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Published in:
Asaio Journal

DOI:
10.1097/MAT.0b013e318031b513

Publication date:
2007

Effects of Relative Blood Volume–Controlled Hemodialysis on Blood Pressure and Volume Status in Hypertensive Patients

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In hypertensive hemodialysis (HD) patients, dry weight reduction to normalize blood pressure (BP) often results in increased frequency of HD hypotension. Because HD with blood volume tracking (BVT) has been shown to improve intra-HD hemodynamic stability, we performed a prospective, randomized study to test whether BVT is more effective than standard hemodialysis (SHD) in the management of hypertension by dry weight reduction. After a run-in period of 4 weeks on SHD, 28 patients were randomly assigned for a 12-week treatment period with either SHD (n = 14) or BVT (n = 14). The mean pre-HD and post-HD weight did not change over time in either group. In the BVT group, pre-HD systolic and diastolic BP decreased on average 22.5 mm Hg and 8.3 mm Hg, respectively (both $p < 0.05$), whereas BP did not change in the SHD group. Extracellular water and cardiothoracic ratio decreased significantly (all $p < 0.05$) in the BVT group but not in the SHD group. Brain natriuretic peptide levels declined only in the BVT group, without reaching statistical significance. The frequency of HD hypotensive episodes decreased significantly ($p < 0.05$) in the BVT group and was unchanged in the SHD group. HD with BVT was associated with a significant reduction in pre-HD BP. At the same time, the frequency of intra-HD hypotensive episodes decreased. Although the mean weight did not change, the reductions in cardiothoracic ratio and extracellular water suggest that HD with BVT resulted in optimization of volume status. *ASAIO Journal* 2007; 53:357–364.

Hypertension in chronic hemodialysis (HD) patients is a potential risk factor for cardiovascular disease.[1] Inadequate removal of excess volume during HD plays a major role in the development of hypertension.[2–4] Blood pressure (BP) lowering, either by dry weight reduction or by antihypertensive medication, often results in an increased frequency of dialysis hypotension, thereby limiting the acceptance and thus the effect of these interventions on BP control.

Because a reduction in blood volume plays an important role in the development of HD hypotension, automatic feedback systems have been developed to control intra-HD changes in relative blood volume (ΔRBV). One of these systems is based on the concept of blood volume tracking (BVT): Based on target values for ultrafiltration (UF) volume and treatment duration, the BVT system guides the actual RBV along a preset individual RBV trajectory by continuously adjusting the UF rate and dialysate conductivity.[5] HD with BVT has been shown to improve intra-HD and post-HD cardiovascular stability in hypotension-prone patients in comparison with standard HD (SHD).[5–9]

At present, there are no randomized studies that have compared SHD to BVT with regard to dry weight optimization and BP control in hypertensive HD patients. The aim of this prospective, randomized study was first, to test whether BVT is more effective than SHD in the management of hypertension by dry weight reduction in patients with long-term HD with hypertension, and, second, to test if BVT is more effective than SHD in the prevention of HD hypotension during the process of dry weight reduction.

Subjects and Methods

Prevalent HD patients with hypertension and presumed volume overload were asked to participate in this study. Hypertension was defined as a pre-HD and/or post-HD BP of >150/90 mm Hg in more than 50% of HD sessions. In addition, eligible patients had to use either one class of antihypertensive drugs (for the indication hypertension) or have a cardiothoracic ratio (CTR) of >0.5 on a standing chest radiograph. Patient exclusion criteria were 1) absence of informed consent; 2) need to perform HD with predilution because BVT does not function properly during predilution; 3) frequent transfusions with packed red blood cells (more than two transfusions per month) because blood transfusion interferes with the calculation of RBV.

Study Design

The total study duration was 16 weeks. The first 4 weeks were used as a run-in period. During this period, all patients were on SHD, and the dialysis staff attempted to gradually lower dry weight to control hypertension. At the end of the run-in period, patients were randomly assigned to either SHD or BVT. The randomization procedure included 34 sealed containers. Each container included one form with either SHD or BVT in a 1:1 ratio. A member of the dialysis staff who did not participate in the trial matched the sealed containers to a patient's inclusion number. Except for the dialysis modality, patients in either group received identical medical care. This included gradual lowering of dry weight in patients who were

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Submitted for consideration September 2006; accepted for publication in revised form November 2006.

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DOI: 10.1097/MAT.0b013e318031b513

judged to be overhydrated by their nephrologists. The randomization procedure was carried out by a member of the dialysis staff who did not participate in the trial.

Subsequently, patients were dialyzed for 12 weeks with either SHD or BVT. In both groups, the HD staff tried to control hypertension by a gradual reduction in dry weight. At the end of the run-in period and at the end of the 12-week treatment period, patients underwent the following tests to assess volume status: 1) chest radiography, 2) bioimpedance analysis, and 3) blood sampling for brain natriuretic peptide (BNP) analyses. To make proper comparisons, all these tests were performed before and/or after a midweek HD session. If patients did not satisfy the inclusion criteria at the end of the run-in period, they were excluded from the study.

Additional blood was drawn to determine: Kt/V, hemoglobin, albumin, and plasma sodium levels. Post-HD blood samples for Kt/V and plasma sodium levels were drawn 15 minutes after the end of the HD session.

Patients received a light lunch and two cups of coffee or tea during HD. Patients were dialyzed in the supine position during most of the treatment. Written informed consent was obtained from all participating patients. The study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the local medical ethics committee.

Table 1. Patient Characteristics at Baseline (Mean ± SD)

	SHD	BVT
Age (years)	64.9 ± 12.5	64.1 ± 12.1
Sex (M/F)	6/8	7/7
Time on dialysis (years)	2.4 ± 1.2	2.4 ± 1.9
Diabetes (number of patients)	3	5
Hemoglobin (mmol/L)	7.6 ± 0.5	7.6 ± 0.7
Albumin (g/L)	39.9 ± 2.5	39.4 ± 2.3
Kt/V	1.28 ± 0.2	1.26 ± 0.2
Cause of ESRD		
Hypertension	5	4
Diabetes	2	3
Focal segmental glomerulosclerosis	2	2
IgA nephropathy	2	0
Chronic pyelonephritis	0	1
MPGN	1	0
Alport syndrome	0	1
Unknown	2	3
Cardiovascular comorbidity		
Cerebrovascular accident	1	1
Myocardial infarction	3	2
Aortic valve stenosis (pressure gradients ranging from 15 to 40 mm Hg)	1	4
Residual diuresis (number of patients)	3	3

SHD, Standard hemodialysis: BVT, blood volume treatment; ESRD, end-stage renal disease; MPGN, membranoproliferative glomerulonephritis.

Dialysis Settings

All patients were dialyzed with bicarbonate dialysis with the Integra Physio HD apparatus (Hospal-Gambro, Lyon, France) for 3 times 4 hours per week with a low-flux polysulfone hollow-fiber dialyzer, F8 (Fresenius Medical Care, Bad Homburg, Germany). ΔRBV during HD was measured with Hemoscan (Hospal-Gambro).[10] Blood flow rates were 250 to 350 mL/min, and dialysate flow rate was 500 mL/min. Blood and dialysate flows were kept constant in individual patients. Dialysate temperature was 36.0°C. Dialysate composition for SHD was as follows: sodium, 139 mmol/L; potassium, 1.0 mmol/L; calcium, 1.5 mmol/L; magnesium, 0.5 mmol/L; chloride, 108 mmol/L; bicarbonate, 34 mmol/L; acetate, 3 mmol/L; and glucose, 1.0 g/L.

BVT System

BVT was performed with the Integra Physio (Hospal-Gambro). The BVT system is described in detail elsewhere.[6–8,10] In short, ΔRBV are measured every minute during HD, based on assessment of variations in hemoglobin concentration. The software responds to ΔRBV and continuously adjusts the UF rate and dialysate conductivity (lower and upper limits 13.3 and 16.0 ms/cm, respectively) through a feedback mechanism. The main objective of the system is to guide the RBV along a predetermined individual RBV trajectory. Simultaneously, the BVT system aims at achieving the preset UF volume target and avoids sodium overload by means of a kinetic sodium model that establishes a preset equivalent conductivity. The equivalent conductivity represents the dialysate conductivity that produces the same sodium mass balance at the end of a BVT treatment session as SHD with constant dialysate conductivity.[6] The equivalent conductivity was set at 13.8 ms/cm, with a lower and upper tolerance of 13.6 and 14.0 ms/cm, respectively. The settings for the RBV target were assessed according to the course of the RBV and the BP during at least six SHD sessions during the run-in period. Dialysate composition during HD with BVT was identical to that with SHD, except for dialysate sodium, which varied according to the concept of BVT.

Adjustment of Dry Weight and Antihypertensive Medication

Patients on SHD and BVT were taken care of by the same nephrologists. Prescriptions regarding dry weight and antihy-

Table 2. Results at Baseline and After 12 Weeks of Treatment (Mean ± SD)

	SHD	BVT
Pre-HD weight (kg), Baseline	70.3 ± 12.2	82.8 ± 16.6
After 12 weeks	70.2 ± 11.9	82.6 ± 15.6
Post-HD weight (kg), Baseline	68.1 ± 12.0	80.7 ± 16.5
After 12 weeks	68.1 ± 11.6	80.3 ± 15.2
Total UF volume (mL), Baseline	2860 ± 602	2832 ± 518
After 12 weeks	2723 ± 668	3066 ± 646
ΔRBV at the end of HD (%), Baseline	−9.9 ± 2.7	−9.1 ± 1.9
After 12 weeks	−8.9 ± 3.1	−8.8 ± 2.0
Pre-HD plasma sodium (mmol/L), Baseline	138.8 ± 3.0	139.9 ± 2.2
After 12 weeks	139.2 ± 2.5	139.8 ± 2.2
Post-HD plasma sodium (mmol/L), Baseline	139.9 ± 2.0	139.9 ± 2.1
After 12 weeks	139.8 ± 2.1	139.9 ± 2.1

SHD, Standard hemodialysis; BVT, blood volume treatment; HD, hemodialysis; UF, ultrafiltration volume; RBV, relative blood volume.

pertensive medication were made solely by these nephrologists during their weekly visits to the participating patients. The dialysis staff was instructed to attempt to gradually lower dry weight to control hypertension on a session-to-session basis as long as the post-HD weight was above the presumed dry weight. Dry weight was evaluated clinically (peripheral edema, signs of pulmonary congestion, intradialytic and interdialytic BP course, muscle cramps) in combination with the CTR on chest radiography.

The preferred antihypertensive medications in our institution are β-blockers, angiotensin-converting enzyme blockers, and A-II receptor blockers. Calcium entry blockers are used only if hypertension persists with the preferred medication. If BP decreased during the process of dry weight reduction, the dose of one class of antihypertensive medication was lowered and stopped if possible, starting with calcium entry blockers. The next class of antihypertensives then was lowered, and so forth. Patients were instructed to take antihypertensive medication after the HD treatment.

To compare the use of the antihypertensive medication between groups, we calculated the average defined daily dose (DDD) of antihypertensive drugs for each individual patient.[11]

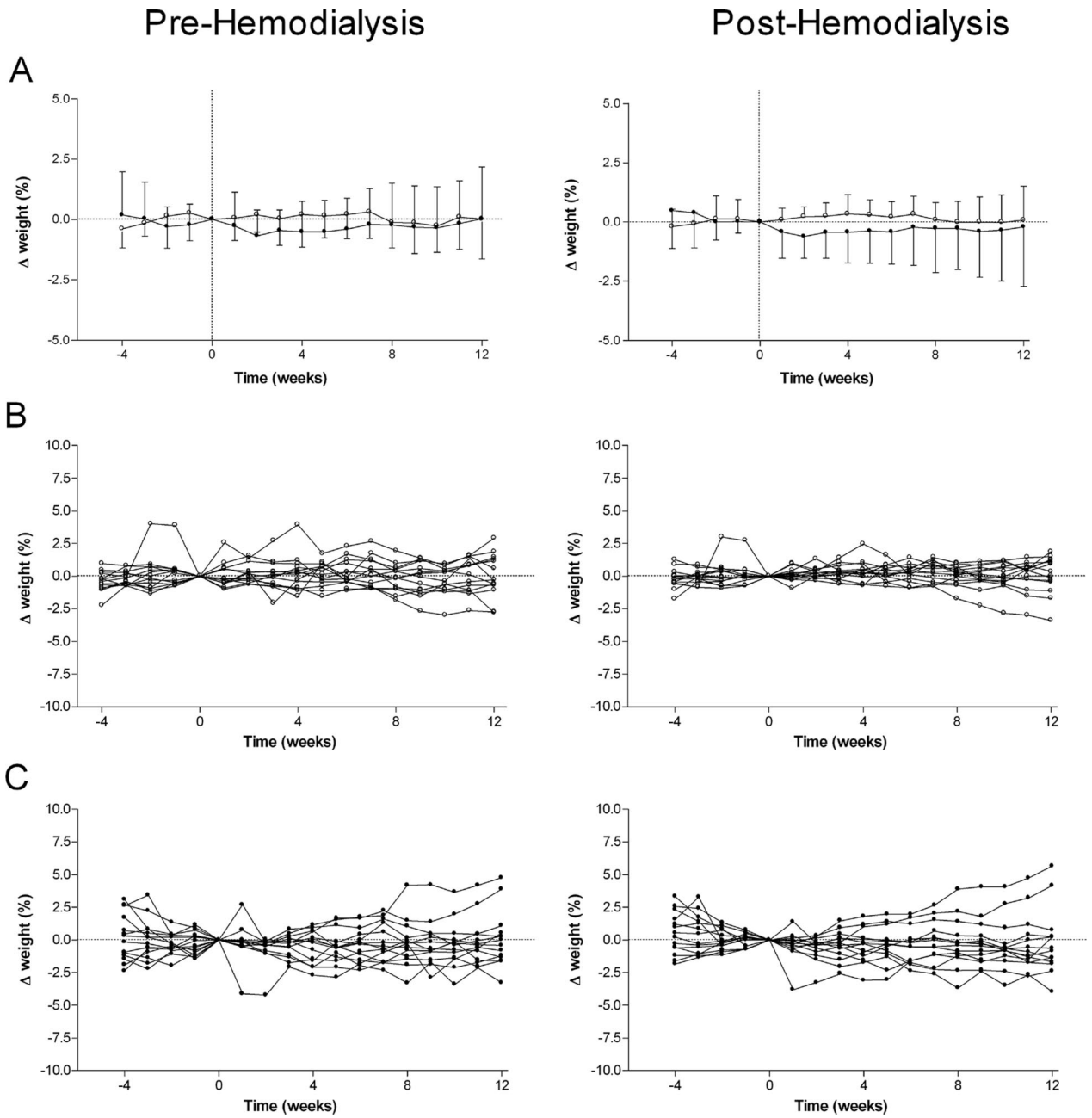

Figure 1. Pre-HD (left panel) and post-HD (right panel) weight change. The weight at baseline is used as the reference point (0%). A shows the average weight change in both groups. Error bars represent standard deviation. B and C show the individual weight changes in the standard hemodialysis group (SHD) and blood volume treatment (BVT) group, respectively. ○ SHD; ● BVT.

Weight, Blood Pressure, Heart Rate, UF Volume, Hypotensive Episodes, and ΔRBV

Each HD session was evaluated for pre-HD and post-HD body weight, pre-HD and post-HD BP, heart rate (HR), UF volume, the occurrence of hypotensive episodes, treatment interventions, and ΔRBV. BP and HR were measured with an automated oscillometric monitor that is incorporated in the HD apparatus.

HD hypotension was defined as a drop in systolic BP of more than 40 mm Hg from the pre-HD value in combination with a treatment intervention by the dialysis nurse (temporary stop of UF and/or infusion of IV fluids). If intravenous fluids were given during HD, the ΔRBV at the end of the treatment was not used in the evaluation because the infusion of fluids interferes with accurate calculation of ΔRBV.

Chest Radiography, Bioimpedance Analysis, and Brain Natriuretic Peptide Levels

As a surrogate marker for volume status, pre-HD standing chest radiography was performed. The CTR (transverse diameter of the heart/ internal diameter of the chest) was assessed by a physician who was blinded to the dialysis modality as well as to the order in which the chest radiographs had been performed.

Extracellular water (ECW) was determined by single-frequency (50 kHz) bioimpedance analysis (BIA), using a BIA-101 (Akern System, Florence, Italy). BIA was performed before and 5 to 10 minutes after the end of HD on the nonaccess side.[12] ECW was corrected for body weight (BW).

Pre-HD and post-HD serum was collected for determination of BNP (microparticle enzyme immunoassay; Abbott Diagnostics) levels. Immediately after the collection of 4 mL EDTA blood, 3 drops of aprotinin (10.000 KIU/mL) were added. Blood samples were centrifuged within 1 hour after sampling for 15 minutes at 3000 rpm and then stored at −80°C until analysis. All samples were analyzed at once.

Statistical Analysis

Data are presented as mean ± standard deviation. BP, HR, hypotensive episodes, weight, and weight loss are presented as weekly averages. The mean values in the randomization week (week 0) were used as the point of reference. The significance of comparisons between baseline and after 12 weeks of either SHD or BVT was made with a paired Student's t test or a Wilcoxon matched-pairs test when appropriate.

For comparisons between groups, analysis of variance, and, when appropriate, an unpaired Student's t test, was used. Probability values of <0.05 were considered significant.

Results

Patients

Thirty-four patients gave informed consent to the study protocol. Twenty-eight of these 34 patients completed the study. The six patients who did not complete the study were all excluded before random assignment. Reasons for not completing the study were kidney transplantation (n = 1), withdrawal of informed consent (n = 4), and transfer to another HD center (n = 1). Of the 28 patients who completed the study, 14 patients had been randomly assigned to SHD and 14 patients to BVT. As shown in **Table 1**, groups were comparable with regard to age, sex, dialysis vintage, frequency of diabetes mellitus, laboratory parameters, Kt/V, cause of end-stage renal disease, and cardiovascular co-morbidity. None of the patients had ankle edema at any time during the study or had pulmonary congestion at either the baseline or the end-of-study chest radiography.

Three patients in each group had residual renal function with urine volumes of 350, 550, and 975 mL/24 h in the SHD group and 150, 690, and 1100 mL/24 h in the BVT group.

In the SHD group, nine patients had an arteriovenous fistula, one a tunneled venous catheter, and four a polytetrafluoroethylene (PTFE) loop. In the BVT group, eight patients had an arteriovenous fistula, two a tunneled venous catheter, and four a PTFE loop.

Weight, UF volume, ΔRBV, and Plasma Sodium Levels

As shown in **Table 2** and **Figure 1A**, mean weight did not change significantly from baseline to the end of the study period in either group. **Figure 1** also shows the individual pre-HD and post-HD weight change in patients on SHD (**Figure 1B**) and BVT (**Figure 1C**). Interestingly, the interindividual variation in weight change was much greater in the BVT group than in the SHD group.

Table 3. Pre-HD and Post-HD Blood Pressure and Antihypertensive Medication (Mean ± SD)

	SHD	BVT
Pre-HD systolic blood pressure (mm Hg),		
Baseline	156.1 ± 14.3	166.1 ± 19.8
After 12 weeks	159.1 ± 17.0	143.6 ± 23.3*
Post-HD systolic blood pressure (mm Hg),		
Baseline	130.2 ± 23.3†	157.1 ± 15.2
After 12 weeks	131.8 ± 20.2	126.6 ± 21.3*
Pre-HD diastolic blood pressure (mm Hg),		
Baseline	82.9 ± 8.7	81.3 ± 12.7
After 12 weeks	84.1 ± 6.2‡	73.0 ± 9.0†
Post-HD diastolic blood pressure (mm Hg),		
Baseline	73.7 ± 8.4	76.8 ± 7.9
After 12 weeks	74.0 ± 7.4	68.7 ± 10.5†
Pre-HD heart rate (bpm), Baseline	82.6 ± 12.6	79.5 ± 12.7
After 12 weeks	82.1 ± 8.1	79.5 ± 10.4
Post-HD heart (bpm), Baseline	82.8 ± 7.7	80.4 ± 12.4
After 12 weeks	80.5 ± 8.0	80.0 ± 14.3
Antihypertensive medication		
No. of defined daily doses, Baseline	0.4 ± 0.5	0.9 ± 1.3
After 12 weeks	0.4 ± 0.6	0.6 ± 0.8
No. of medications, Baseline	0.9 ± 0.7	0.9 ± 1.1
After 12 weeks	0.9 ± 0.8	0.6 ± 0.7

* $p < 0.01$ in comparison with BVT at baseline.
† $p < 0.05$ in comparison with BVT at baseline.
‡ $p < 0.05$ in comparison with BVT at 12 weeks.
SHD, Standard hemodialysis; BVT, blood volume treatment; HD, hemodialysis.

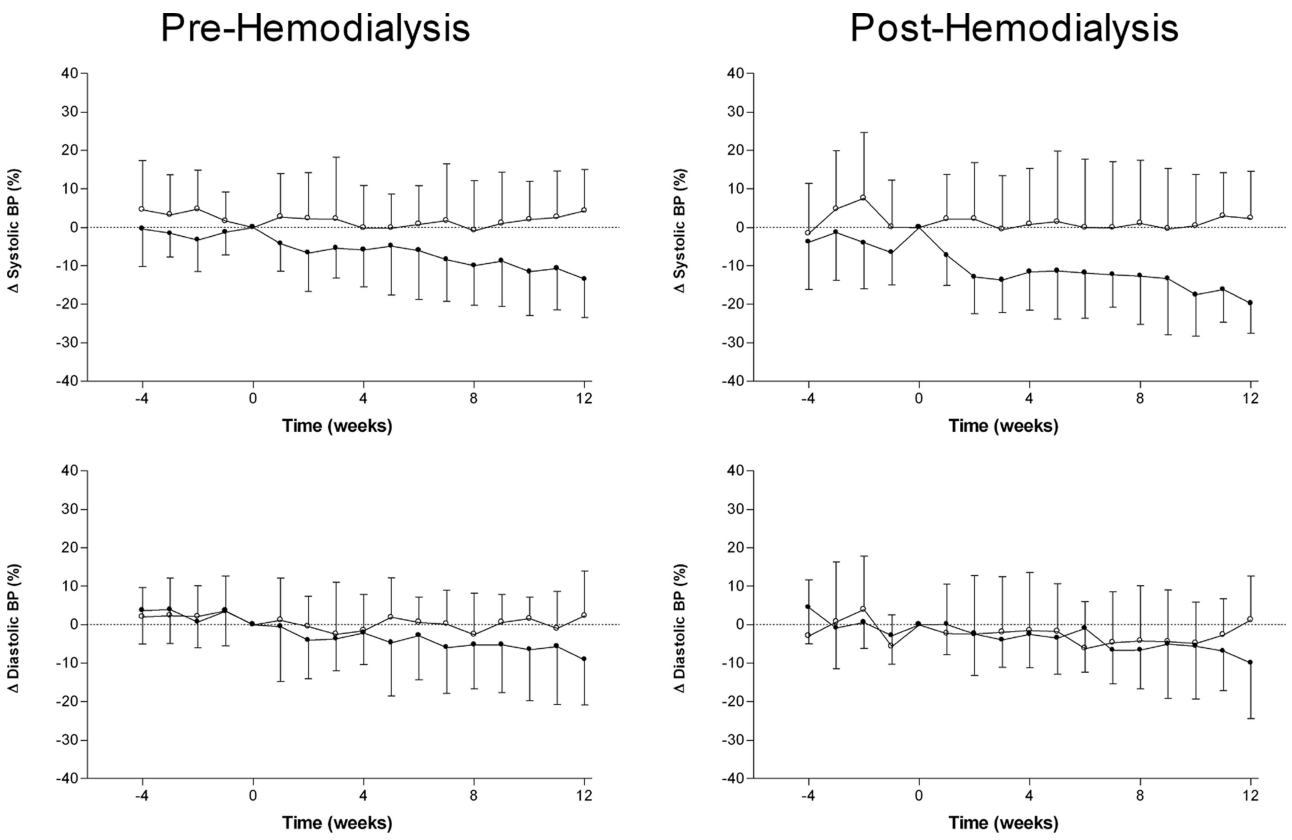

Figure 2. Mean pre-HD (left panel) and post-HD (right panel) systolic (upper panel) and diastolic (lower panel) blood pressure. Error bars represent standard deviation. ○ SHD; ● BVT.

Table 2 also shows the UF volume at baseline and after 12 weeks of treatment. Total UF volume showed a significant interaction on week and group ($p < 0.01$), indicating that in the BVT group the UF volume increased during the course of the study, whereas the UF volume decreased in the SHD group.

ΔRBV at the end of the HD session and pre-HD and post-HD plasma sodium levels in both groups were comparable at baseline and after 12 weeks of treatment (**Table 2**).

Blood Pressure, Heart Rate, and Antihypertensive Medication

Table 3 shows the pre-HD and post-HD BP at baseline and after 12 weeks of treatment. At baseline, pre-HD systolic and pre-HD and post-HD diastolic BP were comparable in both groups. Baseline post-HD systolic BP was higher ($p < 0.05$) in the BVT group.

The pre-HD systolic and diastolic BP did not change in the SHD group. In the BVT group, however, pre-HD systolic and diastolic BP decreased on average 22.5 and 8.3 mm Hg, respectively, from baseline to the end of the study (**Figure 2**). The decrease in systolic BP was significant from 4 weeks onward ($p < 0.05$), and the decrease in diastolic BP was significant at 12 weeks ($p < 0.05$) in comparison with baseline. In the BVT group, post-HD systolic and diastolic BP also decreased significantly ($p < 0.01$ and $p < 0.05$, respectively) from baseline to the end of the study period, whereas it was unchanged in the SHD group. When corrected for differences in baseline BP, pre-HD and post-HD systolic and diastolic BP again decreased significantly ($p < 0.05$) in the BVT group but not in the SHD group.

Heart rate did not differ between both groups at baseline and after 12 weeks of treatment (**Table 3**).

The mean DDD of antihypertensive drugs and the number of antihypertensive medication is also shown in **Table 3**. At baseline, the average DDD in the BVT group was higher than in the SHD group, but the difference was not significant. In the SHD group, the average DDD did not change throughout the study. In the BVT group, the average DDD showed a nonsignificant decrease.

Bioimpedance Studies, Cardiothoracic Ratio, and Brain Natriuretic Peptides

Figure 3 shows the individual values for pre-HD and post-HD extracellular water/body weight (ECW/BW) at baseline and after 12 weeks of treatment. In the SHD group, pre-HD ECW/BW did not change (from 0.25 ± 0.04 to 0.25 ± 0.03), whereas ECW/BW increased significantly ($p < 0.01$) after HD (from 0.22 ± 0.03 to 0.23 ± 0.03). Pre-HD and post-HD ECW/BW decreased significantly ($p < 0.001$) in the BVT group, from 0.25 ± 0.04 to 0.23 ± 0.04 and from 0.23 ± 0.03 to 0.21 ± 0.04, respectively.

Pre-HD and post-HD BNP levels are shown in **Table 4**. At baseline, BNP levels did not differ between groups. After 12 weeks of treatment, BNP levels showed a nonsignificant decline in pre-HD ($p = 0.12$) and post-HD ($p = 0.19$) levels in

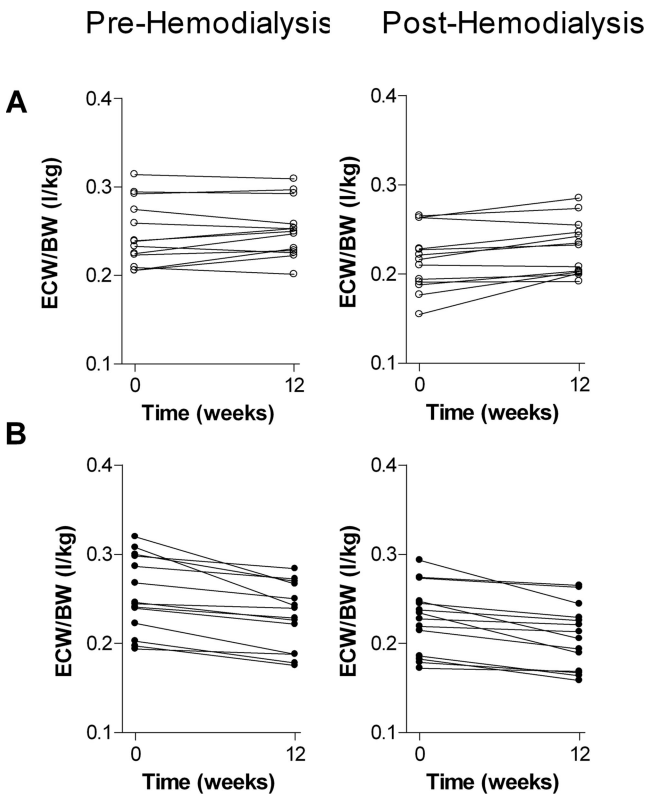

Figure 3. Pre-HD and post-HD individual changes in extracellular water (ECW) corrected for body weight (BW) at baseline and after 12 weeks of treatment. A and B show changes in pre-HD and post-HD ECW/BW in the standard hemodialysis group (SHD) and the blood volume treatment (BVT) group, respectively. ○ SHD; ● BVT.

the BVT group, whereas nonsignificant increases in the SHD group were observed.

The CTR on a pre-HD standing chest radiograph did not change in the SHD group (from 0.522 ± 0.05 to 0.524 ± 0.04), whereas it decreased significantly ($p < 0.01$) in the BVT group (from 0.538 ± 0.05 to 0.517 ± 0.05). Moreover, the mean changes of the CTR between groups differed significantly ($p < 0.01$).

Dialysis Hypotension

As shown in **Figure 4**, the frequency of hypotensive episodes decreased significantly ($p < 0.05$) in the BVT group compared with the run-in period. In the SHD group, the frequency of hypotensive episodes did not change.

Discussion

This study is the first to show in a prospective, randomized fashion that HD with BVT is associated with a significant and clinically relevant reduction in pre-HD and post-HD BP. The decrease in systolic BP was already prominent after 2 to 3 weeks of HD with BVT and was maintained throughout the study. At the same time, the frequency of HD hypotension episodes decreased significantly in the BVT group, whereas it was unchanged in the SHD group.

Control of hypertension in hypertensive HD patients is associated with improved survival.[13] With regard to hypertension control, the Tassin experience is widely known. In a study from this center, excellent BP control was obtained without antihypertensive medication by careful maintenance of dry weight and sodium restriction.[14] A very important part of this HD prescription was the HD duration: Patients were dialyzed for 7 to 8 hours, three times per week. The Tassin group also described the lag phenomenon indicating the delay between the normalization in ECW and the subsequent gradual decrease in BP. In this study, it took more than 8 months of treatment before the gradual BP decline leveled off, although the mean arterial pressure had already decreased from 121 mm Hg to 108 mm Hg within 1 month.[14] In our study, BP started to decrease almost immediately after the initiation of BVT, but BP decline did not reach a plateau phase during the study. It is possible that BP would have decreased further beyond the time frame of this trial and, therefore, a longer follow-up would have been useful. Alternatively, it is possible that not all patients in the BVT group were at their dry weight at the end of the study because several patients did not reach normotension and some still used antihypertensive medication. However, we must emphasize that dry weight reduction may be difficult with a conventional dialysis scheme of three times per week, 4 hours, as in the present study. Frequent nocturnal home HD or nocturnal in-center HD is an important contribution to the efforts made to control hypertension.[15,16]

Remarkably, the average weight did not change in either group. However, the reduction in BP in the BVT group coincided with significant reductions of the CTR and ECW/BW. All these parameters point toward the same direction and suggest that BVT optimized volume status in overhydrated HD patients. Interestingly, there was a large interindividual variation in pre-HD and post-HD weight course in the BVT group, whereas the weight course in the SHD group showed far less variation (**Figure 1**). Weight change, however, is a poor marker for the detection of alterations in the patients volume status because changes in fat or lean body mass may occur unnoticed as the result of a coincident change in ECW.[17] For example, body weight may be unchanged if an increase in fat or lean body mass coincides with a reduction in ECW. In the BVT group, 2 patients showed a large pre-HD and post-HD increase in weight (**Figure 1**). The first patient had pre-HD and post-HD weight gains of 3.9% and 4.1%, respectively, compared with baseline. At the same time, pre-HD CTR (from 0.51

Table 4. Brain Natriuretic Peptide (Mean ± SD, Minimum-Maximum)

	SHD	BVT
Pre-HD BNP, baseline	221.6 ± 324.6 (7.6–1084)	148.3 ± 283.1 (12.2–1084)
After 12 weeks	232.9 ± 311.7 (11.4–1103)	90.3 ± 109.0 (7.7–413.1)
Post-HD BNP, baseline	172.2 ± 249.8 (10–865.1)	118.8 ± 190.7 (14.3–745.5)
After 12 weeks	214.7 ± 301.2 (9.7–1086)	87.1 ± 124.4 (5.8–478.4)

SHD, Standard hemodialysis; BVT, blood volume treatment; HD, hemodialysis; BNP, brain natriuretic peptide.

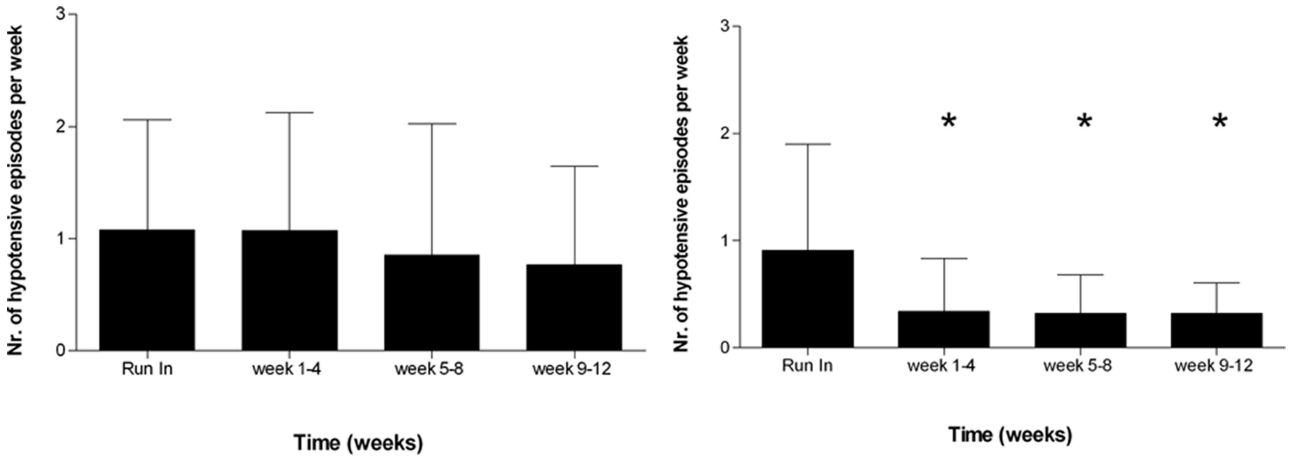

Figure 4. Mean frequency of hypotensive episodes during hemodialysis, expressed as the number of episodes per week per 4-week period in the standard hemodialysis (SHD) group (left panel) and in the blood volume treatment (BVT) group (right panel). Error bars represent standard deviation. * $p < 0.05$ in comparison with the run-in period.

to 0.48), ECW/BW (from 0.24 to 0.22 L/kg), and BNP (from 101.2 to 69.4 pmol/L) all declined during the study. The second patient had pre-HD and post-HD weight increases of 4.7% and 5.6%, respectively, compared with baseline. Also in this patient, pre-HD CTR (from 0.57 to 0.55), ECW/BW (from 0.27 to 0.25 L/kg), and BNP (from 82.7 to 37.2 pmol/L) all declined during the study. These apparent discrepancies may be explained by an increase in lean body mass in these and possibly other patients during HD with BVT. Unfortunately, we did not include nutritional parameters in our study design. Nevertheless, one might speculate that the reduction in the frequency of HD hypotension led to an increased well-being during and after HD and—as a result—an increased food intake in the BVT group.

The better hemodynamic stability and improved volume status with BVT was not paralleled by better RBV preservation in comparison with SHD. The ΔRBV in both groups decreased to a similar magnitude both at baseline and after 12 weeks of treatment (**Table 2**). The finding of a substantial RBV reduction at baseline in both groups is interesting because several groups have reported that patients who display a substantial reduction in RBV during HD are likely to have a correct volume status or, in some cases, are even below optimal dry weight.[18–20] This study, however, shows that moderately overhydrated patients can also display substantial reductions in RBV.

There are several drawbacks to this study. First, this study was not double-blinded because it is not possible to compare SHD and BVT in a double-blinded protocol in clinical practice. However, to avoid bias as much as possible, we made a distinction between the physician who coordinated this trial and the nephrologists who evaluated and adjusted dry weight and antihypertensive medication. Bias could have been introduced because the patients on BVT received more attention during the HD treatment, since the BVT system needs occasional adjustment during the treatment (*vide infra*). Second, in the SHD group, the post-HD systolic BP at baseline was significantly lower in comparison with the BVT group. This could indicate that, by chance, these patients were less overhydrated at baseline than those randomly assigned to BVT. The slightly higher CTR at baseline in the BVT group also points in this direction, although the difference between the groups was not significant. It is therefore possible that it was more difficult for patients in the SHD group to achieve reductions in pre-HD systolic BP. However, when corrected for the difference in baseline systolic BP between BVT and SHD, the decline in the BVT group remained significant. An argument against a difference in baseline hydration status is the identical baseline ECW/BW in both groups. Third, although we used several tests (CTR, BIA, and BNP) to evaluate the volume status of our patients, we did not include inferior vena cava (IVC) measurements. Possibly, IVC measurements would have been an asset to this study. However, all the mentioned methods for evaluating a patient's volume status, including IVC, have their limitations.[17] Therefore, dry weight is by definition determined by clinical assessment and usually reflects the lowest weight a patient can tolerate without intradialytic symptoms and hypotension in the absence of overt fluid overload.[21] Nevertheless, the results from this study must be confirmed in future studies. These studies should preferably include nutritional parameters as well as IVC diameters in addition to the markers we have used for volume status.

The success of the BVT system with regard to BP reduction can probably be explained partially by the fact that it indicates, based on individually set targets for ΔRBV, UF volume and equivalent conductivity, whether or not more fluid can be withdrawn during a particular HD session. The dialysis staff then has the possibility to change the originally set goal for UF volume and/or ΔRBV, based on the patient's current condition. Indeed, in the BVT group, total UF volume increased during the course of the study, whereas it did not in the SHD group. In a patient group with substantial comorbidity, the BVT system can thus be considered as an extra support for the HD staff to reach dry weight by adequate UF. However, for adequate use of the BVT system, one should have knowledge of the merits and limitations of the ΔRBV measurement.[22]

Conclusion

In this small, randomized clinical trial, HD with BVT resulted in a reduction of elevated pre-HD BP, while at the same time the frequency of HD hypotension decreased. The close association between the reduction in BP and the decrease in

CTR and ECW/BW suggests that HD with BVT optimized volume status in previously overhydrated HD patients.

Acknowledgments

Casper Franssen is the recipient of an unrestricted research grant by Gambro-Hospal Company. Gambro-Hospal had no role in the design and conduct, data analysis, and manuscript preparation of this study.

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