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Relationship between volume status and blood pressure during chronic hemodialysis

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Background. The relationship between volume status and blood pressure (BP) in chronic hemodialysis (HD) patients remains incompletely understood. Specifically, the effect of interdialytic fluid accumulation (or intradialytic fluid removal) on BP is controversial.

Methods. We determined the association of the intradialytic decrease in body weight (as an indicator of interdialytic fluid gain) and the intradialytic decrease in plasma volume (as an indicator of postdialysis volume status) with predialysis and postdialysis BP in a cross-sectional analysis of a subset of patients ($N = 468$) from the Hemodialysis (HEMO) Study. Fifty-five percent of patients were female, 62% were black, 43% were diabetic and 72% were prescribed antihypertensive medications. Dry weight was defined as the postdialysis body weight below which the patient developed symptomatic hypotension or muscle cramps in the absence of edema. The intradialytic decrease in plasma volume was calculated from predialysis and postdialysis total plasma protein concentrations and was expressed as a percentage of the plasma volume at the beginning of HD.

Results. Predialysis systolic and diastolic BP values were 153.1 ± 24.7 (mean ± SD) and 81.7 ± 14.8 mm Hg, respectively; postdialysis systolic and diastolic BP values were 136.6 ± 22.7 and 73.9 ± 13.6 mm Hg, respectively. As a result of HD, body weight was reduced by 3.1 ± 1.3 kg and plasma volume was contracted by 10.1 ± 9.5%. Multiple linear regression analyses showed that each kg reduction in body weight during HD was associated with a 2.95 mm Hg ($P = 0.004$) and a 1.65 mm Hg (P = NS) higher predialysis and postdialysis systolic BP, respectively. In contrast, each 5% greater contraction of plasma volume during HD was associated with a 1.50 mm Hg ($P = 0.026$) and a 2.56 mm Hg ($P < 0.001$) lower predialysis and postdialysis systolic BP, respectively. The effects of intradialytic decreases in body weight and plasma volume were greater on systolic BP than on diastolic BP.

Conclusions. HD treatment generally reduces BP, and these reductions in BP are associated with intradialytic decreases in both body weight and plasma volume. The absolute predialysis and postdialysis BP levels are influenced differently by acute intradialytic decreases in body weight and acute intradialytic decreases in plasma volume; these parameters provide different information regarding volume status and may be dissociated from each other. Therefore, evaluation of volume status in chronic HD patients requires, at minimum, assessments of both interdialytic fluid accumulation (or the intradialytic decrease in body weight) and postdialysis volume overload.

Key words: body weight, dry weight, fluid removal, hypertension, plasma volume, postdialysis volume overload.

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Hypertension is common in chronic hemodialysis patients and likely contributes to the excess morbidity and mortality in these patients [1–7]. Although the causes of hypertension are multifactorial, the importance of volume status on blood pressure in hemodialysis patients has long been recognized [8, 9]. To assess the effect of volume status on blood pressure, several previous studies have examined the effect of interdialytic weight gain or intradialytic reduction in body weight on blood pressure; however, the results from these studies are conflicting [10–18]. While all of these previous studies have used either interdialytic weight gain or intradialytic decreases in body weight alone to evaluate volume status, this approach does not assess postdialysis volume status. Thus, the studies assume that all patients are normovolemic at the end of the hemodialysis treatment. Others have examined the diameter of the inferior vena cava [19], total body water volume [20, 21] or extracellular fluid volume [22] at the end of hemodialysis as measures of postdialysis volume status and showed that blood pressure also can be influenced significantly by these parameters. However, those measures of postdialysis volume status are not used routinely in clinical practice, since they require special techniques and their target normovolemic values have high interpatient variability.

Lopot et al have recently suggested that the lack of a decrease in blood volume during hemodialysis treatment could be used to detect postdialysis volume overload [23]. This approach is practical since the intradialytic decrease in blood or plasma volume can be routinely assessed in chronic hemodialysis patients [24]. Lopot et al hypothesized that patients with small intradialytic decreases in blood volume are overhydrated since they have rapid plasma refilling rates [25]. In the current study, intradialytic decreases in body weight were used to assess interdialytic weight gain and provide an estimate of the degree of predialysis fluid overload, while intradialytic decreases in plasma volume were used to provide an estimate of the degree of postdialysis volume overload. The associations between these volume parameters and blood pressure of chronic hemodialysis patients were examined.

METHODS

Patients and dialysis prescriptions

The background, rationale and design of the Hemodialysis (HEMO) Study have been previously described in detail [26]. Briefly, the HEMO Study is a prospective, multicenter clinical trial using a 2×2 factorial design to evaluate the importance of the delivered dose of dialysis and dialysis membrane flux (equated with membrane permeability to β_2-microglobulin) in reducing the mortality and morbidity of chronic hemodialysis patients. Considerable effort was made to include patients with comorbid conditions similar to those of the chronic hemodialysis population in the United States. Patients were excluded from randomization into the HEMO Study if they had residual renal clearance of urea greater than 1.5 mL/min/35 L of urea distribution volume. Eligible patients were randomized into four different treatment groups that differed in the dialysis dose (either a target equilibrated urea Kt/V of 1.05 or 1.45) and the type of hemodialysis membrane (either low flux or high flux). The blood flow rate, dialysate flow rate, dialyzer model and treatment time were tailored to individual patients to achieve the target equilibrated urea Kt/V. Although the nephrologists were encouraged to achieve the target dose within the shortest possible time, it was necessary in some cases to lengthen the treatment time in order to remove the interdialytic fluid gain from individual patients. The minimum acceptable treatment time was 2.5 hours per session. Written, informed consent was obtained from each patient prior to entry into the study.

The choice of dialyzer model was limited to those with in vitro urea mass transfer-area coefficients greater than 500 mL/min at a dialysate flow rate of 500 mL/min [27], and dialyzer reuse was initially permitted for a maximum of 20 times. Subsequent limitations to the number of times a dialyzer could be reused were based on observations of dialyzer clearances of β_2-microglobulin during the study [28]. Other aspects of the treatment, including the dry weight prescription and dialysate sodium concentration, were prescribed by the primary nephrologist without regard to the dialysis dose or the type of dialysis membrane. Dry weight was defined as the postdialysis body weight below which the patient developed symptomatic hypotension or muscle cramps in the absence of edema. All dialysis machines used in this study were governed by volumetric control.

Data collection

Data for this report were collected prospectively during one treatment session four months after each patient had been randomized to a particular treatment group for the validation of dialyzer clearances for urea and β_2-microglobulin. This study session could be either the first, second or third session of the week. In the current analyses of these data, all patients were grouped together, independent of their randomized treatment group, dialyzer model, the number of times the dialyzer had been reused, blood flow rate, dialysate flow rate, dialysate sodium concentration or treatment time. Predialysis and postdialysis body weights were measured using a scale, and predialysis and postdialysis systolic and diastolic blood pressures were measured using a sphygmomanometer with the patient in a sitting position. A predialysis blood sample was taken directly from the vascular access, and a postdialysis blood sample was collected from the arterial blood tubing 20 seconds after completing the treatment and reducing the blood pump speed to less than or equal to 80 mL/min. Blood samples were centrifuged 30 to 90 minutes after collection, and the plasma was shipped to a central laboratory (Spectra East, Rockleigh, NJ, USA) for determination of total protein concentration using an automated assay based on the biuret reaction (Hitachi 747, Indianapolis, IN, USA). The intra-assay coefficient of variation for this assay is 0.6% at a mean concentration of 4.4 mg/dL, and the interassay coefficient of variation is 0.95% at a mean concentration of 6.4 mg/dL. All clinical and laboratory data were transmitted to a central Data Coordinating Center (Department of Biostatistics and Epidemiology, The Cleveland Clinic Foundation, Cleveland, OH, USA) for statistical analyses.

Calculations

The intradialytic decrease in body weight was calculated as the predialysis body weight minus the postdialysis body weight. Mean arterial blood pressure was calculated as the diastolic pressure plus one-third of the pulse pressure (the systolic blood pressure minus the diastolic blood pressure). The intradialytic change in blood pres-

Table 1. Patient characteristics ($N = 468$)

Parameter *units*	Mean ± SD
Demographics	
Age *years*	58 ± 14
Gender *% female*	55
Race *% black*	62
Diabetic status *% diabetic*	43
Medications[a]	
Prescribed any antihypertensive medication *% of patients*	72
Prescribed ACE inhibitors *% of patients*	24
Prescribed beta blockers *% of patients*	21
Prescribed calcium channel blockers *% of patients*	48
Prescribed alpha inhibitors *% of patients*	5
Prescribed other antihypertensive medications *% of patients*	20

[a] Patients may be prescribed more than one antihypertensive medication

sure readings was defined as the postdialysis minus the predialysis value. The intradialytic decrease in plasma volume (ΔPV) was calculated as a fraction of the predialysis value by the following equation:

$$\Delta PV = (PV_{pre} - PV_{post})/PV_{pre} = (TP_{post} - TP_{pre})/TP_{post}$$

where TP denotes the total plasma protein concentration and the subscripts pre and post denote predialysis and postdialysis values, respectively. This equation was derived using the assumption that there was no loss of protein from the vascular compartment and that the plasma compartment behaves as a well-mixed single pool during the hemodialysis treatment (that is, $PV_{pre} \times TP_{pre} = PV_{post} \times TP_{post}$). These analyses do not take into account the possibility that the lowest blood pressure reading or the largest ΔPV value may have occurred in the middle of the hemodialysis treatment.

Statistics

Blood pressures were analyzed as a function of the intradialytic decrease in body weight and the intradialytic decrease in plasma volume using both simple linear regression [29] and multiple regression [30] analyses. Simple linear regression analysis was used to individually relate the blood pressure indices to intradialytic decreases in body weight or plasma volume, without adjustment for other factors. Multiple regression analysis was used to jointly relate the blood pressure indices to both the decrease in body weight and the decrease in plasma volume while controlling for the following potential confounding factors: age, race, gender, and diabetic status. Previous work has shown the each of these factors influence blood pressure in hemodialysis patients [17, 18]. Probability (P) values less than 0.050 were considered significant.

RESULTS

A summary of the demographic characteristics of the patients studied is shown in Table 1, and their measured blood pressures and volume parameters are shown in Table 2. There was a slight predominance of females, a majority of black patients and a substantial fraction of diabetic patients. These demographic characteristics are similar to those of the current end-stage renal disease population in the United States [31], except for the large percentage of black patients that reflects the population served by many of the clinical centers in the HEMO Study [26]. The mean intradialytic decrease in body weight was slightly larger than those reported in most other studies. Figure 1 shows the frequency distribution of the intradialytic decrease in body weight and the intradialytic decrease in plasma volume. There was a wide range of values observed for both volume parameters. The mean intradialytic decrease in plasma volume was approximately 10% and represents the only reported data to date of this parameter in a large sample of chronic hemodialysis patients. The distribution of predialysis and postdialysis systolic and diastolic blood pressure is shown in Figure 2.

Table 2. Blood pressures and volume parameters ($N = 468$)

Parameter *units*	Mean ± SD
Blood pressures	
Predialysis systolic *mm Hg*	153.1 ± 24.7
Predialysis diastolic *mm Hg*	81.7 ± 14.8
Post-dialysis systolic *mm Hg*	136.6 ± 22.7
Post-dialysis diastolic *mm Hg*	73.9 ± 13.6
Volume parameters	
Predialysis body weight *kg*	72.9 ± 16.6
Post-dialysis body weight *kg*	69.8 ± 16.2
Intradialytic decrease in body weight *kg*	3.1 ± 1.3
Intradialytic decrease in plasma volume (ΔPV) *%*	10.1 ± 9.5

Intradialytic changes in systolic blood pressure were associated with intradialytic decreases in both body weight ($P = 0.012$) and plasma volume ($P = 0.011$) in simple linear regression analyses. Larger decreases in body weight (Fig. 3A) and larger decreases in plasma volume (Fig. 3B) were associated with larger intradialytic decreases in systolic blood pressure. The associations of intradialytic changes in mean arterial blood pressure and diastolic blood pressure with intradialytic decreases in body weight and plasma volume were not statistically significant. In multiple linear regression analyses including both intradialytic decreases in body weight and plasma volume as predictor variables, neither factor was significantly associated with intradialytic changes in systolic blood pressure. This may in part be explained by a relatively high correlation of decrease in body weight with decrease in plasma volume ($r = 0.414$, $P < 0.001$), making it difficult to distinguish independent effects of these factors in multiple regression analysis.

Higher values of predialysis systolic ($P = 0.008$, Fig. 4), diastolic ($P = 0.032$) and mean arterial blood pressure ($P = 0.009$) were all associated with larger intradialytic

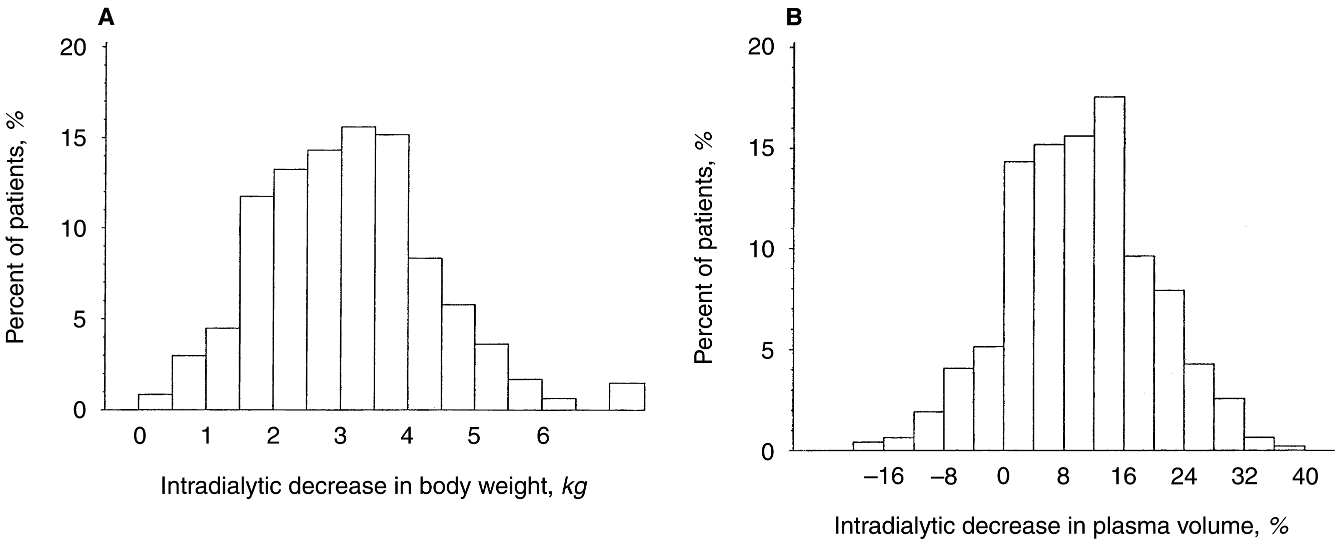

Fig. 1. Frequency distribution of (*A*) intradialytic decreases in body weight and (*B*) intradialytic decreases in plasma volume. $N = 468$; in A, mean = 3.1 and SD = 1.3; in B, mean = 10.1 and SD = 9.5.

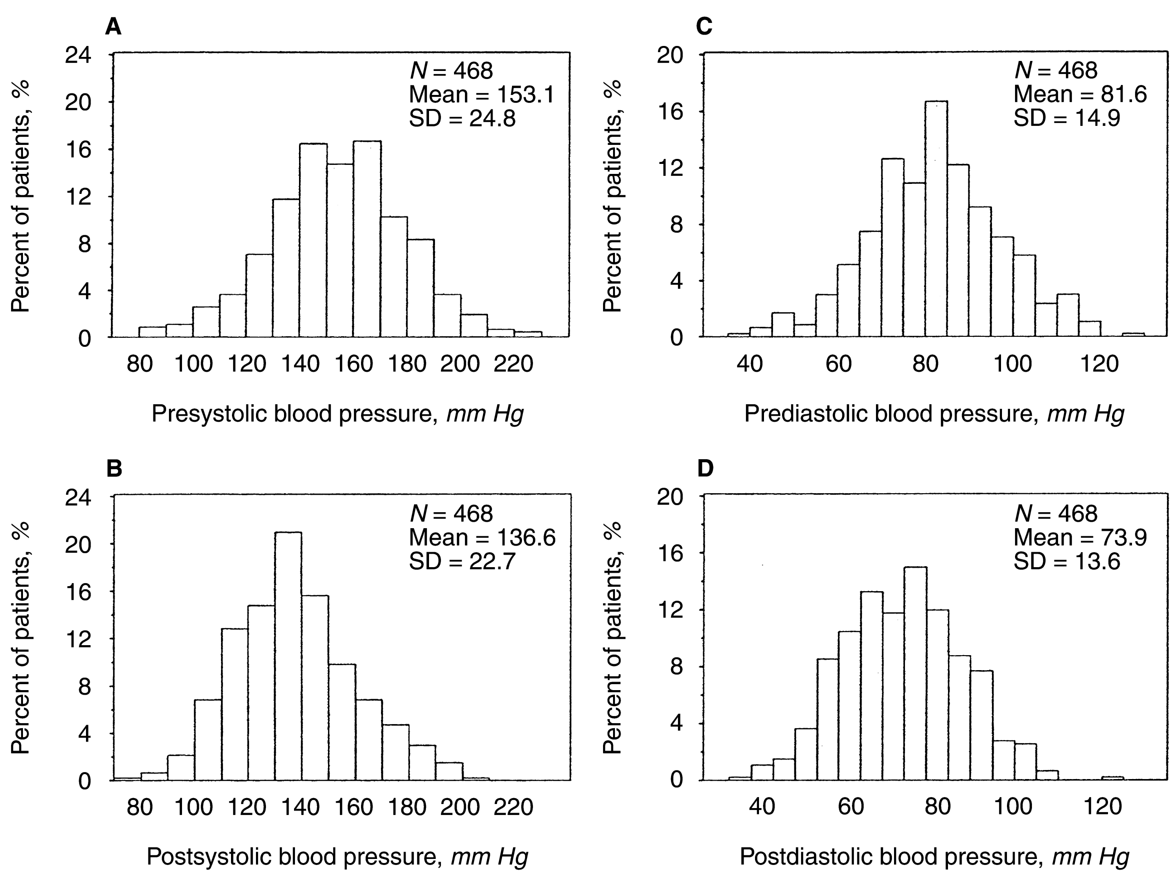

Fig. 2. Frequency distribution of predialysis systolic blood pressure (*A*), postdialysis systolic blood pressure (*B*), predialysis diastolic blood pressure (*C*) and postdialysis diastolic blood pressure (*D*).

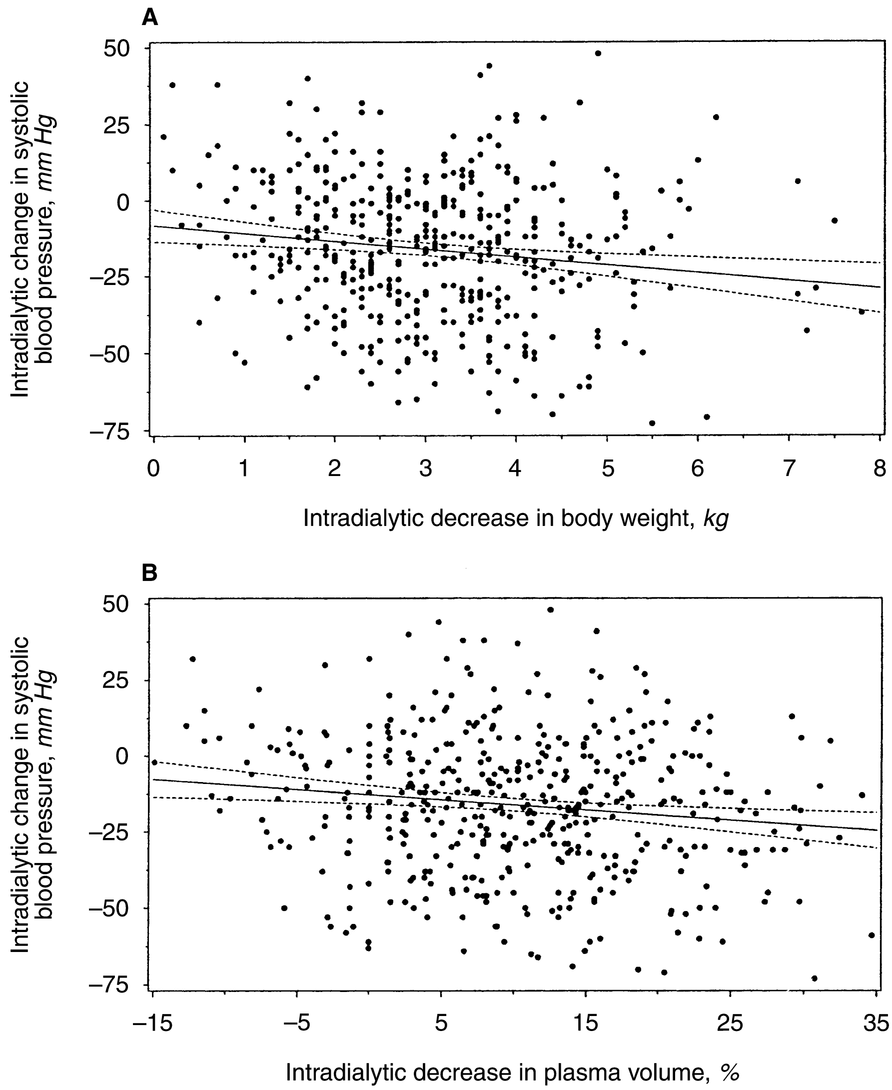

Fig. 3. Relationship between the intradialytic changes in systolic blood pressure and (*A*) the intradialytic decrease in body weight or (*B*) the intradialytic decrease in plasma volume. The simple linear regression coefficients (or slopes) of these relationships were: (A) −2.10 ± 0.83 (standard error) mm Hg/kg and (B) −2.94 ± 0.12 (standard error) mm Hg/%, respectively.

decreases in body weight (a measure of interdialytic fluid gain) in simple linear regression analyses. In contrast, none of the predialysis blood pressures was significantly associated with intradialytic decreases in plasma volume in simple linear regression analyses. When considered in multiple linear regression analyses, however, predialysis blood pressures were associated with intradialytic decreases in both body weight and plasma volume (Table 3). Note that the regression coefficients describing the influence of intradialytic decreases in body weight and plasma volume differ in sign, that is, higher predialysis systolic and diastolic blood pressures were associated with larger intradialytic decreases in body weight but smaller intradialytic decreases in plasma volume. In particular, the regression coefficients in the first row of Table 3 indicate that controlling for the decrease in plasma volume and the other covariates, a 1 kg greater decrease in body weight was associated with a 2.95 ± 1.01 mm Hg higher predialysis systolic blood pressure. On the other hand, after controlling for the decrease in body weight and the other covariates, a 5% greater decrease in plasma volume was associated with a 1.50 ± 0.67 lower predialysis systolic blood pressure. Figure 5 illustrates the magnitude of the effect of intradialytic decreases in body weight on predialysis systolic blood pressure in a multiple linear regression analysis that adjusts for different values of the intradialytic decrease in plasma volume and for patient age, race, gender and diabetic status. There were substantial differences in predialysis systolic blood pressure between patients with large reductions in body weight (greater than 4 kg) and those with small reductions (less than 2 kg).

Figure 6 shows the relationship between postdialysis systolic blood pressure and intradialytic decreases in plasma volume. Lower values of postdialysis systolic ($P < 0.001$) and mean arterial ($P = 0.015$), but not

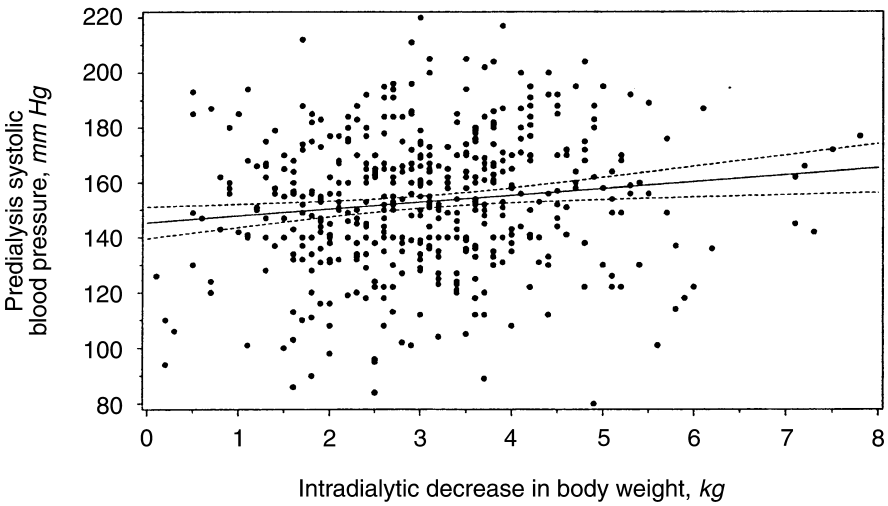

Fig. 4. Relationship between predialysis systolic blood pressure and the intradialytic decrease in body weight as determined by simple linear regression analysis. The slope was 2.32 ± 0.87 (standard error) mm Hg/kg.

Table 3. Regression coefficients or slopes (±standard errors) from multivariate regression analyses of predialysis blood pressure on the predictor variables, intradialytic decrease in body weight (ΔBW) and the intradialytic decrease in plasma volume (ΔPV)

Predialysis blood pressure *mm Hg*	r^2	Predictor variables	
		Per kg ΔBW	Per 5% ΔPV
Systolic	0.032	2.95 ± 1.01	−1.50 ± 0.67
P value		0.004	0.026
Diastolic	0.133	0.77 ± 0.57	−0.86 ± 0.38
P value		NS	0.025

All regression coefficients were corrected for patient age, race, gender and diabetic status. The *P* values indicate the significance of the independent variable to the model, and r^2 indicates the squared multiple correlation for the full regression models including ΔBW, ΔPV, age, race, gender and diabetic status.

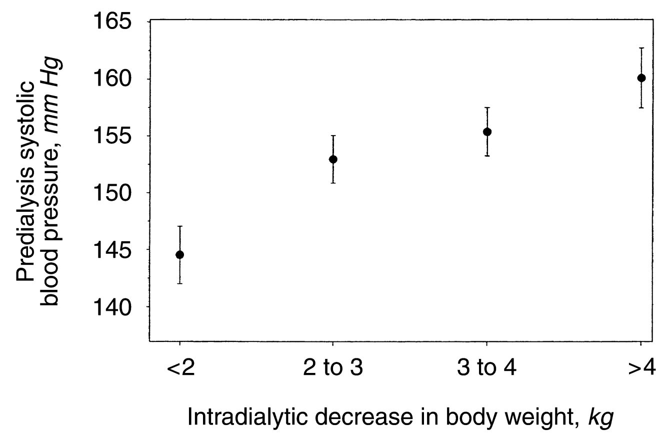

Fig. 5. Calculated values of predialysis systolic blood pressure (mean ± SE) adjusted for differences in the intradialytic decrease in plasma volume (and patient age, race, gender and diabetic status) plotted versus the intradialytic decrease in body weight. The range of the independent variable was divided into approximately four equal quartiles.

diastolic, blood pressure were associated with larger intradialytic decreases in plasma volume in simple linear regression analyses. In simple linear regression analyses, none of the postdialysis blood pressures was significantly associated with intradialytic decreases in body weight. When considered in multiple linear regression analyses, however, postdialysis blood pressures were associated with intradialytic decreases in both body weight and plasma volume (Table 4). Note again that the regression coefficients describing the influence of intradialytic decreases in body weight and plasma volume differ in sign, that is, higher postdialysis systolic blood pressures were associated with larger intradialytic decreases in body weight but smaller intradialytic decreases in plasma volume. Figure 7 illustrates the magnitude of the effect of intradialytic decreases in plasma volume on postdialysis systolic blood pressure in a multiple linear regression analysis that adjusts for different values of the intradialytic decrease in body weight and for patient age, race, gender and diabetic status. Differences were observed in postdialysis systolic blood pressure between patients with large contractions in plasma volume (greater than 16%) and those with small contractions (less than 4%).

DISCUSSION

The present study shows that differences in blood pressure among chronic hemodialysis patients partially reflect differences in volume status. The squared multiple correlations (r^2) for the multiple regression models were relatively low, signifying that variables other than intradialytic decreases in body weight and plasma volume as well as patient age, race, gender and diabetic status also must influence blood pressure [32–34]. Nevertheless, the magnitude of the regression coefficients suggests that the clinical effects of these variables on blood pressure are not insignificant. For example, the multiple regression models indicate that each kg reduction in body weight

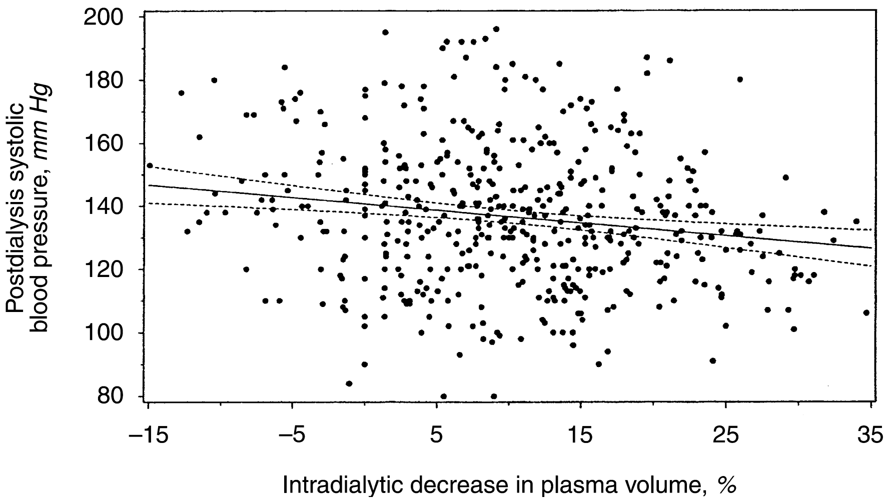

Fig. 6. Relationship between postdialysis systolic blood pressure and the intradialytic decrease in plasma volume as determined by simple linear regression analysis. The slope was −0.40 ± 0.11 (SE) mm Hg/%.

Table 4. Regression coefficients or slopes (±standard errors) from multivariate regression analyses of post-dialysis blood pressure on the predictor variables, intradialytic decrease in body weight (ΔBW) and the intradialytic decrease in plasma volume (ΔPV)

Postdialysis blood pressure *mm Hg*	r^2	Predictor variables	
		Per kg ΔBW	Per 5% ΔPV
Systolic	0.044	1.65 ± 0.91	−2.56 ± 0.61
P value		NS	<0.001
Diastolic	0.116	0.74 ± 0.53	−1.12 ± 0.35
P value		NS	0.002

All regression coefficients were corrected for patient age, race, gender and diabetic status. The *P* values indicate the significance of the independent variable to the model, and r^2 indicates the squared multiple correlation for the full regression models including ΔBW, ΔPV, age, race, gender and diabetic status.

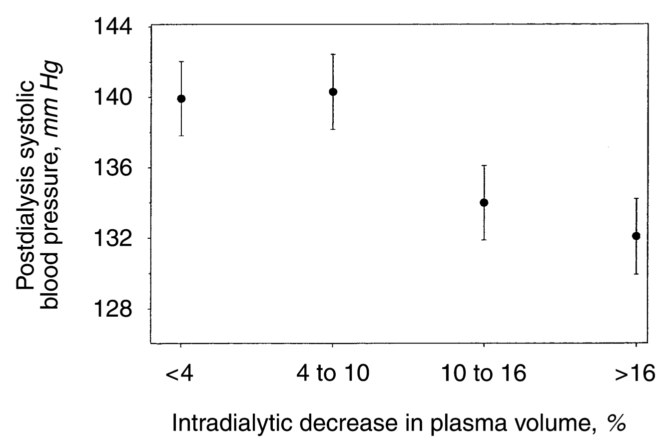

Fig. 7. Calculated values of postdialysis systolic blood pressure (mean ± SE) adjusted for differences in the intradialytic decrease in body weight (and patient age, race, gender and diabetic status) plotted versus the intradialytic decrease in plasma volume. The range of the independent variable was divided into approximately four equal quartiles.

during hemodialysis was associated with a 2.95 ± 1.01 mm Hg and a 1.65 ± 0.91 mm Hg higher predialysis and postdialysis systolic blood pressure, respectively, and each 5% greater contraction of plasma volume during hemodialysis was associated with a 1.50 ± 0.67 mm Hg and a 2.56 ± 0.61 mm Hg lower predialysis and postdialysis systolic blood pressure, respectively. Such associations were largely observed in systolic blood pressures; they were largely absent in diastolic and mean arterial blood pressures. The relatively weak association between diastolic blood pressure and volume status may be real, or it may be due to the relative difficulty in accurately measuring diastolic blood pressure [35]. Thus, in this study large intradialytic decreases in systolic blood pressure were associated with large intradialytic decreases in both body weight and plasma volume. High predialysis blood pressure was primarily associated with large reductions in body weight, whereas high postdialysis blood pressure was largely associated with small intradialytic decreases in plasma volume. It is noteworthy that the impact of volume status was significant on both predialysis and postdialysis systolic blood pressures, those that have been strongly associated with both mortality [5, 6] and cardiovascular morbidity [4] in chronic hemodialysis patients.

Effect of volume status on intradialytic changes in blood pressure

It has long been recognized that blood pressure usually falls during hemodialysis with fluid removal; the decrease in blood pressure is greater with larger amounts of fluid removed and with higher ultrafiltration rates [36]. The importance of volume status on blood pressure in chronic hemodialysis patients has recently been questioned in several reports showing that intradialytic changes in blood pressure are independent of either the interdialytic weight gain or the intradialytic reduction in body weight [10, 12, 15, 37]. These studies were limited to small patient samples, and these investigators analyzed intradialytic changes in blood pressure in patients with small differences in interdialytic weight gains. Others, however, have reported a significant positive correlation between intradialytic decreases in blood pressure and either the interdialytic weight gain or the ultrafiltration rate during hemodialysis treatment [11, 14, 17, 18]. The magnitude of the effect of fluid removal on intradialytic changes in blood pressure observed in the current study was similar to that observed in these studies; however, it comprised a large sample of patients with a wide range of intradialytic decreases in body weight. Lins et al suggested that the intradialytic decrease in plasma volume was a better predictor of the intradialytic decrease in systolic blood pressure than the intradialytic decrease in body weight [10]. While our results confirm that intradialytic decreases in plasma volume are associated with intradialytic decreases in systolic blood pressure, we could not demonstrate that intradialytic decreases in plasma volume were a better predictor than those in body weight.

Effect of intradialytic decreases in body weight on predialysis and postdialysis blood pressure

The importance of the intradialytic reduction in body weight or the interdialytic weight gain on predialysis blood pressure is also controversial. Sherman, Daniel and Cody reported only limited correlation between interdialytic weight gain and predialysis mean arterial pressure [11], but three recent cross-sectional analyses reported a significant association of predialysis blood pressure with intradialytic reduction in body weight or the ultrafiltration rate [14, 17, 18]. Our observations confirm the results from these latter studies and suggest that larger intradialytic decreases in body weight are associated with higher predialysis blood pressures.

Effect of intradialytic decreases in plasma volume on predialysis and postdialysis blood pressure

It has been assumed in many previous studies that clinical determination of dry weight is accurate; therefore, all patients were assumed to be normovolemic at the end of hemodialysis. The present analysis does not make any a priori assumptions regarding postdialysis volume overload, but assesses, albeit indirectly, this parameter by measuring intradialytic changes in plasma volume as proposed by Lopot et al [23]. Our analyses show that small intradialytic decreases in plasma volume are associated with both high predialysis and postdialysis blood pressures, consistent with the hypothesis that these patients have inappropriately high dry weight.

Others have recently proposed alternative methods of evaluating postdialysis volume status, such as the diameter of the inferior vena cava [19], the plasma concentration of atrial natriuretic peptide [38], extracellular volume assessed by multifrequency bioelectric impedance [22], or total body water volume assessed by single frequency bioelectric impedance [20, 21]. While these other volume parameters also may prove useful, intradialytic decreases in plasma or blood volume can be easily determined during routine hemodialysis [24]. Our results, as well as those of others [21], suggest that the effect of postdialysis volume overload has its primary effect on postdialysis, not predialysis, blood pressures.

Several methodological issues in the current study are worthy of discussion. First, all analyses were performed using the magnitude of the intradialytic decrease in body weight not normalized by patient size. We have performed similar analyses using this parameter normalized to body weight and arrived at identical conclusions (data not shown). Second, instead of the intradialytic reduction in body weight, interdialytic weight gain could be used to assess excess volume gained during the interdialytic interval. In the chronic hemodialysis patient who is at steady state and whose postdialysis body weight is relatively constant after each treatment, the intradialytic reduction in body weight is a good approximation to the interdialytic weight gain. Third, the interdialytic decrease in plasma volume was calculated assuming that there was no loss or gain of plasma proteins from the circulation during hemodialysis. This assumption has been challenged in certain studies [39, 40], but the errors incurred by using this approach are likely small and insignificant. Fourth, the regression coefficients calculated from the multiple linear regression analyses for both predialysis and postdialysis blood pressures show stronger volume-dependent relationships than the regression coefficients calculated from the simple linear regression analyses (compare the slope in the legend of Fig. 4 with the corresponding value in Table 3 and the slope in the legend of Fig. 5 with the corresponding value in Table 4). This comparison suggests that one potential reason for previous conflicting results regarding the effect of volume status on blood pressure in chronic hemodialysis patients is that both volume overload immediately postdialysis and during the interdialytic interval have not been evaluated simultaneously.

Several additional caveats from the analyses performed in this study should be noted. First, the current study was based on a large sample of chronic hemodialysis patients who had minimal residual renal function; thus, the association of blood pressure with volume parameters assessed in this study may be greater than that observed previously in patients with substantial renal function. Second, postdialysis blood pressures were measured soon after the completion of treatment, but blood pressure may rebound thereafter [41]. Prior reports on the correlation of immediate postdialysis blood pressures with volume status are conflicting [4, 42, 43]. Third, the current study only indirectly evaluated the volume of total body water, instead of extracellular volume. Others have emphasized that the volume of extracellular fluid is more important in determining blood pressure [44, 45]. Fourth, the analyses in this study have assumed that the relationships between blood pressures and intradialytic decreases in body weight are linear; however, recent work suggests that these relationships are likely nonlinear [18]. Nevertheless, we have performed additional multiple regression analyses using these nonlinear relationships and also have observed similar significant relationships between blood pressures and intradialytic decreases in plasma volume. Fifth, in this study we measured net changes in plasma volume from the beginning to the end of the hemodialysis treatment, but it is currently possible to measure intradialytic changes in blood or plasma volume continuously and in real time during hemodialysis using a variety of devices [24]. The use of such blood volume monitors may permit more effective fluid removal by altering treatment parameters (for example, ultrafiltration rate, dialysate sodium concentration and dialysate temperature) either manually or by using biofeedback-controlled devices. Sixth, we have assumed that interdialytic changes in plasma volume reflect only postdialysis volume overload as originally proposed by Lopot et al [23]. It is well known, however, that cardiac status alters the relationship between blood pressure and fluid removal during hemodialysis treatment [46, 47]. Indeed, recent work shows that blood pressure decreases more substantially in patients with cardiac failure than in those without cardiac failure for equivalent intradialytic decreases in plasma volume [48]. Last, our study did not specifically examine treatment time or dialysis dose on blood pressure. These parameters have been previously shown to be associated with blood pressure in hemodialysis patients [2, 5, 22]. Because of the design of the HEMO study, however, treatment time correlates with, and is therefore confounded by, equilibrated urea Kt/V values. Thus, it will not be possible to assess whether longer treatment time or higher urea Kt/V values independently influence blood pressure in this study.

In conclusion, this study shows that volume status influences both predialysis and postdialysis blood pressure. The intradialytic reduction in body weight (or interdialytic fluid gain) is helpful but insufficient to describe volume status and predict blood pressure in chronic hemodialysis patients. These observations further suggest that more rigorous methods of determining dry weight are needed. The recent call for prospective studies on the effect and treatment of hypertension in dialysis patients [49] must incorporate direct and extensive assessment of volume status into the protocols.

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REFERENCES

1. Fernández JM, Carbonell ME, Mazzuchi N, Petruccelli D: Simultaneous analysis of morbidity and mortality factors in chronic hemodialysis patients. *Kidney Int* 41:1029–1034, 1992
2. Charra B, Calemard E, Ruffet M, *et al*: Survival as an index of adequacy of dialysis. *Kidney Int* 41:1286–1291, 1992
3. Tomita J, Kimura G, Inoue T, *et al*: Role of systolic blood pressure in determining prognosis of hemodialyzed patients. *Am J Kidney Dis* 25:405–412, 1995
4. Conlon PJ, Walshe JJ, Heinle SK, *et al*: Predialysis systolic blood pressure correlates strongly with mean 24-hour systolic blood pressure and left ventricular mass in stable hemodialysis patients. *J Am Soc Nephrol* 7:2658–2663, 1996
5. Zager PG, Nikolic J, Brown RH, *et al*: "U" curve association of blood pressure and mortality in hemodialysis patients. *Kidney Int* 54:561–569, 1998
6. Port FK, Hulbert-Shearon TE, Wolfe RA, *et al*: Predialysis blood pressure and mortality risk in a national sample of maintenance hemodialysis patients. *Am J Kidney Dis* 33:507–517, 1999
7. Mazzuchi N, Carbonell E, Fernández-Cean J: Importance of blood pressure control in hemodialysis patient survival. *Kidney Int* 58:2147–2154, 2000
8. Hegstrom RM, Murray JS, Pendras JP, *et al*: Two year's experience with periodic hemodiaysis in the treatment of chronic uremia. *Trans Am Soc Artif Intern Organs* 8:266–280, 1962
9. Vertes V, Cangiano JL, Berman LB, Gould A: Hypertension in end-stage renal disease. *N Engl J Med* 280:978–981, 1969
10. Lins LE, Hedenborg G, Jacobson SH, *et al*: Blood pressure reduction during hemodialysis correlates to intradialytic changes in plasma volume. *Clin Nephrol* 37:308–313, 1992
11. Sherman RA, Daniel A, Cody RP: The effect of interdialytic weight gain on predialysis blood pressure. *Artif Organs* 17:770–774, 1993
12. Luik AJ, Gladziwa U, Kooman JP, *et al*: Influence of interdialytic weight gain on blood pressure in hemodialysis patients. *Blood Purif* 12:259–266, 1994
13. Coomer RW, Schulman G, Breyer JA, Shyr Y: Ambulatory blood pressure monitoring in dialysis patients and estimation of mean interdialytic blood pressure. *Am J Kidney Dis* 29:678–684, 1997
14. Ifudu O, Dawood M, Homel P, Friedman EA: Excess interdialytic weight gain provokes antihypertensive drug therapy in patients on maintenance hemodialysis. *Dial Transplant* 26:541–559, 1997
15. Luik AJ, van Kuijk WHM, Spek J, *et al*: Effects of hypervolemia on interdialytic hemodynamics and blood pressure control in hemodialysis patients. *Am J Kidney Dis* 30:466–474, 1997
16. Ventura JE, Spósito M: Volume sensitivity of blood pressure in end-stage renal disease. *Nephrol Dial Transplant* 12:485–491, 1997
17. Rahman M, Dixit A, Donley V, *et al*: Factors associated with inadequate blood pressure control in hypertensive hemodialysis patients. *Am J Kidney Dis* 33:498–506, 1999
18. Rocco MV, Yan G, Heyka RJ, *et al*: Risk factors for hypertension in chronic hemodialysis patients: Baseline data from the HEMO Study *Am J Nephrol* 21:280–288, 2001
19. Cheriex EC, Leunissen KML, Janssen JHA, *et al*: Echography of the inferior vena cava is a simple and reliable tool for estimation of 'dry weight' in haemodialysis patients. *Nephrol Dial Transplant* 4:563–568, 1989
20. Dionisio P, Valenti M, Bergia R, *et al*: Influence of the hydration

state on blood pressure values in a group of patients on regular maintenance hemodialysis. *Blood Purif* 15:25–33, 1997
21. Lins RL, Elseviers M, Rogiers P, *et al*: Importance of volume factors in dialysis related hypertension. *Clin Nephrol* 48:29–33, 1997
22. Katzarski KS, Charra B, Luik AJ, *et al*: Fluid state and blood pressure control in patients treated with long and short haemodialysis. *Nephrol Dial Transplant* 14:369–375, 1999
23. Lopot F, Kotyk P, Bláha J, Forejt J: Use of continuous blood volume monitoring to detect inadequately high dry weight. *Int J Artif Organs* 19:411–414, 1996
24. Leypoldt JK, Cheung AK: Evaluating volume status in hemodialysis patients. *Adv Renal Repl Ther* 5:64–74, 1998
25. Wizemann V, Leibinger A, Mueller K, Nilson A: Influence of hydration state on plasma volume changes during ultrafiltration. *Artif Organs* 19:416–419, 1995
26. Eknoyan G, Levey AS, Beck GJ, *et al*: The hemodialysis (HEMO) study: Rationale for selection of interventions. *Semin Dial* 9:24–33, 1996
27. Leypoldt JK, Cheung AK, Agodoa LY, *et al*: Hemodialyzer mass transfer-area coefficients for urea increase at high dialysate flow rates. *Kidney Int* 51:2013–2017, 1997
28. Cheung AK, Agodoa LY, Daugirdas JT, *et al*: Effects of hemodialyzer reuse on clearances of urea and β_2-microglobulin. *J Am Soc Nephrol* 10:117–127, 1999
29. Godfrey K: Simple linear regression in medical research, in *Medical Use of Statistics* (2nd ed), edited by Bailar JC III, Mosteller F, Boston, NEJM Books, 1992, pp 201–232
30. Tabachnick BG, Fidell LS: *Using Multivariate Statistics* (2nd ed). New York, Harper Collins, 1989
31. *U.S. Renal Data System: USRDS 1999 Annual Data Report*. Bethesda, The National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases, 1999
32. de Leeuw PW: Pathophysiology of hypertension in patients on renal replacement therapy. *Blood Purif* 12:245–251, 1994
33. Ritz E, Koomans HA: New insights into mechanisms of blood pressure regulation in patients with uraemia. *Nephrol Dial Transplant* 11(Suppl 2):52–59, 1996
34. Luik AJ, Charra B, Katzarski K, *et al*: Blood pressure control and hemodynamic changes in patients on long time dialysis treatment. *Blood Purif* 16:197–209, 1998
35. Kaplan NM: *Clinical Hypertension* (7th ed). Baltimore, Williams & Wilkins, 1998
36. Henderson LW: Symptomatic hypotension during hemodialysis. *Kidney Int* 17:571–576, 1980
37. Savage T, Fabbian F, Giles M, *et al*: Interdialytic weight gain and 48-h blood pressure in haemodialysis patients. *Nephrol Dial Transplant* 12:2308–2311, 1997
38. Fishbane S, Natke E, Maesaka JK: Role of volume overload in dialysis-refractory hypertension. *Am J Kidney Dis* 28:257–261, 1996
39. Kirschbaum B: Comparison of indirect methods to estimate plasma volume changes during hemodialysis. *Int J Artif Organs* 12:307–313, 1989
40. Schneditz D, Roob J, Oswald M, *et al*: Nature and rate of vascular refilling during hemodialysis and ultrafiltration. *Kidney Int* 42:1425–1433, 1992
41. Dolson GM, Ellis KJ, Bernardo MV, *et al*: Acute decreases in serum potassium augment blood pressure. *Am J Kidney Dis* 26:321–326, 1995
42. Kooman JP, Gladziwa U, Böcker G, *et al*: Blood pressure during the interdialytic period in haemodialysis patients: Estimation of representative blood pressure values. *Nephrol Dial Transplant* 7:917–923, 1992
43. Agarwal R: Role of home blood pressure monitoring in hemodialysis patients. *Am J Kidney Dis* 33:682–687, 1999
44. Guyton AC, Hall JE: *Textbook of Medical Physiology* (9th ed). Philadelphia, W.B. Saunders, 1996
45. Charra B, Bergström J, Scribner BH: Blood pressure control in dialysis patients: Importance of the lag phenomenon. *Am J Kidney Dis* 32:720–724, 1998
46. Ritz E, Rambausek M, Mall G, *et al*: Cardiac changes in uremia and their possible relation to cardiovascular instability on dialysis. *Contrib Nephrol* 78:221–229, 1990
47. Poldermans D, Man in't Veld AJ, Rambaldi R, *et al*: Cardiac evaluation in hypotension-prone and hypotension-resistant hemodialysis patients. *Kidney Int* 56:1905–1911, 1999
48. van der Sande FM, Mulder AW, Hoorntje SJ, *et al*: The hemodynamic effect of different ultrafiltration rates in patients with cardiac failure and patients without cardiac failure: Comparison between isolated ultrafiltration and ultrafiltration with dialysis. *Clin Nephrol* 50:301–308, 1998
49. Salem M: Hypertension in the hemodialysis population? High time for answers. *Am J Kidney Dis* 33:592–594, 1999