison with the constant UF rate in standard HD. ◯ Gray circle $p < 0.001$ versus HD initiation in HD with BV-UFC, * $p < 0.001$ versus standard HD, + $p < 0.01$ versus standard HD, ++ $p < 0.05$ versus standard HD, HD, hemodialysis; UF, ultrafiltration, BV-UFC, blood volume change- guided ultrafiltration control

Outcome

The primary outcome was the prevalence of IDH during HD. The secondary outcomes were episodes of interventions for symptomatic IDH, changes in intradialytic BP, *%ΔBV* at the end of HD, and achievement of the target UFV during HD in each patient.

Statistical analyses

Data are presented as the mean ± standard deviation. Student's t-tests for paired values were used for the comparison of clinical parameters between standard HD and HD with BV-UFC. The *%ΔBV* values and UF rate changes in each group during HD were evaluated using repeated-measures analysis of variance with general linear models and Tukey tests. Chi-squared tests were used to assess the comparisons of IDH prevalence, the number of patients with IDH, episodes of interventions for symptomatic IDH, the number of patients with symptomatic IDH, and achievement of the target UFV at the end of HD, complemented by an adjusted residual analysis. All analyses were performed using IBM SPSS Statistics version19.0 for Windows (SPSS Inc., Chicago, IL, USA). A p value of <0.05 was considered statistically significant.

Results

Baseline characteristics

Of the 75 patients screened, 64 met the inclusion criteria and were enrolled in this study. Overall, 16 patients did not complete the study because of lack of data (n = 12) and withdrawal from the study (n = 4) and were excluded from the analysis (Fig. 3). Therefore, 48 patients completed the study. The patients' general characteristics are summarized in Table 1. No significant differences in the UFV, systolic and diastolic BP measurements, heart rate, and Kt/V urea between standard HD and HD with BV-UFC were found in this study. Furthermore, 40 patients (83.3%) took antihypertensive medication, and 26 patients (54.2%) took it before the HD session.

Primary outcome: prevalence of IDH during HD

IDH was recognized in 197 (51.3%) HD sessions in standard HD and 198 (51.6%) HD sessions in HD with

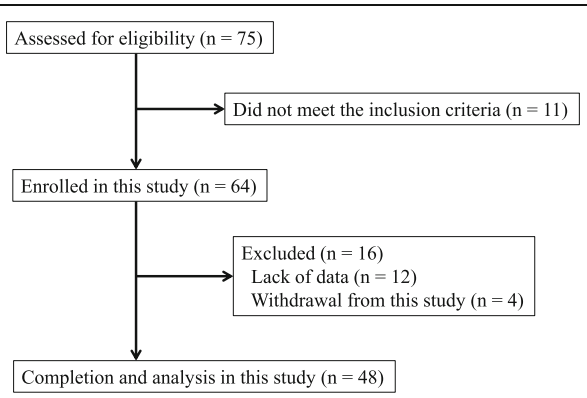

Fig. 3 Patient flow chart

Table 1 Patients' general characteristics

	Characteristics at study initiation		
Number of patients (men/women)	48 (15/33)		
Age (years)	64.2 ± 7.3		
HD duration (years)	7.5 ± 7.3		
Dry weight (kg)	61.3 ± 15.7		
Disease			
Diabetes mellitus	19		
Chronic glomerulonephritis	12		
Nephrosclerosis	3		
ADPKD	6		
Others	8		
Comorbidities			
Cardiovascular disease	0/48		
Cerebrovascular disease	4/48		
Medication, *n* (%)			
Antihypertensive medicines	40 (83.3)		
Renin-angiotensin system blocker	31 (64.6)		
Calcium channel blocker	33 (68.8)		
Beta blocker	12 (25.0)		
Alpha blocker	8 (16.7)		
Vitamin D analogue	39 (79.6)		
Phosphate binder	41 (85.4)		
Erythropoiesis-stimulating agent	46 (95.8)		
Laboratory findings			
Hb (g/dL)	10.9 ± 0.8		
BUN (mg/dL)	67.4 ± 15.5		
Serum creatinine (mg/dL)	11.3 ± 2.3		
Na (mEq/L)	138.7 ± 1.7		
K (mEq/L)	5.0 ± 0.7		
Cl (mEq/L)	104.1 ± 2.7		
Ca (mg/dL)	8.7 ± 0.6		
P (mg/dL)	5.4 ± 1.3		
Total protein (g/dL)	6.4 ± 0.4		
Serum albumin (g/dL)	3.7 ± 0.3		
	Standard HD	HD with BV-UFC	*p*-value
n (total number of HD sessions)	384	384	
Ultrafiltration (L/session)	2.80 ± 0.84	2.79 ± 0.80	0.780
Systolic blood pressure (mmHg)	151 ± 19	151 ± 19	0.933
Diastolic blood pressure (mmHg)	80 ± 11	80 ± 12	0.158
Heart rate (beats/min)	69.3 ± 9.3	69.8 ± 10.1	0.093
Kt/V urea	1.45 ± 0.25	1.48 ± 0.24	0.720

HD hemodialysis, *ADPKD* autosomal dominant polycystic kidney disease, *Hb* hemoglobin, *BUN* blood urea nitrogen, *BV-UFC* blood volume change- guided ultrafiltration control

BV-UFC. No significant difference in IDH prevalence was found between the groups (p = 0.942, Fig.4). In standard HD, the number of patients who had episodes of IDH was 44 patients, and the number of IDH episodes in each patient with IDH during this study was 4.5 ± 2.4 times, whereas in HD with BV-UFC, the number of patients who had episodes of IDH was 43 patients, and the number of IDH episodes in each patient with IDH was 4.6 ± 2.4 times. There were no significant differences in the number of patients who had IDH episodes (p = 0.726) and in the number of IDH episodes in each patient with IDH (p = 0.804) between the groups.

Secondary outcomes

Episodes of interventions for symptomatic IDH

The episodes of intervention for symptomatic IDH was recognized in 15 (3.9%) HD sessions in standard HD and 17 (4.4%) HD sessions in HD with BV-UFC. In standard HD, the intervention included 9 sessions of saline infusion and 6 sessions of change from the supine position to the Trendelenburg position. In HD with BV-UFC, the intervention also included 9 sessions of saline infusion and 8 sessions of change to the Trendelenburg position. No significant difference in those for symptomatic IDH was found between the groups (p = 0.718). In standard HD, the number of patients who had episodes of symptomatic IDH was 9 patients, and the number of symptomatic IDH episodes in each symptomatic IDH patient was 1.6 ± 1.0 times, whereas in HD with BV-UFC, the number of patients who had episodes of symptomatic IDH was 9 patients, and those of symptomatic IDH episodes in each symptomatic IDH patient was 1.9 ± 1.1 times. There was no significant difference in the number of symptomatic IDH episodes (p = 0.653) between the groups. However, there was a significant difference in the distribution of timing of the intervention for symptomatic IDH episodes during HD between the groups (p=0.022, Fig. 5), i.e., the number of the interventions for symptomatic IDH episodes in HD with BV-UFC during 2 to 3h HD session was significantly higher than those in standard HD (p < 0.01), whereas the number of those in standard HD during the last 1h HD session was significantly higher than those in HD with BV-UFC (p <0.05).

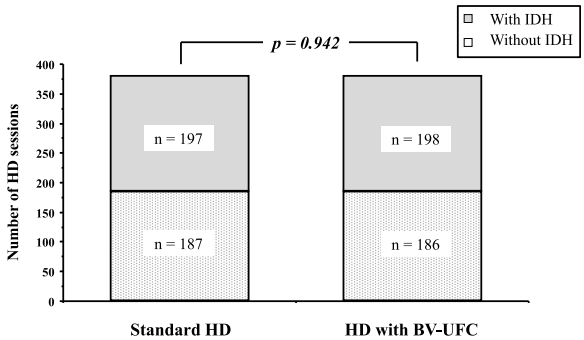

Fig. 4 Comparison of the prevalence of IDH during HD between standard HD and HD with BV-UFC. HD, hemodialysis; IDH, intradialytic hypotension, BV-UFC, blood volume change- guided ultrafiltration control

Changes in intradialytic BP

In standard HD, the systolic BP from 2 h after HD initiation to the end significantly decreased compared with the BP at baseline (p <0.001; Table 2). The systolic BP at the end also significantly decreased compared with the values 3 h after HD initiation (p <0.05). In HD with BV-UFC, the systolic BP from 1 h after HD initiation to the end significantly decreased compared with the baseline BP (p <0.01 vs. 1 h after HD initiation; and p <0.001 vs. others). However, the difference in systolic BP between 3 h and the end of HD was not significant (p = 0.955). There were no differences in diastolic BP in standard HD, whereas little but significant differences in diastolic BP in HD with BV-UFC were confirmed at 2 and 3 h after HD (both p < 0.05 vs. HD initiation). However, these differences in diastolic BP disappeared at the end of HD in HD with BV-UFC.

%ΔBV at the end of HD

The *%ΔBV* in HD with BV-UFC significantly decreased from 15 to 180 min compared with that in standard HD (p <0.05 vs. 180 min; and p <0.001 vs. others), whereas the *%ΔBV* in standard HD significantly decreased from 200 min to the end compared with that in HD with BV-UFC (p <0.05 vs. 200 min; and p <0.001 vs. others). Finally, at the end of HD, the decrease in *%ΔBV* in HD with BV-UFC was significantly fewer than that in standard HD (-12.1 ± 4.8% vs. -14.4 ± 5.2%, p <0.001, Fig. 6). Furthermore, to confirm precision of the sample mean in *%ΔBV* monitoring during HD, the standard error of the mean was calculated. In standard HD, the standard error in *%ΔBV* ranged from 0.02% to 0.3%, and in HD with BV-UFC, ranged from 0.03% to 0.3%, which were considered relatively small values in each group.

Achievement of the target UFV during HD

In this study, achievement of the target UFV at the end of HD was defined as within ± 0.3 kg of the dry weight. The target UFV was not achieved in 3 of the 384 HD sessions in standard HD and 5 of the 384 HD sessions in HD with BV-UFC. No significant difference in the achievement of the target UFV at the end of HD was found between the groups (p = 0.722).

Discussion

IDH has been mainly associated with a BV reduction, which is induced by UF over a short period, and

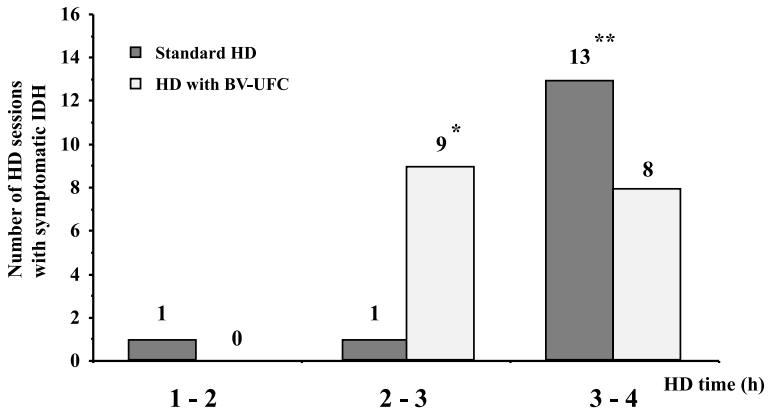

Fig. 5 Comparison of interventional episodes for symptomatic IDH divided into the time of occurrence during HD between standard HD and HD with BV-UFC. *p <0.05 versus standard HD, **p <0.01 versus HD with BV-UFC, HD, hemodialysis; IDH, intradialytic hypotension, BV-UFC, blood volume change- guided ultrafiltration control

impaired cardiovascular compensatory mechanisms in patients undergoing HD [17, 20]. Recently, the prevalence of IDH, which was defined as a decrease in systolic BP ≥ 20 mmHg, reached 63.8-68.9%, and interventions were implemented in 8.5-9.6% of standard HD sessions [5, 17]. In this study, the prevalence of IDH was nearly 50% and approximately 4% for symptomatic IDH interventions in both HD with BV-UFC and standard HD. Therefore, it can be presumed that there are no significant differences between HD with BV-UFC and standard HD in terms of hemodynamic stability during HD. The effect of automatic feedback systems that could control the UF rate in response to the relative changes in BV during HD have been reported to be useful in preventing the occurrence of IDH [21–23]. However, this system was also recently reported not to reduce the rate of symptomatic IDH events [24] and the degree of systolic BP reduction [25], and the present study could not confirm the effect of this system on IDH prevention. A potential reason for why this system did not reduce the prevalence of IDH was the limit of accuracy in BV monitoring itself including the suitability of $\%\Delta BV$ during HD [26]. In addition, patients were prioritized based on hemodynamic stability in this study and there would be possible to include the patients who systemic BP was relatively high before HD. Furthermore, in addition to the use of antihypertensive medicines in 40 patients out of 48 patients in this study, 26 patients took these agents before HD, which was possible to influence the BP decrease after HD initiation. Therefore, these might be the reasons that IDH was frequently confirmed after HD initiation.

In the present study, a difference in $\%\Delta BV$ at the end of HD could be significantly confirmed between standard HD and HD with BV-UFC. The $\%\Delta BV$ decreased linearly in standard HD, as previously reported [27, 28], from 30 min after HD initiation to the end, and the value reached -14.4 ± 5.2%. Meanwhile, in HD with BV-UFC, according to the gradual decrease of UF rate during the automatic UF rate- adjustment period, the slope of BV reduction became small compared with that in standard HD; therefore, the $\%\Delta BV$ values at the end of

Table 2 Comparisons of systolic BP and diastolic BP between standard HD and HD with BV-UFC

	BP baseline	1 h	2 h	3 h	End of HD
Systolic BP (mmHg)					
Standard HD	151 ± 19	148 ± 18	145 ± 17*	144 ± 17*	140 ± 17*,**
HD with BV-UFC	151 ± 19	146 ± 19##	143 ± 19#	140 ± 19#	139 ± 19#
Diastolic BP (mmHg)					
Standard HD	80 ± 11	78 ± 11	78 ± 11	78 ± 10	79 ± 10
HD with BV-UFC	80 ± 12	78 ± 11	78 ± 11$	78 ± 11$	78 ± 11

* p <0.001 versus HD initiation in standard HD
** p <0.05 versus 3 h after HD initiation in standard HD
# p <0.001 versus HD initiation in HD with BV-UFC
p <0.01 versus HD initiation in HD with BV-UFC
$ p <0.05 versus HD initiation in HD with BV-UFC
BP blood pressure, *HD* hemodialysis, *BV-UFC* blood volume change- guided ultrafiltration control

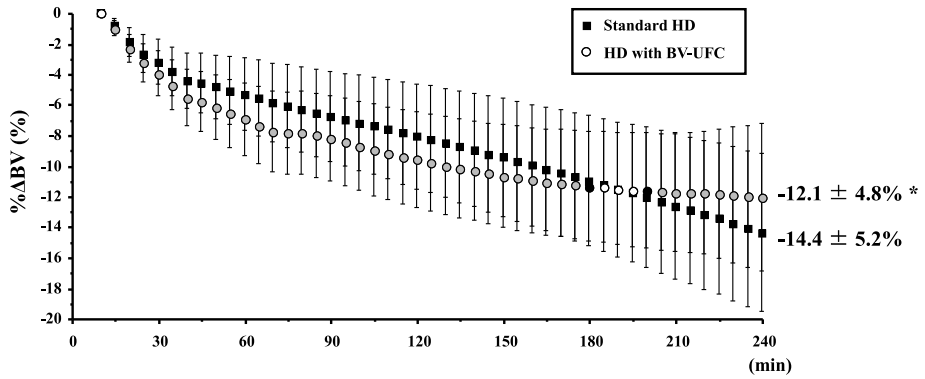

Fig. 6 Comparison of %Δ*BV* in HD with BV-UFC and the constant rate of ultrafiltration in standard HD. ● $p < 0.05$ versus standard HD, ◯ Gray circle $p < 0.001$ versus standard HD, *p <0.001 versus %Δ*BV* value at the end of HD in standard HD, %Δ*BV*, relative change in blood volume; HD, hemodialysis, BV-UFC, blood volume change- guided ultrafiltration control

HD were significantly fewer (-12.1 ± 4.8%, p <0.001 vs. standard HD). The suppression of changes in *%ΔBV* at the last phase of HD in HD with BV-UFC would be associated with the prevention of symptomatic IDH episodes, which might result in the significant difference in the number of interventions for symptomatic IDH episodes during the last 1h HD compared with standard HD. Furthermore, in patients with chronic kidney disease, sympathetic nerve activity was reportedly higher than that in healthy control and further increased according to the decrease in extracellular volume [29]. In addition, sympathetic hyperactivity in patients undergoing short daily HD was significantly suppressed by the decrease in the magnitude of fluid fluctuation [30]. Therefore, the relief of a relative BV reduction, which means less fluid fluctuation, in HD with BV-UFC may contribute to the suppression of the sympathetic hyperactivity.

Regarding the meaning of the setting in UF rate divided into four parts during HD with the BV-UFC system, a constant UF rate period at first phase was set to confirm the stability in systemic BP under the same condition in standard HD. As a second phase, higher UF rate period would be expected to be easily removed excessive body fluid at the early phase of HD therapy. Furthermore, an automatic UF rate- adjustment period was set under the adjustment along the target *%ΔBV* value to prevent the excessive *%ΔBV* reduction during the middle to last phase of HD session. Finally, an automatic constant UF rate period was set to reach the dry weight at the end of HD during the last 20 min of HD session. Therefore, determination of two indices (UF rates during the higher UF rate period and the target *%ΔBV* value during the automatic UF rate- adjustment period) was necessary before HD initiation in HD with BV-UFC. Before this study, the values in each patient were determined by observing hemodynamic stability during the run-in period. In standard HD with a constant UF rate, the recommended maximum UF rate is ≤15 mL/(kg·h) [31, 32]. However, in patients with IDH, removing more fluid during the first hour of HD and reducing the rate later were recommended under the concept of UF profiling control [33, 34] because of the higher rates of plasma refilling in response to UF at the early phase of the HD session, particularly within 1 h after the HD session [34]. In this study, UF rate during the higher UF rate period in HD with BV-UFC was 15.7 ± 4.2 mL/(kg·h). Thereafter, the *%ΔBV* value within the automatic UF rate- adjustment period, on average, was set at -4.0% during 150 min. To reach the dry weight in standard HD with constant UF rates, the *%ΔBV* range had been proposed previously [11]. Based on this report, at the end of 4 h HD session, *%ΔBV* per the percent change in body weight during HD was recommended from -1.75% to -3.73% [11]. In this study, dry weight was 61.3kg and the residual UFV at the initiation of the automatic UF rate- adjustment period was 1.9 L, which was equivalent to 3.10% of the percent change in body weight. Therefore, recommended *%ΔBV* range during this period was calculated from -3.39% to -7.23%. In this study, assumed *%ΔBV* range during this period to prevent the excessive BV reduction was relatively low level compared with that previously recommended in standard HD.

In HD with BV-UFC, the UF rates were continuously changing along with the *%ΔBV* changes during the automatic UF rate- adjustment period, which had been set before HD, and the UFV during this period cannot be strictly determined. Therefore, one of our major concerns was whether a delay in achieving the target UFV at the end of HD occurs in HD with BV-UFC. Being overweight at the end of HD by ≥ 0.3 kg was independently associated with an increased long-term risk of all-cause and cardiovascular mortality in patients undergoing HD

[35]. Therefore, achievement of the target UFV at the end of HD was defined as within ± 0.3 kg of the dry weight in this study. As a result, no significant differences were found in HD sessions with a delay in achieving the target UFV between HD with BV-UFC and standard HD.

This study had several limitations. First, the sample size was relatively small. Second, the setting of the higher UF rate and $\%\Delta BV$ decrease during the automatic UF rate-adjustment period in each patient may have differences because these values were determined based on the hemodynamic stability during HD at the discretion of each hospital. Third, because HD therapy was crossed over between standard HD and HD with BV-UFC as the first and second HD sessions during this study, the therapeutic effect of HD with BV-UFC might not reach the steady state throughout the observation in this study. Therefore, it might be considered that this study could not correctly evaluate the therapeutic benefits of HD with BV-UFC, including BP stability during HD. Furthermore, the gradients between serum sodium and dialysate sodium levels, which were associated with body- fluid movement between intracellular and extracellular fluids, and body and dialysate temperatures are important factors in preserving hemodynamic stability during HD [36]. However, in this study, serum sodium levels were confirmed at limited times, and body and dialysate temperature were not recorded throughout this study. Therefore, we cannot directly comment on the influences of sodium gradients between blood and dialysate, as well as those of the body and dialysate temperatures on hemodynamic stability during HD. Therefore, additional studies are needed to confirm the therapeutic effect of HD with BV-UFC in detail in the future.

Conclusion

HD with BV-UFC did not reduce the prevalence of IDH compared with standard HD. The relief of a relative BV reduction at the end of HD may be beneficial in patients undergoing HD with BV-UFC.

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Authors' contributions

SO, NH and KT conceived and designed this study. SO, KI, TU, KT, SK, TS, KH, HM, YU, TH, CI, OI, KY, YM and KT performed this study. SO and KI analyzed the data. YM, NH and KT supervised the data collection and manuscript preparation. SO and KI drafted the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

All data analyzed during this study are included in this published article.

Ethics approval and consent to participate

This study was registered at the University Hospital Medical Information Network (study No. UMIN000024670, date of registration: December 1, 2016) in Japanese Primary Registry Network; approved by the institutional review board of Saitama Medical Center, Jichi Medical University, Japan (RINS 16-003); the study was conducted in accordance with the Declaration of Helsinki (2004 Tokyo revision). All patients signed informed consent forms before participation.

Consent for publication

For publication of this study, agreement was obtained from each patient.

Competing interests

Nikkiso Corporation provided support in the form of covering costs required for this study. There are no patents, products in development associated with this study to declare.
NH is working as an associate editor of this journal. NH did not involve in the reviewing process of this article.

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