Relative Plasma Volume Monitoring During Hemodialysis Aids the Assessment of Dry Weight

Arjun D. Sinha, Robert P. Light, Rajiv Agarwal

Abstract—Among hemodialysis patients, the assessment of dry weight remains a matter of clinical judgment because tests to assess dry weight have not been validated. The objective of this study was to evaluate and validate relative plasma volume (RPV) monitoring as a marker of dry weight. We performed RPV monitoring using the Crit-Line monitor at baseline and at 8 weeks in 150 patients participating in the Dry-Weight Reduction in Hypertensive Hemodialysis Patients Trial. The intervention group of 100 patients had dry weight probed, whereas 50 patients served as time controls. RPV slopes were defined as flat when they were less than the median (1.33% per hour) at the baseline visit. Among predominantly (87%) black hemodialysis patients, we found that flat RPV slopes suggest a volume-overloaded state for the following reasons: (1) probing dry weight in these patients led to steeper slopes; (2) those with flatter slopes at baseline had greater weight loss; (3) both baseline RPV slopes and the intensity of weight loss were found to be important for subsequent change in RPV slopes; and, most importantly, (4) RPV slopes predicted the subsequent reduction in interdialytic ambulatory systolic blood pressure. Those with the flattest slopes had the greatest decline in blood pressure on probing dry weight. Both baseline RPV slopes and the change in RPV slopes were important for subsequent changes in ambulatory systolic blood pressure. We conclude that RPV slope monitoring is a valid method to assess dry weight among hypertensive hemodialysis patients. (Hypertension. 2010;55:305-311.)

Key Words: hypertension ■ hemodialysis ■ dry weight ■ plasma volume ■ diagnostic test

Although the adequacy of solute clearance in patients on chronic hemodialysis is routinely measured as part of dialysis quality assessment, volume status has no validated marker.1 Even after 50 years of dialysis, the assessment of volume remains a matter of clinical judgment;2 unfortunately, the clinical examination performs poorly to assess volume.3 Although probing for dry weight can lead to intradialytic hypotension and uncomfortable symptoms, inadequate volume removal can lead to chronic volume overload with hypertension and left ventricular hypertrophy, which may evoke cardiovascular events and increase mortality.4,5

There has been a long-standing interest in developing volume markers.6 In general, 4 major types of objective measures of volume status have been investigated.7 These measures include the following: biochemical markers (eg, N-terminal pro–B-natriuretic peptide8), imaging markers (eg, inferior vena cava diameter9), bioimpedance analysis,10 and relative plasma volume (RPV) monitoring.11 Among these, RPV monitoring is relatively easy, commercially available, and inexpensive to perform.12 To monitor RPV, a device is attached to the hemodialysis blood tubing that continuously and accurately measures the hematocrit by optical absorbance.13 Assuming no change in the red cell mass during hemodialysis and uniform mixing of red cells within the vasculature, the percentage increase in hematocrit during ultrafiltration estimates the percentage of decrease in blood volume.13

Most studies of RPV monitoring have revolved around efforts to predict and thus prevent intradialytic hypotension and symptoms.13 Using this monitor, we have earlier reported that RPV monitoring correlates with venous echocardiography, as well as with symptoms of and interventions for intradialytic hypotension.14 A few studies have examined the ability of the RPV monitor to assess volume status using the slope of the RPV decrease over the hemodialysis session and correlating that with other objective measures of volume status.11,15,16 All of these studies have been small. Kooman et al.,17 in a recent review, concluded the following:

Blood volume monitoring as a tool to assess dry weight needs further validation and standardization. Summarizing technological tools may certainly aid the clinician in the assessment of fluid state, but should always be interpreted in the clinical context of the patient. Controlled studies are needed to definitively establish the role of technological tools in detecting dry weight.

The purpose of this study was to evaluate among hypertensive hemodialysis patients the diagnostic ability of RPV slope monitoring to assess dry weight. Accordingly, we...
sought the relationship of probing dry weight on RPV slopes. We then evaluated the relationship of baseline RPV slopes and change in RPV slopes on their ability to predict interdialytic ambulatory blood pressure (BP).

Methods
This is a prespecified analysis of patients participating in the previously published Dry-Weight Reduction in Hypertensive Hemodialysis Patients Trial. Briefly, we recruited patients ≥18 years of age on long-term hemodialysis for ≥3 months who had hypertension defined as mean interdialytic ambulatory BP of ≥135/85 mm Hg. After a 6-hemodialysis run-in phase, during which baseline data were collected, patients were randomized in 1:2 proportion into control group versus ultrafiltration trial group for 8 weeks. Pre-BP and post-BP and weights were averaged over the 6-treatment run-in phase. During this 24-dialysis treatment phase, patients were seen at each dialysis visit and had dry weight probed as assessed by symptoms and signs related to hypovolemia. The ultrafiltration group underwent an additional weight loss of 0.1 kg/10.0 kg of body weight per dialysis without increasing the time or frequency of dialysis. This additional weight loss was combined with the ultrafiltration volume required to remove interdialytic weight gain to achieve the desired reduction in dry weight. If ultrafiltration was not tolerated on the basis of symptoms and signs, such as muscle cramps, need for excessive saline, or symptomatic hypotension, the additional prescribed weight loss was reduced by 50%. If ultrafiltration was still not tolerated, the additional weight loss was further reduced by 50% until even 0.2-kg incremental weight loss per dialysis was not tolerated. At this point, the patient was said to be at his or her dry weight. Thus, by this protocol, each patient had to experience symptoms of volume depletion to be at dry weight. The control group had regular physician visits but no additional reduction in dry weight. No changes in antihypertensive medication were permitted during the trial.

BP Monitoring
Ambulatory BP monitoring was performed after the midweek hemodialysis session for 44 hours at baseline, 4 weeks, and 8 weeks. BPs were recorded every 20 minutes during the day (6:00 AM to 10:00 PM) and every 30 minutes during the night (10:00 PM to 6:00 AM) using a SpaceLabs 90207 ABP monitor (SpaceLabs Medical Inc) in the nonaccess arm. Recordings began immediately after hemodialysis and terminated immediately before the subsequent dialysis. Accuracy of ambulatory BP recordings was confirmed against auscultated BP at baseline. Hourly means were calculated. These means were then averaged over the entire course of recording to provide systolic and diastolic interdialytic ambulatory BPs. The mean interdialytic ambulatory BP served as the reference standard.

RPV Monitoring
Of the 150 participants, 145 participants underwent successful intra-dialytic RPV monitoring, which was performed once during the 2-week period at baseline before any intervention and in the last week of the 8-week trial. RPV monitoring was performed with Crit-Line III-TQA, which is a clinically available device that incorporates photo-optical technology to noninvasively measure absolute hematocrit (HemaMetrics). Hematocrit is measured every 20 seconds throughout the duration of hemodialysis. Measurements made by the machine have been validated against hematocrits measured by centrifugation. We exported the machine-stored time and hematocrit data to a relational database for further analysis. The study protocol was approved by the institutional review boards and the Veterans’ Affairs Research and Development Committee. All of the patients provided written, informed consent.

Statistical Methods
The change in plasma volume with ultrafiltration dialysis approximates first-order elimination kinetics. RPV change was calculated as described here. First, we calculated the fraction of blood free of hematocrit using the formula 100−hematocrit%. Next, we took the natural log of this fraction as the dependent variable. An advantage of log transformation is that the coefficients on the time variables approximately reflect the percentage of change in RPV. Independent variables included the following: (1) time elapsed since the beginning of dialysis; (2) indicator variables for group (ultrafiltration and control), visits (baseline and 8 weeks), and their interaction; and (3) interactions of these indicator variables with time elapsed. A mixed model was used to allow for repeated measurements within individuals. Details of the analyses are shown in the supplemental Methods section (available in the online Data Supplement at http://hyper.ahajournals.org).

All of the analyses were conducted using Stata 10.1 (Stata Corp). The P values reported are 2 sided and taken to be significant at <0.05.

Results
Table 1 shows the baseline clinical characteristics of the study population by quartiles of RPV slopes. Most of these characteristics were well matched. By play of chance, steeper RPV slopes at baseline were more often seen in those randomized to the ultrafiltration group. This disadvantaged the ultrafiltration group, because we subsequently showed that BP response depended on quartiles of RPV slopes. Those with steeper slopes had greater ultrafiltration volume, which is not surprising given the physiology that underlies RPV monitoring.

Unadjusted modeled changes in RPV between control and ultrafiltration groups are shown in Figure 1A. The intercepts of RPV slopes were not significantly different from each other and, therefore, were removed from the model. The resulting model was parsimonious, and its model fit was similar to the parent model. In the control group, there was no change in RPV slope from baseline to final visit. In fact, the RPV slopes were so similar that the RPV curves in controls from baseline to final were superimposed. The ultrafiltration group at baseline had an RPV slope similar to controls and experienced a significant steepening of slope over 8 weeks.

The ultrafiltration group had additional volume reduction therapy, which, as expected, led to reduction in postdialysis weight from baseline to 8 weeks. If postdialysis weight change was the sole cause of changes in RPV slopes, then adjustment in the ultrafiltration group for postdialysis weight change would abolish the RPV change. Figure 1B illustrates that if weight changes were accounted for, they did not alter the magnitude or significance of change in RPV slopes.

If flat RPV slopes denote expanded extracellular fluid volume, then those with flat slopes would have decline in weight. Conversely, if steeper RPV slopes denote a contracted extracellular fluid volume, then those with steeper slopes would have increase in weight. Figure 2 shows weight loss as a function of baseline RPV slope. The mean weight overall was 81.6 kg. Those assigned to the ultrafiltration group were 0.55 kg lighter (P<0.2). In the control group, an increase of 0.15 kg in postdialysis weight was noted (P>0.2). Compared with the change in the control group, those in the
Interdialytic ambulatory BP, mm Hg 143.5/110.0 (0.028). Regardless of the study group, patients with steep slopes lost weight. Consideration of RPV slopes in the model improved the estimation of weight loss over the course of the trial ($P=0.005$).

Table 2 shows RPV slopes by quartiles of weight change. Quartile 1 had the least weight loss and quartile 4 the greatest weight loss over 8 weeks. The baseline RPV slopes in the control group were similar at baseline. On the other hand, the baseline RPV slopes in the ultrafiltration group were dissimilar depending on the quartile; those in the higher quartiles...
had flatter baseline slopes. The change from baseline in RPV slope depended on quartiles of weight loss in the control group. The change from baseline in RPV slope was also dependent on quartiles of weight loss in the ultrafiltration group. Even when the change from baseline in RPV slope in the control group was subtracted from change from baseline in RPV slope in the ultrafiltration group, the changes remained highly significant and dependent on quartiles of weight change.

The change from baseline in RPV slope was also dependent on quartiles of weight loss in the ultrafiltration group; those with the steepest slopes at baseline had a flattening of slope, whereas those with the flattest slopes at baseline had the steepest RPV slope at the end of trial (Table S1, available in the online Data Supplement at http://hyper.ahajournals.org). The combined effects of baseline RPV slopes and weight loss on subsequent changes in RPV slopes are shown in Figure 3. Those who had low weight loss had flattening of slopes regardless of whether their slopes were steep or flat at onset. Those who had higher weight loss had steepening of slopes only when probed for dry weight. Those in the control group who did not have their dry weights probed had discordant responses. The high weight loss and steep slope group had a limited number of patients; the steepening in RPV slope
observed is based on the outcomes of only 6 patients. The interaction effect between baseline RPV slope and weight loss on change in RPV slopes was highly significant ($P<0.001$). Compared with the steep-slope group, the odds of losing weight in the ultrafiltration group was 3.12 (95% CI: 1.08 to 9.5; $P=0.019$) in the flat RPV slope group. The odds ratio of losing weight in the control group was 0.59 (95% CI: 0.13 to 2.85; $P=0.44$). The test of homogeneity of the odds ratio was significant ($P<0.05$).

Table S2 shows 44-hour interdialytic ambulatory systolic BP in the control and ultrafiltration groups by quartiles of baseline RPV slopes. The changes from baseline BP over 8 weeks are also shown. Both in control and ultrafiltration groups, baseline systolic BP was similarly elevated. This difference did not differ between quartiles. A fall in systolic BP was seen in the control group; this fall occurred independent of baseline quartile of the RPV slope. A greater fall in systolic BP was seen in the ultrafiltration group. However, this fall in systolic BP had a linear trend with increasing quartiles. Thus, those with the flatterest RPV slopes at baseline experienced the greatest decline in BP on probing dry weight.

Figure 4 shows the effect of initial and final RPV slopes on changes in systolic ambulatory BP. BP did not change when the slope was steep initially and became flatter subsequently. The most profound effect on BP reduction was seen when the initial RPV slope was flat and then steepened subsequently. When dry weight was not probed (control group), patients who had no change in slopes had no significant change in BP (note that the CI of the change goes through 0). However, those who went from flat to steep slope had a significant reduction in systolic BP. Models that excluded initial RPV slope or final RPV slopes or both were significantly worse than nested models.

Finally, we noted that RPV slopes directly affected the frequency of cramps during dialysis, the need for saline boluses, and the need to reduce ultrafiltration. The frequency of these events was accelerated when dry weight was probed in patients who had steeper slopes (data not shown).

## Discussion

Among hypertensive individuals on long-term hemodialysis, we found the following reasons that support the use of RPV slopes as markers of dry weight. First, RPV slopes are

<table>
<thead>
<tr>
<th>Group/Time</th>
<th>Q1, %/h</th>
<th>Q2, %/h</th>
<th>Q3, %/h</th>
<th>Q4, %/h</th>
<th>Heterogeneity Between Quartiles (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control baseline</td>
<td>1.62 (0.22)</td>
<td>1.02 (0.25)</td>
<td>1.61 (0.3)</td>
<td>1.51 (0.57)</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>CFB control</td>
<td>-0.07 (0.02)</td>
<td>0.23 (0.01)</td>
<td>-0.41 (0.02)</td>
<td>0.08 (0.03)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pairwise $P$ for change</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>UF baseline</td>
<td>1.69 (0.17)</td>
<td>1.92 (0.26)</td>
<td>1.55 (0.21)</td>
<td>1.15 (0.18)</td>
<td>0.06</td>
</tr>
<tr>
<td>UF CFB</td>
<td>0.57 (0.01)</td>
<td>-0.18 (0.03)</td>
<td>-0.76 (0.03)</td>
<td>0.54 (0.02)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pairwise $P$ for change</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>CFB UF - CFB control</td>
<td>0.64 (0.02)</td>
<td>-0.41 (0.03)</td>
<td>-0.35 (0.03)</td>
<td>0.46 (0.04)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>$P$ for $\Delta - \Delta$</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
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</tr>
</tbody>
</table>

Data show the quartiles of weight change (Q1 through Q4) from baseline to 8 weeks. Q4 experience the greatest reduction in weight. CFB indicates change from baseline; UF, ultrafiltration.

Figure 3. Weight loss and baseline RPV slope are both important in modulating the change from baseline (CFB) in RPV slopes. Low weight loss represents weight loss of $<0.3$ kg from baseline to the end of trial. Flat slopes represent slopes flatter than 1.33% per hour. A significant interaction effect was seen between baseline RPV slope and weight loss, suggesting that the effect of these 2 factors is multiplicative on subsequent change in RPV slopes. Error bars represent the SEMs. The row just above the x axis represents the number of individuals in that group.

Figure 4. Assessment of Dry Weight 309
responsive to probing dry weight (Figure 1); patients who have dry weight probed (ultrafiltration group) have steepening of slopes. Second, when dry weight is probed, RPV slopes predict the magnitude of weight change (Figure 2). Third, baseline RPV slopes reflect volume status. Flat RPV slopes suggest a volume-overloaded state; probing dry weight in these patients leads to subsequent steeper slopes (Table 2). In contrast, steepening of RPV slopes occurs less often in those who have steeper RPV slopes at baseline (Table S1). Fourth, both baseline RPV slopes and the intensity of weight loss are important for subsequent changes in RPV slopes (Table S2 and Figure 3). For example, patients with flatter slopes and above-median weight loss steepen their RPV slopes. This steepening of RPV slopes depends on probing dry weight (assignment to ultrafiltration group); the steepening of RPV slopes is much less in those who do not have dry weight probed (the control group). Fifth, RPV slopes predict the subsequent reduction in interdialytic ambulatory systolic BP; those with the flattest slopes had the greatest decline in BP on probing dry weight. Thus, flat slopes identify volume-responsive hypertension. Sixth, both baseline RPV slopes and the change in RPV slopes are important for subsequent changes in ambulatory systolic BP (Figure 4). Seventh, baseline RPV predicts the time to onset of intradialytic cramps and the need to stop ultrafiltration and administer saline boluses.

Currently, the change over time in postdialysis weight is taken as a marker of volume reduction. We found that greater weight loss is associated with a greater steepening of slope, regardless of randomization. However, weight loss alone was insufficient to explain changes in RPV slopes evoked by probing dry weight. This supports the notion that postdialysis weight alone is a poor proxy of dry weight. Dry weight can be better estimated with RPV slope monitoring. This is so because those with the flattest RPV slopes experienced the greatest steepening of slopes on probing dry weight. More importantly, those with the flattest RPV slopes who had the greatest steepening of slopes also experienced the greatest declines in 44-hour systolic ambulatory BP on probing dry weight. Furthermore, those with the steepest slopes had more symptoms and interventions on probing dry weight.

Although the changes in RPV slopes are related to the magnitude of weight loss, the relationship between weight loss and RPV slope is inconsistent (Figure 3 and Table 2). Changes in postdialysis weight accounted for some changes in RPV slopes but were not sufficient to account for all of the changes. Some possibilities for the lack of relationship between postdialysis weight change and change in RPV slopes may be as follows. First, postdialysis weight may not reflect the true change in ultrafiltration volume during dialysis, because often patients eat and drink during dialysis. Second, postdialysis weight changes may not be accurately capture alteration in body composition and, therefore, fluid-volume compartments over 8 weeks of the study.

Our results support the observations of Lopot et al., who were among the first to suggest that RPV monitoring may be valuable in the assessment of dry weight. They reported that RPV monitor-guided reduction in dry weight reduced echocardiographic inferior vena cava diameter among patients who were found to be volume overloaded. Similarly, Rodriguez et al. reported in a cohort study of 28 patients that RPV monitoring led to changes in dry weight in all of the patients. Steuer et al. reported that 18% of the patients in a dialysis unit had <5% reduction in relative blood volume. Over 6 weeks, they reduced the weight by an average of 0.8 kg, which resulted in a larger decrease in relative blood volume with a low incidence of symptoms. The median RPV slope in our study was 1.33% per hour, which, over 4 hours, would lead to a reduction in RPV of a magnitude similar to that reported by Steuer et al. Thus, nearly half of the patients in our study were volume overloaded by the definition from Steuer et al., probably because we studied only those patients who were hypertensive. The mean weight loss over 8 weeks in our study was 1 kg, also similar to Steuer et al. We also found steepening of RPV slope when fluid was removed, similar to their study. Our data also support the work of Dasselaar et al., who evaluated the role of blood volume tracking compared with standard therapy in the management of hypertension in hemodialysis patients by reducing dry weight. They reported that among 14 patents randomized to blood volume tracking-guided dry weight reduction, predialysis BP was reduced by 22.5/8.3 mm Hg; extracellular fluid water and cardiothoracic ratio was also reduced. Among pediatric hemodialysis patients, RPV monitoring has been used to guide dry-weight reduction; this results in lower interdialytic ambulatory BP and reduces the rate of hospitalizations. Our data also confirm the observations of Zellweger et al., who demonstrated that dry-weight reduction is more likely when relative blood volume changes are lower. Taken together, these data support the notion that therapy guided by RPV slope may serve as a valid tool to
assess volume and prescribe augmented volume reduction therapy among hemodialysis patients.

Our study has some limitations. We conducted RPV monitoring only once at baseline and once at the end of the trial. Multiple recordings may have improved the precision of RPV slopes for individual patients. Although the analysis of RPV monitoring was prespecified, patients were not randomized on the basis of RPV. Thus, a cause-and-effect relationship between RPV slopes and subsequent improvement in interdialytic ambulatory BP may be premature. Finally, there were few nonblack patients in our study. Whether the results of our study are generalizable to nonblack patients will need to be demonstrated in future trials.

Perspectives
The assessment of dry weight in patients on long-term hemodialysis has been a long-term challenge. Our study provides a simple and a widely available tool that can aid the evaluation of dry weight. RPV slopes derived by this measurement can predict the success of subsequent weight loss and improvement in BP. Periodic monitoring of RPV may assist in the management of dry weight and control of hypertension among long-term hemodialysis patients. The median RPV slope at baseline seen in our study was 1.33% per hour. Patients with flatter RPV slopes may, thus, be volume overloaded. Although RPV slope may serve as a marker of volume, its utility needs to be confirmed in clinical trials.

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Disclosures
None.

References
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Relative plasma volume monitoring during hemodialysis aids the assessment of dry-weight

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Statistical Methods

Relative Plasma Volume

In the mixed model, the random effects were subject and time elapsed. An unstructured covariance matrix allowed the slopes and intercepts to vary independently of each other and maximal likelihood estimation was obtained. The visits were also modeled as random effects to account for the study participation effect. Since the RPV was log transformed, the coefficients on the slope terms in this model were converted back to percent change in RPV per hour by using the following formula: \(100 \times (1 - \exp(\beta))\) where \(\beta\) is the coefficient on the reading time.

Most dialysis patients have measurement of volume through sequential changes in post-dialysis weight. The change from baseline to final visit in post-dialysis weight was calculated for each patient. To ascertain the effect of change from baseline in weight over 8 weeks on the RPV slopes we incorporated the change in weight from baseline in the above statistical model. We did so by forming this change from baseline in weight into quartiles. Whether the patient was in the control group or ultrafiltration group, each patient was classified into quartiles of body-weight change. We then tested the significance of quartiles on relative plasma volume slopes. If body weight change was the sole mediator of changes in RPV slopes, we reasoned that adjustment for quartiles of change in body weight will remove the relationship between RPV slope and probing dry-weight.

We next tested the effect of RPV slopes at baseline on subsequent change in RPV slopes. RPV slopes at baseline were calculated for each patient by ordinary least squares regression and this value was used to generate quartiles from the steepest RPV slope (quartile 1) to flattest RPV slope (quartile 4). The effect of these quartiles was then tested in a mixed model with the dependent variable being the RPV slope.

To test the combined effect of baseline RPV slopes and subsequent weight loss on RPV slopes we first dichotomized the RPV slopes and weight loss above and below median. Those above the median had flatter RPV slopes and greater weight loss. To predict RPV slopes, we created a model that included all main effects up to four-way interaction between 4 independent factors: groups (control vs ultrafiltration), visits (baseline vs final), median RPV slope (steeper vs flatter), and median weight loss (less vs more). A mixed effects model was used to calculate the slopes. The random effect part of the equation was the one described earlier. To test the significance of the two factors, RPV slope and weight loss, we first created models without either of these factors and then a model with one of these factors. The model fit of the two nested models were evaluated using the likelihood ratio test. We similarly compared the 2 models with 3 factors (group, visits, and weight; or group, visits and RPV slopes) with a model with all 4 factors using the likelihood ratio test.

Relationship between Relative Plasma Volume and Ambulatory BP

Next we calculated the RPV slopes with ordinary least squares regression for each individual at baseline. These RPV slopes were divided into quartiles. These slope quartiles were used as independent variables to predict 44-hour interdialytic ambulatory systolic BP and changes in ambulatory systolic BP on probing dry-weight. Since RPV
monitoring was performed at baseline at 8 weeks, the corresponding ambulatory BP was used for these analyses. The changes in ambulatory BP were modeled using a mixed model. In this mixed model, ambulatory systolic BP was the dependent variable. Independent variables were the following: 1) indicator variables for group (ultrafiltration and control), visits (baseline and 8 weeks), and their interaction; and 2) interactions of these indicator variables with quartiles of RPV slope. The random effects were subjects and visits and an unstructured covariance matrix was used.

To explore the combined effect of baseline RPV slopes and change in RPV slopes on BP we dichotomized the RPV slopes at baseline about the median. We then calculated the RPV slopes at end of trial and dichotomized them about the median. We produced a 4 way interaction model with group, visits, baseline RPV slopes, and end of study RPV slopes as independent variables to predict 44-hour interdialytic ambulatory systolic BP.
Table S1: Relative plasma volume (RPV) slopes (%/hr) by quartiles of RPV at baseline.

<table>
<thead>
<tr>
<th>Group/Time</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Heterogeneity between quartiles (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Baseline</td>
<td>2.84 (0.16)</td>
<td>1.94 (0.27)</td>
<td>1.04 (0.16)</td>
<td>0.31 (0.15)</td>
<td>&lt;0.0001</td>
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<tr>
<td>CFB control</td>
<td>-0.54 (0.02)</td>
<td>0.01 (0.03)</td>
<td>-0.08 (0.01)</td>
<td>0.67 (0.02)</td>
<td>&lt;0.0001</td>
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<tr>
<td>pairwise p for change</td>
<td>&lt;0.0001</td>
<td>&gt;0.2</td>
<td>&lt;0.0001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>UF Baseline</td>
<td>2.99 (0.12)</td>
<td>1.69 (0.11)</td>
<td>0.98 (0.13)</td>
<td>0.2 (0.14)</td>
<td>&lt;0.0001</td>
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<tr>
<td>CFB UF</td>
<td>-0.17 (0.01)</td>
<td>0.13 (0.02)</td>
<td>0.2 (0.02)</td>
<td>1.19 (0.02)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>pairwise p for change</td>
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<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>CFB UF - CFB control</td>
<td>0.37 (0.02)</td>
<td>0.12 (0.03)</td>
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<td>0.52 (0.03)</td>
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<td>p for delta-delta</td>
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</table>

Q1-Q4 represent quartiles of RPV at baseline. Q1 represents the steepest RPV slope. CFB = change from baseline, UF = ultrafiltration, RPV = Relative plasma volume.
Table S2: 44 hour ambulatory systolic BP by quartiles of RPV at baseline.

<table>
<thead>
<tr>
<th>Group/Time</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Heterogeneity between quartiles (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Baseline</td>
<td>145.1 (2.8)</td>
<td>138.8 (4.5)</td>
<td>150.6 (2.6)</td>
<td>145.8 (2.5)</td>
<td>0.12</td>
</tr>
<tr>
<td>CFB control</td>
<td>-10.1 (4.8)</td>
<td>-10.5 (7.6)</td>
<td>-4 (4.1)</td>
<td>-9.7 (4.4)</td>
<td>&gt;0.20</td>
</tr>
<tr>
<td>pairwise p for change</td>
<td>0.017</td>
<td>0.082</td>
<td>0.16</td>
<td>0.013</td>
<td></td>
</tr>
<tr>
<td>UF Baseline</td>
<td>142.6 (2.1)</td>
<td>145.6 (1.8)</td>
<td>148.4 (2.2)</td>
<td>148.3 (2.2)</td>
<td>0.17</td>
</tr>
<tr>
<td>CFB UF</td>
<td>-9.6 (3.4)</td>
<td>-13.8 (3)</td>
<td>-15.1 (3.6)</td>
<td>-22.3 (3.8)</td>
<td>0.09</td>
</tr>
<tr>
<td>pairwise p for change</td>
<td>0.002</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>CFB UF- CFB control</td>
<td>0.5 (5.9)</td>
<td>-3.2 (8.1)</td>
<td>-11.1 (5.4)</td>
<td>-12.6 (5.8)</td>
<td>*</td>
</tr>
<tr>
<td>p for delta-delta</td>
<td>&gt;0.2</td>
<td>&gt;0.2</td>
<td>0.02</td>
<td>0.014</td>
<td></td>
</tr>
</tbody>
</table>

Q1-Q4 represent quartiles of RPV at baseline. Q1 represents the steepest RPV slope. CFB = change from baseline, UF = ultrafiltration, RPV = Relative plasma volume. * Test of linear trend <0.05 in combined control and UF groups.