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Association of Predialysis Calculated Plasma Osmolarity With Intradialytic Blood Pressure Decline

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Abstract

Background—The rapid reduction in plasma osmolality during hemodialysis (HD) may induce temporary gradients that promote the movement of water from the extracellular to the intracellular compartment, predisposing to development of intra-dialytic hypotension (IDH).

Study Design—Observational cohort study.

Setting & Participants—The cohort comprises 3,142 prevalent patients receiving thrice-weekly HD from a single dialysis provider organization.

Predictor—Pre-dialysis calculated plasma osmolarity (calculated after the two-day interval as 2*serum sodium + serum urea nitrogen/2.8 + serum glucose/18).

Outcome—Magnitude of systolic blood pressure (SBP) decline (pre-dialysis SBP - nadir intra-dialytic SBP) and risk of IDH (SBP decline >35 or nadir SBP <90 mmHg).

Measurements—Unadjusted and multivariable adjusted generalized linear models were fit to estimate the association of calculated osmolarity with intra-dialytic SBP decline and the odds of developing IDH.

Results—The mean age of participants was 62.6 ± 15.2 (SD) years; 57.1% were male; 61.0% were diabetic. The mean pre-dialysis calculated osmolarity was 306.4 ± 9.5 mOsm/kg. After case-mix adjustment, each 10-mOsm/L increase in predialysis calculated osmolarity was associated

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with 1.48 (95% CI, 0.86–2.09) mm Hg (p<0.001) greater decline in intradialytic SBP and 10% greater odds of IDH (OR, 1.10; 95% CI, 1.05–1.15). In adjusted models, lower predialysis sodium, higher SUN and higher serum glucose were associated with greater decline in intra-dialytic SBP.

Limitations—Measured serum osmolality, timing of changes in intra-dialytic osmolality, dialysate osmolality and dialysate temperature were not available.

Conclusions—Higher pre-dialysis calculated osmolarity is associated with greater decline in intra-dialytic SBP and greater risk of IDH in long-term HD patients. Strategies to minimize rapid shifts in osmolality should be tested prospectively to minimize excess SBP decline in susceptible patients.

Keywords

intra-dialytic hypotension; osmolality; hemodialysis

Intra-dialytic hypotension (IDH)—defined as significant and abrupt decline in systolic blood pressure (SBP) during the hemodialysis (HD) procedure that causes symptoms and/or requires an intervention—is estimated to affect up to one third of outpatient HD sessions.[1–3] IDH events are associated with a greater incidence of myocardial stunning,[4] cerebral atrophy[5] and greater all-cause mortality.[6] The underlying pathogenesis of intra-dialytic SBP decline is likely to be multi-factorial, including the presence of autonomic neuropathy,[7] higher rates of ultrafiltration[8] and temporary changes in osmolality induced by the HD procedure itself.[9]

The mean pre-dialysis serum osmolality in HD patients is reported to range from 291–339 mOsm/kg, and may decline by up to 33 mOsm/kg during dialysis,[10–13] primarily due to changes in sodium (SNa), glucose, and urea (the three major constituents of serum osmolality). We previously reported that greater rates of decline in serum urea nitrogen (SUN) during HD are associated with a greater risk of developing IDH.[9] Previous studies have reported that the use of higher dialysate sodium (DNa)[14] and other hyperosmolar substances[15–16] may limit the development of transient osmotic gradients and thereby promote intra-dialytic hemodynamic stability.

We wished to determine the association of pre-dialysis calculated osmolarity with the magnitude of decline in intra-dialytic SBP. We hypothesized that higher pre-dialysis calculated osmolarity would be associated with greater intra-dialytic SBP decline.

Methods

Study Design and Population

The study protocol was deemed exempt by the Partners Healthcare Institutional Review Board. We performed a non-concurrent cohort study of prevalent patients receiving HD in Satellite Healthcare facilities in 2012. Patients became eligible for participation on the earliest date within this time period on which they were at least 18 years of age and had been receiving HD for greater than 180 days (n=3722). Those not on thrice weekly HD (n=291), those with session length >5 hours (n=23) and those without available variables to calculate the pre-dialysis calculated osmolarity (n=231) or intra-dialytic SBP decline (SBP readings

<40 or >240 mmHg or missing; n=18) were excluded. As the majority of laboratory values (97%) were measured on the first dialysis day of the week (i.e. Monday or Tuesday), we excluded patients with blood drawn on other days (n=17). The final cohort consisted of 3,142 individuals and 21,646 HD sessions.

Exposures and Outcomes

The primary exposure of interest was the calculated osmolarity, equal to (2*serum sodium) + (SUN/2.8) + (serum glucose/18). Secondary exposures of interest included pre-dialysis serum sodium, glucose and SUN (recorded from routine monthly blood draws). The primary outcome was the magnitude of intra-dialytic SBP decline, defined as the pre-dialysis SBP less the nadir intra-dialytic SBP. Routine blood pressures were measured every 30 minutes during dialysis; the median number of measurements per session was eight. The secondary outcome of interest was the development of intra-dialytic hypotension, defined as a decline in SBP >35 mmHg, or any intra-dialytic SBP <90 mmHg.

Study Data

Demographic data including sex, race, co-morbid conditions and age were recorded at baseline. Dialysis treatment and hemodynamic parameters were recorded at each individual HD session; only sessions with corresponding laboratory data were included in the analyses. Laboratory measurements were obtained prior to the first HD session of the week (after the two-day inter-dialytic interval) on a monthly basis and processed in a central laboratory. All patients were dialyzed against a dialysate glucose concentration of 100 mg/dL.[17] The DNa concentrations used in these treatments ranged from 126 to 148 mmol/L, including 16.1% that utilized sodium modeling algorithms.

Statistical Analysis

Continuous variables were examined graphically and recorded as means ± standard deviations for normally distributed data, or medians with inter-quartile ranges for non-normally distributed data. Comparisons were made using analysis of variance or Kruskal-Wallis tests as appropriate. Categorical variables were examined by frequency distribution, recorded as proportions and comparisons made using the χ^2 test.

Initially, unadjusted generalized linear regression models (using a normal distribution and identity link function) were fit to assess the association of calculated osmolarity with intra-dialytic SBP decline. Subsequently, in Model 1, adjustment was made for age, sex (male vs. female), race (black vs. non-black), diabetes, ischemic heart disease, congestive heart failure, access type (fistula, graft, catheter), pre-dialysis SBP and ultrafiltration rate (UFR in mL/kg/h). Model 2 was adjusted for the same variables as Model 1, in addition to pre-dialysis serum calcium, albumin, and bicarbonate. Subsequently, further models were fit, using a binomial distribution and logit link function, to determine the association of calculated osmolarity with the odds of developing intra-dialytic hypotension. As extreme hyperglycemia may influence the calculated osmolarity, sensitivity analyses were performed when excluding those with pre-dialysis glucose concentrations >132 mg/dL. In order to evaluate the individual components that contribute to the calculated osmolarity, secondary analyses were performed in the manner already described to determine the association of

pre-dialysis SNa, glucose and SUN with the magnitude of intra-dialytic SBP decline and odds of developing IDH. Finally, via the inclusion of cross-product terms, exploratory analyses were performed to assess for effect modification of the association of calculated osmolarity with SBP decline according to higher (>140 mmol/L or modeling) versus lower (≤140 mmol/L) DNa use and UFR, with sub-group analyses presented for lower and higher DNa use and tertiles of UFR.

Covariates for all models were selected on the basis of clinical and biological plausibility, without use of probabilistic selection criteria. Nominal two-sided p-values of <0.05 were considered statistically significant. Analyses were performed using Stata MP 13.1 (College Station, TX).

Results

Study Participants

The mean age of the patients was 62.6 ± 15.2 (standard deviation) years; 12.9% were black and 61.0% were diabetic. Individuals in the highest tertile of baseline calculated osmolarity tended to be younger and male and have higher pre-dialysis SNa, SUN, serum glucose and albumin, but lower pre-dialysis serum bicarbonate concentrations (Table 1). Those in the highest tertile of calculated osmolarity also tended to have higher pre-dialysis SBP, greater ultrafiltration volume and UFR, greater intra-dialytic SBP decline and greater frequency of IDH (Table 2). During a median follow up time of 5.3 months, the mean pre-dialysis calculated osmolarity was 306.4 ± 9.5 mOsm/kg.

Predialysis Calculated Osmolarity and Intradialytic SBP Decline

In unadjusted models, each 10-mOsm/L increment in the pre-dialysis calculated osmolarity was associated with a 2.22 (95% confidence interval [CI], 1.51–2.93) mm Hg greater decline in intra-dialytic SBP. In the fully adjusted model (Model 2), the association was attenuated, but remained statistically significant (1.48 [95% CI, 0.86–2.09] mm Hg), even after exclusion of patients with pre-dialysis serum glucose > 132 mg/dL (0.98 [95% CI, 0.23–1.70] mmHg [Table 3]). Effect estimates were qualitatively and quantitatively similar after individual additional adjustment for categories of blood flow, dialysate bicarbonate and dialysate calcium (data not shown). When analyzed in tertiles of calculated osmolarity, a monotonic association was apparent (Figure 1). Similar patterns of association were evident when IDH was considered as the outcome of interest (Table 3).

Predialysis Serum Sodium, SUN, Glucose and Intradialytic SBP Decline

In secondary analyses, the associations of SNa, SUN and serum glucose with intra-dialytic SBP decline were examined. In the fully adjusted model (Model 2), lower SNa, higher SUN and higher glucose were independently associated with greater SBP decline (Table 4). After the exclusion of individuals with pre-dialysis glucose >132 mg/dL, the association of glucose with SBP decline became non-significant. Effect estimates were qualitatively and quantitatively similar after individual additional adjustment for categories of blood flow, dialysate bicarbonate and dialysate calcium (data not shown). Similar patterns of association were evident when IDH was considered as the outcome of interest (Table 5).

Exploratory Analyses

Addition of higher vs. lower DNa as a covariate to the fully adjusted model (Model 3) revealed no evidence of significant change to the point estimate of the association of calculated osmolarity with intra-dialytic SBP decline (1.48 [95% CI, 0.87–2.10] mm Hg). However, in sub-group analyses according to higher or lower DNa use, calculated osmolarity remained associated with hypotension in the lower DNa sub-group only (Table 3). In the analyses of SNa, SUN and serum glucose, only higher SUN remained consistently associated with SBP decline across DNa sub-groups (Tables 4 & 5).

In other exploratory analyses we found evidence for effect modification of the association of calculated osmolarity with SBP decline by UFR (p for interaction<0.001). In these analyses, greater calculated osmolarity only remained associated with greater SBP decline in the lower two tertiles of UFR, although the mean calculated osmolarity was lower in tertile 3 than in tertile 2 (Table 6).

Discussion

In this study of dialysis-associated SBP changes, we report that higher pre-dialysis calculated osmolarity, measured after the two-day inter-dialytic interval, is independently associated with greater decline in intra-dialytic SBP and greater odds of having IDH.

In normal physiological states, the calculated osmolarity, equal to (2*serum sodium) + (SUN/2.8) + (serum glucose/18), approximates the measured osmolality.. As sodium is the major contributor to the serum osmolality, one might expect higher pre-dialysis SNa to be associated with greater SBP decline. We found the opposite to be the case, but noted a significant negative correlation between glucose and SNa in our study (r=−0.32; P<0.001), suggesting that severe hyperglycemia may partially obscure the association of SNa with outcomes of interest. However, even after exclusion of those with higher glucose levels, the direction of association of SNa with SBP decline did not change. A more likely explanation, consistent with our current findings (correlation between SNa and UF volume: r= −0.18; P<0.001), may be that lower SNa associates with greater inter-dialytic weight gain[18] (and perhaps lower solute intake), identifying those who are more likely to have intra-dialytic hypotension as a result of higher UFRs.[19] Interestingly, we found that higher calculated osmolarity was not associated with greater SBP decline in the highest tertile of UFR, suggesting that in this particular sub-group, the risk of hypotension from a higher rate of fluid removal may outweigh any contribution from changes in osmolality. However, an alternative explanation may again be that greater interdialytic weight gain results in a lower pre-dialysis osmolality, obscuring any association with greater SBP decline. In support of this assertion, we reported that the pre-dialysis calculated osmolarity for the highest tertile of UFR was indeed lower than that of the middle tertile.

The relatively high calculated osmolarity in HD patients, compared with patients who have normal kidney function, largely reflects the contribution of higher SUN concentrations. In states of rapid flux (such as HD), it is possible that rapid urea clearance from the extracellular compartment may predispose to the generation of temporary osmotic gradients,[20–23] promoting transcellular movement of water and resultant hypotension. Of

note, higher pre-dialysis SUN may partially reflect better nutritional status in some hemodialysis patients[24]—therefore, it is important to point out that protein restriction is not to be advocated as a means to reduce SUN for the prevention of IDH. Knowledge related to the mechanisms of water and urea movement across body compartments continues to evolve[25–26] and future experimental work will shed further light on this important area.

Higher blood glucose concentrations may also contribute to higher pre-dialysis osmolality measurements in long-term HD patients. The optimal dialysate glucose prescription is one that minimizes the risk of hypoglycemia, while also limiting exposure to excessively high glucose concentrations.[27] However, in individuals with hyperglycemia, fixed lower dialysate glucose may actually lead to larger blood–dialysate gradients and a more rapid lowering of blood glucose during the HD procedure. Prior reports have demonstrated reduced frequency of IDH in diabetic patients when dialyzed against 200 mg/dL versus 100 mg/dL dialysate glucose.[28] Our findings support the theory that larger blood–dialysate glucose concentration gradients may also predispose to greater intra-dialytic blood pressure decline.

Excess SBP decline during HD is a common occurrence and associated with worse all-cause and cardiovascular mortality, even in the absence of symptoms.[29–30] Whether interventions to minimize rapid changes in osmolality that result in a 2– to 4–mm Hg lesser decline in SBP would lead to improved outcomes is not known, but these margins may be all the more important for end-organ perfusion in HD patients with stiff vessels that are dependent on maintenance of adequate perfusion pressure.[31] It is therefore imperative to identify modifiable risk factors that may limit excessive drops in blood pressure during HD. One such example relates to the pressor effects of arginine vasopressin (AVP). Pre-dialysis AVP levels in HD patients are higher than those of the individuals without kidney disease (presumably reflecting the higher baseline osmolality). However, temporary lowering of plasma osmolality during HD may result in a blunted response of AVP to hypotension.[32] On the other hand, minimizing the decline in serum osmolality during HD by the administration of hypertonic fluids has been shown to augment AVP release and promote blood pressure stability.[10, 33–34] We previously reported that the rapidity of decline in SUN associated with greater odds of intra-dialytic hypotension in a post-hoc analysis of the HEMO (Hemodialysis) Study.[9] This observation may also partly explain why isolated ultrafiltration (with minimal changes in plasma osmolality) tends to have less associated hypotension.[35] Our current finding, that higher predialysis calculated osmolarity is associated with greater magnitude of SBP decline, is consistent with these observations.

There are numerous reports detailing interventions aimed at minimizing the rate of osmolality decline that may be useful in the treatment of patients prone to hypotensive events. Dialysis physicians initially increased the DNa concentration, finding that this reduced the frequency of dialysis-related symptoms[16] and improved hemodynamic stability.[36–37] Prior reports of increased thirst and inter-dialytic weight gain tempered the initial enthusiasm of these findings, [8, 37] but more recently the use of biofeedback-controlled sodium profiling appears to have less associated interdialytic weight gain. [38] Whether treatment, or aggressive focus on prevention, of pre-dialysis hyperglycemia (taking care to avoid hypoglycemia) would attenuate the risk of IDH is currently unknown. Other strategies include the administration of hypertonic mannitol and other hypertonic solutions. [10, 15, 34, 39]

In our analyses, we did not find any evidence for effect modification or confounding of our model estimates by the DNa concentration. In this regard, it must be remembered that higher DNa is generally prescribed for patients who are already known to suffer from IDH – this confounding by indication has been reported previously and may actually be expected to lead to an association of higher DNa use with greater SBP decline.[40] Furthermore, as higher DNa may not be expected to associate with pre-dialysis calculated osmolarity, but rather to associate with less rapid decline in intra-dialytic osmolality, it is not surprising that it does not behave as a confounding variable in our analyses. However, it is interesting to note that greater calculated osmolarity only remained significantly associated with hypotension in the lower DNa subgroup. Although underpowered, and potentially subject to significant confounding as explained above, this observation suggests that the association of osmolality with intra-dialytic SBP decline may be altered by the use of differing DNa concentrations. Unfortunately we did not have actual pre- and post-HD samples to determine the measured osmolality changes in individual subjects.

We and others have reported a potential survival benefit for certain individuals dialyzing against higher DNa,[41–43] although several large dialysis organizations have put forward proposals to lower the DNa concentration, based largely on observational evidence.[44] This stance has already met with some opposition.[45] It therefore seems imperative to perform interventional trials to identify best practices for the safe and effective delivery of HD.

The strengths of this study include the availability of a relatively large number of patients with detailed intra-dialytic hemodynamic data from individual HD sessions. There are, however, several limitations that warrant discussion. As this is an observational study, there remains the possibility of residual confounding from variables not considered, or insufficient adjustment from those that were. For example, data limitations prevented us from taking into account dialysate temperature, measured osmolality and medication use in our analyses. The demographic make-up of our sample differs from that of the general US population (lower proportion of African-Americans), thus limiting the broader generalizability of our findings. It is notable that this study analyzed laboratory data from the first HD day of the week (i.e. Monday or Tuesday) and therefore followed the longer two-day inter-dialytic interval, when pre-dialysis osmolality may be expected to be highest. Within the current confines of thrice-weekly HD for the vast majority of patients in the United States, it is possible that alternative dialysis prescriptions could be required for different days of the week.

In conclusion, higher pre-dialysis calculated osmolarity, due primarily to elevations in urea and glucose, is associated with greater magnitude of decline in intra-dialytic SBP and greater odds of having a hypotensive event. Strategies to limit pre-dialysis elevations in osmolality (such as treatment or avoidance of hyperglycemia before dialysis) and strategies to minimize the rapidity of osmotic shifts (such as isolated ultrafiltration, longer dialysis session length or greater HD frequency) should be tested to minimize the frequency and magnitude of SBP decline and its associated morbidity and mortality.

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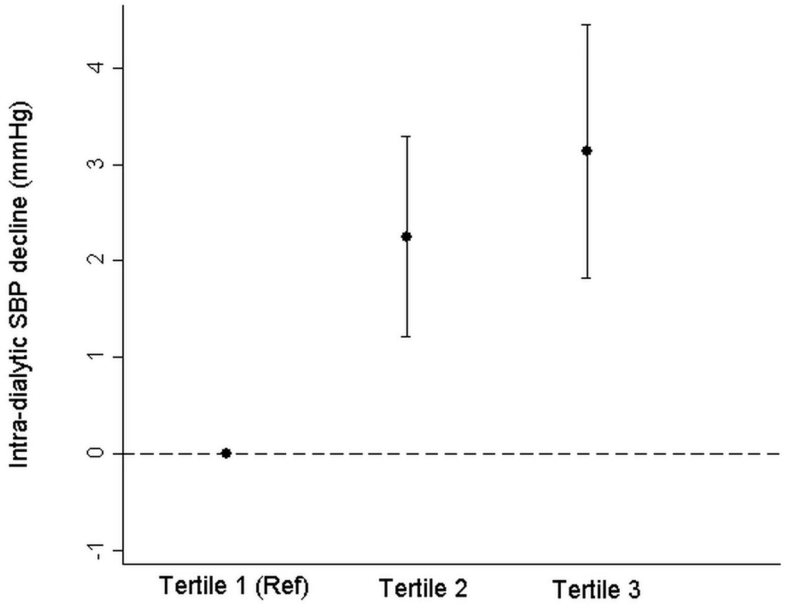

Figure 1.

Generalized linear models were fit to estimate the association of tertiles of pre-dialysis calculated osmolality with the magnitude of intra-dialytic SBP decline (Tertile 1 was taken as the reference), after adjusting for age, gender (male versus female), race (black versus non-black), diabetes, ischemic heart disease, congestive heart failure, access type (fistula, graft, catheter), pre-dialysis SBP, UFR, serum calcium, albumin, and bicarbonate.

Table 1

Baseline characteristics of the cohort according to tertiles of pre-dialysis calculated osmolarity

	Total (N=3,142)	Calculated Osmolarity Tertile			P[a]
		1 (n=1,048)	2 (n=1,049)	3 (n=1,045)	
Age (y)	62.6 ± 15.2	64.0 ± 14.9	62.5 ± 14.9	61.4 ± 15.5	<0.001
Male sex	1795, 57.1	555, 53.0	596, 56.8	644, 61.6	<0.001
Black race	406, 12.9	145, 13.8	141, 13.4	120, 11.5	0.2
Diabetes	1918, 61.0	624, 59.5	643, 61.3	651, 62.3	0.4
IHD	529, 16.8	181, 17.3	174, 16.6	174, 16.6	0.9
CHF	772, 24.6	252, 24.0	274, 26.1	246, 23.5	0.4
Access type					0.2
AVF	1965, 62.6	639, 61.0	659, 62.8	667, 63.8	
AVG	570, 18.1	200, 19.1	202, 19.3	168, 16.1	
Catheter	607, 19.3	209, 19.9	188, 17.9	210, 20.1	
Session Length					0.4
≤180 min	1818, 57.9	585, 55.8	611, 58.3	622, 59.5	
181–209 min	781, 24.9	270, 25.8	252, 24.0	259, 24.8	
>209 min	543, 17.2	193, 18.4	186, 17.7	164, 15.7	
Postdialysis weight (kg)	76.2 ± 20.9	76.4 ± 21.4	76.3 ± 20.3	76.0 ± 20.9	0.9
Serum Sodium (mmol/L)	136.8 ± 3.2	134.9 ± 3.1	137.1 ± 2.6	138.4 ± 2.9	<0.001
Serum Albumin (g/dL)	3.8 ± 0.4	3.7 ± 0.4	3.9 ± 0.4	3.9 ± 0.4	<0.001
SUN (mg/dL)	65.9 ± 19.8	51.6 ± 14.6	64.1 ± 14.0	82.0 ± 17.4	<0.001
Serum Bicarbonate (mmol/L)	24.0 ± 3.3	24.3 ± 3.4	23.9 ± 3.3	23.7 ± 3.4	<0.001
Serum Glucose (mg/dL)	142.3 ± 70.2	128.4 ± 57.3	145.3 ± 71.8	153.3 ± 77.7	<0.001
Calculated osmolarity (mOsm/L)	305.1 ± 9.5	295.0 ± 5.7	305.2 ± 2.2	315.2 ± 5.3	<0.001

Note: Values for categorical variables are given as number (percentages); values for continuous variables, as mean ± standard deviation. Conversion factors for units: glucose in mg/dL to mmol/L, ×0.05551; SUN in mg/dL to mmol/L, ×0.357.

IHD, ischemic heart disease; CHF, congestive heart failure; AVF, arteriovenous fistula; AVG, arteriovenous graft; SUN, serum urea nitrogen.

[a]P values refer to testing the null of no difference between groups, using analysis of variance for continuous variables and χ^2 tests for categorical variables.

Table 2

Baseline hemodialysis treatment blood pressure characteristics according to tertiles of pre-dialysis calculated osmolarity

	Total (N=3,142)	Calculated Osmolarity Tertile			p[a]
		1 (n=1,048)	2 (n=1,049)	3 (n=1,045)	
Pre-dialysis SBP (mmHg)	150.4 ± 26.1	148.0 ± 26.9	150.7 ± 25.7	152.4 ± 25.6	<0.001
Minimum Intradialytic SBP (mmHg)	110.0 ± 26.9	110.7 ± 27.6	109.2 ± 26.3	110.2 ± 26.8	0.4
Postdialysis SBP (mmHg)	135.5 ± 24.3	136.4 ± 24.8	135.0 ± 24.3	135.1 ± 24.0	0.3
SBP decline (mmHg)	40.5 ± 28.5	37.5 ± 29.2	41.7 ± 27.6	42.4 ± 28.6	<0.001
SBP variability[b] (mmHg)	15.8 ± 8.4	15.5 ± 8.2	16.0 ± 8.4	15.9 ± 8.5	0.4
UF volume (L)	3.0 ± 1.2	3.0 ± 1.3	3.0 ± 1.2	3.1 ± 1.1	0.001
UFR (ml/kg/h)	12.8 ± 4.9	12.2 ± 5.2	12.8 ± 4.7	13.4 ± 4.8	<0.001
IDH	1,733 (55.2)	542 (51.7)	598 (57.0)	593 (56.8)	0.02

Note: Values for categorical variables are given as number (percentage); values for continuous variables, as mean ± standard deviation.

Hemodialysis-associated blood pressure variables (± standard deviation) according to baseline dialysate sodium use (≤140 mmol/L vs. >140 mmol/L or modeling).

Abbreviations and definitions: SBP, systolic blood pressure; UF, ultrafiltration; UFR, ultrafiltration rate; IDH, intradialytic hypotension (defined as SBP decline >35 mmHg or nadir intra-dialytic SBP <90 mmHg).

[a] P values refer to testing the null of no difference between groups, using analysis of variance for continuous variables and χ^2 tests for categorical variables.

[b] SBP variability was calculated as the standard deviation of all intra-dialytic SBP measurements.

Table 3

Association of predialysis calculated osmolarity with intra-dialytic SBP decline and hypotension

	Intradialytic SBP decline per 10-mOsm/L greater predialysis calculated osmolarity	Odds of hypotension per 10-mOsm/L greater predialysis calculated osmolarity
Unadjusted model	2.22 (1.51 to 2.93) mm Hg; P<0.001	1.10 (1.05 to 1.15); P<0.001
Model 1	1.28 (0.68 to 1.88) mm Hg; P<0.001	1.08 (1.03 to 1.13); P=0.001
Model 2	1.48 (0.86 to 2.09) mm Hg; P<0.001	1.10 (1.05 to 1.15); P<0.001
Model 2A	0.98 (0.23 to 1.70) mm Hg; P=0.01	1.06 (1.00 to 1.12); P=0.06
Model 3	1.48 (0.87 to 2.10) mm Hg; P<0.001	1.10 (1.05 to 1.15); P<0.001
Lower dialysate sodium	1.71 (1.02 to 2.39) mm Hg; P<0.001	1.11 (1.06 to 1.18); P<0.001
Higher dialysate sodium	0.70 (−0.59 to 2.00) mm Hg; P=0.3	1.02 (0.93 to 1.13); P=0.6

Note: Values in parentheses are 95% confidence interval. Generalized linear models were fit to estimate the association of pre-dialysis calculated osmolality with intra-dialytic SBP decline or odds of intra-dialytic hypotension (decline in SBP >35 mmHg, or any intra-dialytic SBP <90 mmHg). Model 1 adjusted for age, sex, race (black versus non-black), diabetes, ischemic heart disease, congestive heart failure, access type (fistula, graft, catheter), pre-dialysis SBP and ultrafiltration rate. Model 2 adjusted for the same variables as Model 1 in addition to serum calcium, albumin, and bicarbonate. Model 2A excluded those with pre-dialysis serum glucose >132 mg/dL. Model 3 adjusted for the same variables as Model 2, in addition to dialysate sodium use (≤140 mmol/L vs. >140 mmol/L or modeling).

SBP, systolic blood pressure;

Table 4

Association of pre-dialysis serum sodium, SUN and serum glucose and with intra-dialytic SBP decline

	Intradialytic SBP decline per 1-mmol/L greater predialysis serum sodium	Intradialytic SBP decline per 2.8-mg/dL greater predialysis SUN	Intradialytic SBP decline per 18-mg/dL greater predialysis serum glucose
Unadjusted model	0.00 (−0.20 to 0.20); P=0.9	0.33 (0.24 to 0.42); P<0.001	0.50 (0.33 to 0.67); P<0.001
Model 1	−0.25 (−0.43 to −0.08); P=0.01	0.31 (0.23 to 0.39); P<0.001	0.18 (0.03 to 0.33); P=0.02
Model 2	−0.22 (−0.40 to −0.04); P=0.02	0.33 (0.25 to 0.42); P<0.001	0.19 (0.04 to 0.34); P=0.01
Model 2A	−0.26 (−0.48 to −0.05); P=0.02	0.29 (0.19 to 0.39); P<0.001	−0.09 (−0.62 to 0.44); P=0.74
Model 3	−0.22 (−0.40 to −0.04); P=0.02	0.33 (0.25 to 0.42); P<0.001	0.20 (0.05 to 0.35); P=0.01
Lower dialysate sodium	−0.14 (−0.35 to 0.06); P=0.2	0.34 (0.24 to 0.43); P<0.001	0.26 (0.10 to 0.42); P=0.002
Higher dialysate sodium	−0.46 (−0.85 to −0.09); P=0.02	0.35 (0.15 to 0.54); P<0.001	−0.07 (−0.42 to 0.27); P=0.7

Note: Values are provided in mm Hg; values in parentheses are 95% confidence intervals. Generalized linear models were fit to estimate the association of pre-dialysis sodium, SUN and glucose with intra-dialytic SBP decline. Model 1 additionally adjusted for age, sex, race (black versus non-black), diabetes, ischemic heart disease, congestive heart failure, access type (fistula, graft, catheter), pre-dialysis SBP and ultrafiltration rate. Model 2 adjusted for the same variables as Model 1 in addition to serum calcium, albumin, and bicarbonate. Model 2A excluded those with pre-dialysis serum glucose >132 mg/dL. Model 3 adjusted for the same variables as Model 2, in addition to dialysate sodium use (≤140 mmol/L vs. >140 mmol/L or modeling).

SBP, systolic blood pressure; SUN, serum urea nitrogen

Table 5

Association of pre-dialysis serum sodium, SUN, and serum glucose with intra-dialytic hypotension

	Odds of intradialytic SBP per 1-mmol/L greater predialysis serum sodium	Odds of intradialytic SBP per 2.8-mg/dL greater predialysis SUN	Odds of intradialytic SBP per 18-mg/dL greater predialysis serum glucose
Unadjusted	0.99 (0.98 to 1.00); P=0.2	1.02 (1.01 to 1.02); P<0.001	1.03 (1.02 to 1.04); P<0.001
Model 1	0.98 (0.96 to 0.99); P=0.001	1.02 (1.01 to 1.03); P<0.001	1.02 (1.00 to 1.03); P=0.01
Model 2	0.98 (0.97 to 0.99); P=0.01	1.02 (1.02 to 1.03); P<0.001	1.02 (1.00 to 1.03); P=0.01
Model 2A	0.98 (0.96 to 0.99); P=0.01	1.02 (1.01 to 1.03); P<0.001	1.00 (0.96 to 1.05); P=0.9
Model 3	0.98 (0.97 to 1.00); P=0.01	1.02 (1.02 to 1.03); P<0.001	1.02 (1.01 to 1.03); P<0.001
Lower dialysate sodium	0.99 (0.97 to 1.00); P=0.06	1.02 (1.02 to 1.03); P<0.001	1.02 (1.00 to 1.03); P=0.01
Higher dialysate sodium	0.97 (0.94 to 0.99); P=0.02	1.02 (1.00 to 1.03); P=0.02	1.02 (0.99 to 1.05); P=0.3

Note: Values in parentheses are 95% confidence intervals. Generalized linear models were fit to estimate the association of pre-dialysis sodium, BUN and glucose with intra-dialytic hypotension (decline in SBP >35 mmHg, or any intra-dialytic SBP <90 mmHg). Model 1 additionally adjusted for age, sex, race (black versus non-black), diabetes, ischemic heart disease, congestive heart failure, access type (fistula, graft, catheter), pre-dialysis SBP and ultrafiltration rate. Model 2 adjusted for the same variables as Model 1 in addition to serum calcium, albumin, and bicarbonate. Model 2A excluded those with pre-dialysis serum glucose >132 mg/dL. Model 3 adjusted for the same variables as Model 2, in addition to dialysate sodium use (≤140 mmol/L vs. >140 mmol/L or modeling).

SBP, systolic blood pressure; SUN, serum urea nitrogen

Table 6

Association of pre-dialysis calculated osmolarity with intra-dialytic SBP decline, according to tertiles of ultrafiltration rate

	UFR Tertile 1	UFR Tertile 2	UFR Tertile 3
Intradialytic SBP decline per 10-mOsm/L greater calculated Osmolarity (mm Hg)	2.4 (1.5 to 3.3)	1.7 (0.8 to 2.6)	0.3 (−0.6 to 1.2)
P	<0.001	<0.001	0.5
Mean calculated osmolarity (mOsm/L)	305.6±9.6	307.0±9.3	306.5±9.6

Note: Values in parentheses are 95% confidence intervals. Generalized linear models were fit to estimate the association of pre-dialysis calculated osmolarity with intra-dialytic SBP decline. Model 2 adjusted for age, sex, race (black versus non-black), diabetes, ischemic heart disease, congestive heart failure, access type (fistula, graft, catheter), pre-dialysis SBP, UFR, serum calcium, albumin, and bicarbonate.

UFR, ultrafiltration rate