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Comparison of Ambulatory Blood Pressure Patterns in Patients With Intradialytic Hypertension and Hemodialysis Controls

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Abstract

Background/Aims—Intradialytic hypertension (IH) patients have higher mortality risk than other hemodialysis patients and have been shown to have higher ambulatory blood pressure (BP). We hypothesized that interdialytic BP *patterns* would differ in IH patients and hypertensive hemodialysis controls.

Methods—We consecutively screened hemodialysis patients at our university-affliated units. Based on pre and post-HD BP measurements during the prior 2 week period, we identified IH patients and demographically matched hemodialysis controls. We measured ambulatory interdialytic BP, fow-mediated vasodilation, and intradialytic endothelin-1 (ET-1). Using linear mixed-models, we compared BP slopes during the following intervals: 1–24 hours post-dialysis, 25–44 hours post-dialysis, and 1–44 hours post-dialysis.

Results—There were 25 case subjects with IH and 24 controls. Systolic BP during hours 1–44, 1–24, and 25–44 were 143.1 (16.5), 138.0 (21.2), and 150.8 (22.3) mmHg in controls. For IH subjects, they were 155.4 (14.2), 152.7 (22.8), and 156.5 (20.8) mmHg (p=0.008, 0.02, 0.4). In controls, the slopes were +0.6, +0.6, and +0.4 mmHg/hr. In IH subjects, they were +0.1, −0.3, and +0.3 mmHg/hr. The IH 1–24 hour slope differed from the IH 25–44 hour slope (p=0.001) and the

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control 1–24 hour slope (p=0.002). The change in ET-1 from pre to post dialysis was 0.5 (1.5) pg/mL in controls and 1.0 (2.3) pg/mL in IH patients (p=0.4). In a univariate model, there was an association with screening BP and BP slope (p=0.002 for controls and p=0.1 for IH patients).

Conclusions—Interdialytic BP *patterns* differ in IH patients and hemodialysis controls. The elevated post dialysis blood pressure persists for many hours in IH patients contributing to the overall increased BP burden.

Keywords

Hemodialysis; Hypertension; Intradialytic Hypertension; Ambulatory Blood Pressure; Endothelial Cell Dysfunction

Introduction

Hypertension, nearly universal in hemodialysis patients, is a leading risk factor for increased morbidity and mortality in this population. A wide range of blood pressure (BP) measurements both during and between hemodialysis sessions poses a challenge in hypertension management. Compared to individual BP measurements obtained in the hemodialysis unit, the average of BP measurements obtained during the interdialytic period provides better prognostic information for adverse clinical outcomes, including mortality [1]. Because hemodialysis unit measurements are directly available to nephrologists, it is important to 1) recognize the associations between intradialytic BP patterns and overall interdialytic BP burden [2] and 2) further explore the nature of these relationships.

Intradialytic hypertension (IH), an increase in BP from pre to post-hemodialysis, is a recurrent and persistent phenomenon in a subset of hemodialysis patients [3] that has been shown to be an independent risk factor for increased morbidity and mortality [4–6]. Recent observational evidence demonstrates that IH patients have higher ambulatory systolic BP measured during the 44-hour interdialytic period compared to hypertensive hemodialysis controls [2]. There has been no formal analysis of how the interdialytic BP *patterns* differ between these groups. As interdialytic BP measurements are the most reliable BP measurements to predict outcomes in hemodialysis patients, it is critical to identify what factors influence BP most strongly during the interdialytic period, particularly in high-risk patients. Furthermore, while hypotheses exist to explain the intradialytic increases in BP including acute increases in vasoconstrictor peptides [7–9], changes in cardiac performance related to improvement in extracellular volume status [10, 11], or greater endothelial cell dysfunction [12], none of these variables have been examined in the context of how they influence the BP during the interdialytic period.

In this retrospective analysis of a previously published case-control study, we sought to identify and characterize quantitative differences in ambulatory interdialytic BP patterns between IH patients and hemodialysis controls using linear mixed models. Based on qualitative inspection of the BP patterns [2], we hypothesized that the BP slopes of these two patient groups would be significantly different during the initial 24 hours after HD, but similar throughout the remainder of the interdialytic period. We furthermore sought to

explore how clinical and demographic variables that influenced the BP patterns during the first 24 hours after dialysis.

Materials and Methods

Study Population

Full details of this study's methods are previously published [2, 12]. Using consecutive sampling, we screened ESRD patients receiving thrice weekly in-center maintenance hemodialysis at University of Texas Southwestern-affiliated units. Inclusion criteria were: 1) age 18–80 years; 2) hemodialysis vintage ≥1 month; 3) ability to achieve the dry weight as determined clinically by the patient's individual nephrologist; 4) clinical hypertension as defined by BP exceeding the recommended guidelines set forth by the National Kidney Foundation (pre-dialysis systolic BP ≥140 mmHg or post-dialysis systolic BP >130 mmHg [13]). Subjects were defined as case subjects if they demonstrated an increase in systolic BP ≥10 mmHg from pre to post-hemodialysis in 4/6 screening treatments. Subjects were defined as control subjects if they demonstrated a decrease in systolic BP ≥10 mmHg from pre to post hemodialysis in 4/6 screening treatments. The subjects had signed written, informed consent prior to any study procedures taking place. The study was approved by the University of Texas Southwestern Medical Center institutional review board, and all procedures were in accordance with the Declaration of Helsinki. The study was part of a registered trial [14].

Blood Pressure Measurements

Before, during, and after a midweek hemodialysis treatment, brachial artery BP was measured using a standard automated hemodialysis unit sphygmomanometer in the seated position with feet on the floor and the patient's back supported by a chair. Following treatment, while the subjects were still in the hemodialysis unit, interdialytic BP measurement was initiated with a Spacelabs 90207 ambulatory BP monitor. Blood pressure was measured every 30 minutes during daytime (6 am – 10 pm) and hourly at night for 44 hours until the next hemodialysis treatment.

Blood Measurements

Immediately before and after the same midweek hemodialysis treatment, a nurse obtained blood from the patient's hemodialysis access and centrifuged at 1000 rpm for 10 minutes. Samples were shipped to a local laboratory where albumin was measured using spectrophotometry and sodium was measured by direction-selective potentiometry. Remaining serum was stored in a −80 degree Celsius freezer, and endo-thelin-1 (ET-1) was analyzed with ELISA in batch at study conclusion [15]. Other laboratory measurements were obtained from monthly lab draws per hemodialysis unit protocol.

Flow Mediated Vasodilation

Endothelial cell function was assessed with measurement of brachial artery vasodilation in response to shear stress [16]. On a midweek, non-dialysis day, ultrasound of the brachial artery was obtained with an 11-MHz pulsed Doppler ultrasound probe at an insonation angle of 60 degree (Philips ie33, Bothell, WA), and mean blood flow velocity and brachial artery

diameter were measured. A forearm cuff was inflated for five minutes prior to deflation. Two minutes after deflation, repeat measurements of brachial artery diameter were repeated to determine flow-mediated dilation (FMD). Images were digitized and analyzed in a blinded fashion with an automatic wall tracking system (Vascular Analysis Tools, Medical Imaging Analysis). The final FMD was normalized for peak sheer stress [17, 18] and expressed as a percentage change from the baseline diameter. Images were repeated after replacing the forearm occlusion step with oral intake of a single 0.4mg tab of sublingual nitroglycerin.

Pulse wave velocity

On the same midweek, non-dialysis day that FMD was measured, a pulse transducer device (Cardiovascular Engineering, Inc.) was used to obtain arterial tonometry and simultaneous electrocardiogram. Carotid-femoral pulse wave velocity was measured as distance/time using the foot-foot method [19].

Statistical Analysis

Continuous variables are reported as means with standard deviations or median with interquartile range when data is not normally distributed. Between-group comparisons in baseline characteristics were performed with unpaired t-tests for continuous variables. For categorical variables, between-group comparisons were performed with Chi-square test or Fisher's exact test when the frequency was less than 5 for an individual group. The primary outcome is the systolic BP slope defined as the hourly change of systolic BP in the interdialytic period which was analyzed with mixed effect regression analysis using time (hour) modeled for systolic BP. A slope was determined for each of the following 3 predefined intervals: hours 1–24 after dialysis, hours 25–44 after dialysis, and hours 1–44 after dialysis. We then explored mixed effect models to assess the relationship between BP slope during hours 1–24 with several clinical variables (presence of diabetes, age, gender, race, number of antihypertensive medications, tobacco use, FMD, intradialytic change in ET-1, dialysis shift, percentage of interdialytic weight gain, pulse wave velocity, ultrafiltration rate, dialysate to serum sodium gradient, change in intradialytic systolic BP during screening as well as in the treatment preceding ambulatory BP measurement). For these analyses, time was a random effect variable, and others were fixed effect variables modeled for systolic BP.

Results

Patient Characteristics

In the parent case-control study, there were 460 patients screened and 59 that were enrolled (401 were ineligible or not interested) [12]. A total of nine subjects withdrew (four controls and five cases) from that study, and we did not have complete hourly BP measurements for one of the remaining controls. The details of the 49 subjects in this analysis are included in Table 1. The only difference between groups was noted for angiotensin converting enzyme inhibitor (ACE-I) use, which 64% of the IH subjects were taking and 33% of the controls were taking ($p=0.05$). There was no statistically significant difference between groups regarding angiotensin-receptor blocker use (8% vs. 21%, $p=0.2$). There were no differences in dialysis prescription, including dialysate sodium. Serum sodium and albumin

measurements obtained prior to the dialysis treatment immediately preceding the ambulatory blood pressure measurements were similar between groups. There were not any differences in dialysate to serum sodium gradients between the two groups. There were no differences in monthly lab parameters drawn routinely at the dialysis unit.

Intradialytic Blood Pressure and Measurements of Endothelial Cell Function

During the 2-week screening period used to identify case subjects and controls, the mean (standard deviation) pre-dialysis systolic BP were 155.0 (15.7) mmHg in the controls and 144.0 (9.7) mmHg in the IH patients (p=0.005). Post-dialysis systolic BP were 128.3 (11.0) and 159.0 (9.3) mmHg in the two groups, respectively (p<0.001); and the changes in systolic BP from pre to post dialysis were −26.7 (12.5) and + 15.0 (9.1) mmHg in the two groups (p<0.001). During the single hemodialysis treatment occurring immediately prior to the ambulatory BP measurements, all control subjects had decreases in systolic BP from pre to post-dialysis. Among the IH subjects, there were 13 subjects with BP increases and 12 subjects with BP decreases during this treatment. A comparison of measurements obtained in the treatment immediately prior to the ambulatory BP monitoring as well as other measurements of endothelial cell function and fluid changes are shown in Table 2. While pre-dialysis systolic BPs for this single treatment were similar, post-dialysis systolic BP and change in systolic BP from pre to post dialysis were different between these groups.

Interdialytic Blood Pressure Patterns

The average systolic BP during the 44 hour interdialytic time period was 143.1 (16.5) mmHg in the controls and 155.4 (14.2) mmHg in the IH subjects (p=0.008). For the first 24 hours, the average systolic BP was 138.0 (21.2) mmHg in the controls and 152.7 (22.8) mmHg in the IH subjects (p=0.02). During the remainder of the interdialytic time period (hours 25–44), the average systolic BP was 150.8 (22.3) mmHg and 156.5 (20.8) mmHg, respectively (p=0.4).

The systolic BP slope for the controls during the entire 44-hour interdialytic period was +0.6 mmHg/hr (p<0.0001 compared to zero slope, Figure 1). In the controls, the systolic BP slope for hours 1–24 and 25–44 were +0.6 mmHg/hr (p=0.001 compared to zero slope) and +0.4 mmHg/hr (p=0.09 compared to zero slope), respectively. Within the control group there was no difference between these time periods (−0.1 mmHg/hr, p=0.4). In the IH subjects, the systolic BP slope during the entire 44 hour interdialytic time period was +0.1 mmHg/hr (p=0.1 compared to zero slope). The slope for hours 1–24 and 25–44 were −0.3 mmHg/hr (p=0.2 compared to zero slope) and +0.3 mmHg/hr (p=0.3 compared to zero slope), respectively. Within the IH subjects, there was a difference between these two periods (+0.6 mmHg/hr when comparing hours 25–44 to hours 1–24, p=0.001). The between-group differences for controls and IH subjects slopes for hours 1–24 and 25–44 were −0.8 mmHg/hr (p=0.002) and −0.1 mmHg/hr (p=0.7), respectively. There were no differences in the 1–24 hour systolic BP slope among the IH patients who had intradialytic BP increases or decreases in the treatment immediately prior to the ambulatory blood pressure monitoring (+0.2 mmHg/hr for decrease vs increase, p=0.7).

We explored demographic and potentially clinically relevant variables to assess if they had associations with interdialytic BP slope during hours 1–24 in univariate analyses. The change in systolic BP from pre to post dialysis averaged during the screening period was associated with interdialytic systolic BP slope in the control group with a trend for such an association in the IH subjects (Table 3). However, there was no significant association between the change in systolic BP during the treatment prior to measurement of ambulatory BP and the ambulatory BP slope. African American race also had a significant association with slope in the controls, but not the IH subjects. The results of the remaining variables are shown in Table 3.

Discussion

The principal finding of this study was that we found quantitatively distinct interdialytic BP patterns in IH patients compared to our hypertensive hemodialysis controls. Most hemodialysis patients have decreases in BP during dialysis followed by a persistent rise in systolic BP during the interdialytic period. The interdialytic BP pattern in our IH patients was characterized by a trend for decreasing BP for the initial 24 hours after dialysis, and it was followed by a more typical increase in BP for the remainder of the interdialytic period. The controls demonstrated an expected persistent increase in BP throughout the interdialytic period. We did not identify any additional clinical variables related to baseline characteristics or intradialytic hemodynamic changes that consistently influenced this BP slope.

As published previously, the overall ambulatory BP was significantly higher in IH subjects compared to controls [2]. While the average systolic BP measured from hour 25–44 was similar between the two groups, there is a significant difference between the two groups for the average systolic BP measured during the initial 24 hours after dialysis. This study demonstrates the significance of the initial 24 hour time period following HD in defining the overall ambulatory BP burden in patients with IH compared to other hemodialysis patients. Specifically, the elevated post-HD BP in patients with IH is not transient and takes many hours to normalize.

Furthermore, we provide a formal quantitative analysis supporting that the BP patterns, defined by the change in systolic BP each hour, are distinct during this 24 hour time period among patients with different intradialytic BP characteristics. This suggests that the mechanisms responsible for increased BP likely differ between these two groups of patients not only during dialysis, but also throughout a large part of the interdialytic time period. Extracellular volume status is an important determinant of BP in hemodialysis patients, in general. Cohort data of hemodialysis patients shows that the “average” response to a hemodialysis treatment is a two-slope decrease in BP with an acute decrease in BP during the first hour of the treatment followed by a more blunted decrease in BP throughout the remainder of the treatment [20]. Greater ultrafiltration volume or rate during dialysis is associated with more a negative slope, or greater decline in BP, during the latter portion of the treatment. During the interdialytic time period, BP increases with time, with faster increases in BP seen with greater amount of interdialytic weight gain [21]. Controls in our study demonstrated an expected increase in BP throughout the entire interdialytic time

period. Systolic BP in this group increased 0.6 mmHg each hour after dialysis during both the initial 24 hours after dialysis and the entire 44-hour interdialytic time period. The slope did not change in controls from hours 1–24 after dialysis to hours 25–44. In contrast, the BP slope in the IH patients showed a trend towards a decrease with each hour (−0.3 mmHg/hr) during the first 24 hours, and this change was different from not only the same time period in controls (p=0.002, Figure 1), but also when compared to hours 25–44 in the IH patients (p=0.001). We conclude from this study that intradialytic hypertension patients respond to *acute* volume expansion differently than the hypertensive controls based on the between group differences in ambulatory BP slope with similar interdialytic weight gain (and percentage of interdialytic weight gain). Exploratory analyses showed no association in either group with systolic BP slope and the variables interdialytic weight gain, ultrafiltration rate, or dialysate to serum sodium gradient.

Despite similarities in acute change in extracellular volume between our patient groups, we cannot exclude that chronic volume overload did not play a role in the different ambulatory BP patterns. Extracellular volume overload has been proposed to be a mechanism responsible for intradialytic hypertension in general [10, 11, 22, 23], and it remains possible that there were differences in chronic volume overload between these two groups. We acknowledge the important findings of others that the degree of chronic extracellular expansion does influence interdialytic BP patterns in hemodialysis patients such that more volume overloaded patients have more blunted increases in BP between dialysis treatments [22, 24]. Chronic volume expansion might be expected to influence not only the interdialytic BP via a persistent elevation of vascular resistance [25], but it might also influence intradialytic BP due to more rapid intravascular refilling as ultrafiltration takes place during dialysis. Others have found vascular resistance to increase during dialysis in IH patients in general [8], and it is unknown how acute intravascular refilling would influence acute changes in vascular resistance. It is conceivable that if our IH patients were more chronically overloaded with a baseline state of increased vascular resistance, some stimulus of increased vascular resistance during dialysis (whether related to volume changes or not), would result in a prolonged period of heightened vascular resistance before it returns back down to the baseline value. It would be of interest to have simultaneous measurements of extracellular volume, intravascular volume, cardiac output, and vascular resistance in a similar study to specifically address this.

Our prior work has identified a greater endothelial cell dysfunction in IH patients compared to hypertensive hemodialysis controls [12, 15]. Specifically, there is lower baseline FMD and lower levels of circulating endothelial progenitor cells. No prior studies have looked at the quantitative relationship between impaired endothelial cell function and interdialytic BP pattern among patients with IH. In this study, we performed exploratory analyses to determine how markers of endothelial cell function were associated with BP slopes. We did not find any strong association of intradialytic change in ET-1 with the systolic BP slope. So, while intradialytic increases in ET-1 have been proposed to explain increases in BP during HD in IH patients, [7–9, 15] there is no evidence to conclude from our study that the magnitude of an increase in ET-1 affects BP for prolonged periods of time. We also found that neither baseline FMD or PWV had an association with BP slope. We did find associations between screening intradialytic BP change and systolic BP in the controls in a

univariate model with a trend for such an association in the IH patients. Conversely, there was no association with change in systolic BP from pre to post dialysis and BP slope when considering the treatment immediately before the ambulatory BP was measured in either group. This generates the hypothesis that the ambulatory BP pattern may not just be a response to what happened during the prior treatment, but may be more likely related to whatever mechanisms make an individual prone to intradialytic hypertension in the first place. This was supported by the similarity in BP slopes for the IH patients with increases and decreases in intradialytic BP in the treatment immediately prior to the ambulatory BP monitoring. We acknowledge that we cannot confirm these findings from our exploratory analysis without multiple ambulatory BP measurements obtained at different points in time and a larger sample size.

There are numerous other hypotheses for the etiology of IH that warrant further consideration in the context of how ambulatory BP might affected. Silva et al. found that higher dialysate bicarbonate concentration was associated with lower post-dialysis cardiac index and BP, while higher dialysate to serum potassium gradient was associated with more preserved BP and cardiac index [26]. There were no differences in dialysate bicarbonate, dialysate potassium, or dialysate to serum potassium gradient in our study to support these as primary mechanisms responsible for the intradialytic BP differences we saw. Using a lower dialysate sodium has been shown to prevent BP increases in IH patients [27], but we found no difference in serum to dialysate sodium gradient between groups and no association with this gradient on the interdialytic BP slope. Others have found that intradialytic exercise results in a higher intradialytic BP than in controls, but the BP decreases by the end of dialysis [28]. Although specific targeted exercise regimens are not part of our protocol, we did not have ascertainment of relative activity during dialysis in our study to fully address this possibility. As stated above, the role of chronic volume overload and other unidentified vasoconstrictors on the intradialytic changes in vascular resistance remain to be further explored.

Limitations to this study include a lack of extracellular volume measurements from bioimpedance spectroscopy to establish whether one group was chronically more volume overloaded than the other. One study using multifrequency bioimpedance spectroscopy suggests that volume overload is a characteristic of IH based on measurements obtained in a cross sectional study [23]. We also did not have weight measurements between HD treatments to determine if the rate of weight gain was different between these groups. While we know that percentage of weight gain was similar when considering the entire interdialytic period, we cannot confirm if there were differences in weight gain on the non-HD day. Furthermore, we did not have reliable ascertainment of residual renal function to compare this between groups or assess the possible effect this may have had on interdialytic BP patterns. The absence of associations of most variables tested with the ambulatory BP slope may have been limited by inadequate sample size. It is possible that associations exist that would have required a larger study to uncover these relationships. Finally, we are basing our conclusions on a single set of ambulatory BP measurements in a relatively small sample of patients.

Conclusion

We found in this study that interdialytic BP patterns differ significantly between patients with IH and hypertensive hemodialysis controls. There is an absence of the expected systolic BP increase during the initial 24 hours after dialysis in patients with IH. Furthermore, this period of time defines the overall higher BP burden in patients with compared to other hemodialysis patients as both the average BP and the BP slope are similar in the two groups during the latter portion of the interdialytic time period. Our study further establishes how intradialytic BP patterns can provide information on BP during the interdialytic time period.

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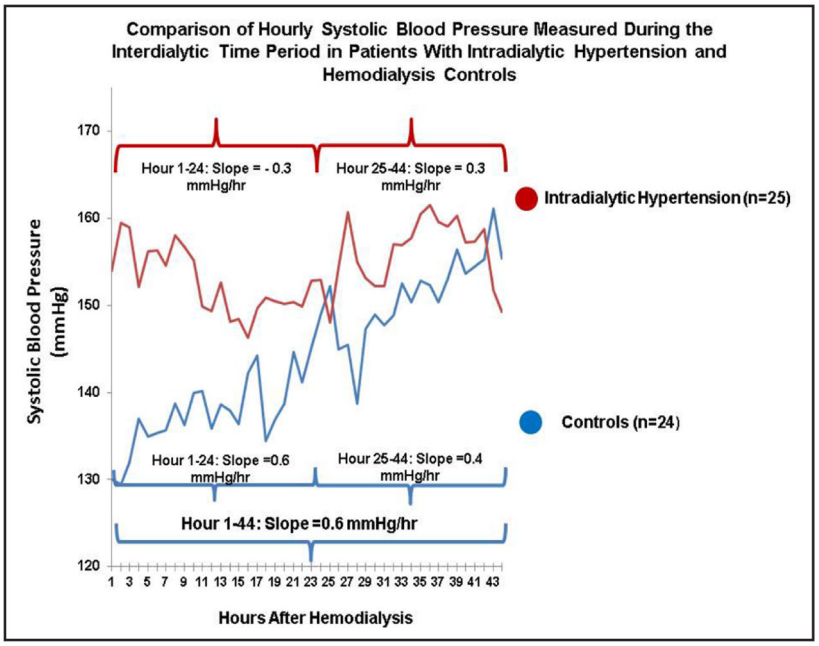

Fig. 1.

The average systolic blood pressure measurement for each hour after hemodialysis is shown for both intradialytic hypertension subjects (red) and hypertensive hemodialysis controls (blue). For the controls, the systolic blood pressure increased 0.6 mmHg/hr throughout the entire interdialytic period. The slope was +0.6 mmHg/hr during hours 1–24 and +0.4 mmHg for hours 25–44. In the intradialytic hypertension subjects, the systolic blood pressure slope was −0.3 mmHg/hr for hours 1–24 (p=0.002 for between group difference) and +0.3 mmHg/hr for hours 25–44 (p=0.7 for between group difference).

Table 1

Baseline Patient Characteristics

	Control (n=24)	Intradialytic Hypertension (n=25)	p-value
Demographic Information and Clinical Data			
Age in years (standard deviation)	54.9 (±8.0)	53.9 (±11.1)	0.7
Percent Male (n)	79 (19)	80 (20)	0.9
Percent Hispanic (n)	58 (14)	64 (16)	0.5
Percent African American (n)	42 (10)	36 (9)	0.8
Percent With Diabetes (n)	83 (20)	88 (22)	0.7
Percent With Coronary Artery Disease (n)	8 (2)	16 (4)	0.7
Percent With History of Stroke (n)	21 (5)	20 (5)	0.9
Percent With Congestive Heart Failure (n)	13 (3)	16 (4)	0.9
Tobacco Use			0.5
Never Smoker: % (n)	38 (9)	32 (8)	
Current Smoker: % (n)	21 (5)	20 (5)	
Quit Within 10 years: % (n)	8 (2)	24 (6)	
Quit More Than 10 years ago: % (n)	33 (8)	24 (6)	
Dialysis Vintage			0.9
Less than 6 months: % (n)	8 (2)	12 (3)	
6–12 months: % (n)	17 (4)	24 (6)	
12–24 months: % (n)	17 (4)	12 (3)	
More than 2 years: % (n)	58 (14)	52 (13)	
Hemodialysis Access			0.9
Graft: % (n)	13 (3)	16 (4)	
Fistula: % (n)	79 (19)	80 (20)	
Catheter: % (n)	8 (2)	4 (1)	
Hemodialysis Shift			0.6
1st % (n)	33 (8)	48 (12)	
2nd % (n)	50 (12)	40 (10)	
3rd %(n)	17 (4)	12 (3)	
Estimated Dry Weight in kilograms (standard deviation)	82.9 (14.7)	81.8 (19.9)	0.7
Dialysis Prescription			
Treatment Time (hours)	3.94 (±0.3)	3.96 (±0.4)	0.8
Blood Flow (mL/min)	454 (±109)	420 (±52)	0.2
Dialysate Flow (mL/min)	665 (±131)	674 (±162)	0.4
Dialysate Calcium (mEq/L)	2.54 (±0.1)	2.54 (±0.1)	0.9
Dialysate Potassium (mEq/L)	1.96 (±0.4)	1.76 (±0.4)	0.09
Dialysate Sodium (mEq/L)	140 (±1.6)	140 (±1)	0.9
Dialysate Bicarbonate (mmol/L)	39.6 (±1.4)	39.8 (±1)	0.5
Laboratory Data			
Serum Creatinine (mg/dL)	9.33 (±2.5)	8.67 (±2.2)	0.3

	Control (n=24)	Intradialytic Hypertension (n=25)	p-value
Kt/V	1.64 (±0.2)	1.69 (±0.3)	0.5
Hemoglobin (g/dL)[1]	12.1 (±1.4)	12.3 (±1.1)	0.5
Serum Albumin (g/dL)[1]	3.91 (±0.2)	3.82 (0.6)	0.5
Parathyroid Hormone (pg/mL)	460 (±550)	347 (±222)	0.4
Serum Phosphorus (mg/dL)	5.20 (±1.5)	5.09 (±1.3)	0.8
Serum Calcium (mg/dL)	8.97 (±0.9)	8.77 (±0.7)	0.4
Serum Potassium (mmol/L)	4.86 (±0.6)	4.65 (±0.6)	0.2
Serum Sodium (mEq/L)[1]	137 (±3.0)	136 (±3.7)	0.1
Dialysate to Serum Sodium Gradient (mEq/L)	3.00 (±3.2)	4.38 (±4)	0.2
Serum to Dialysate Potassium Gradient (mmol/L)	3.03 (±0.8)	2.95 (0.9)	0.9
Antihypertensive Use			
Angiotensin Converting Enzyme Inhibitor % (n)	33 (8)	64 (16)	0.05
Angiotensin Receptor Blocker % (n)	21 (5)	8 (2)	0.2
Beta Adrenergic Receptor Blocker % (n)	66 (16)	68 (17)	0.9
Calcium Channel Blocker % (n)	46 (11)	60 (15)	0.4
Clonidine % (n)	21 (5)	32 (8)	0.5
Hydralazine % (n)	13 (3)	24 (6)	0.5

[1]Measured in Central Lab and Obtained Prior to Dialysis Treatment Preceding Ambulatory Blood Pressure Measurement

Table 2

Comparisons of Measurements Obtained During Study Period

	Controls (n=24)	Intradialytic Hypertension (n=25)	p-value
Pre-Dialysis Systolic Blood Pressure (mmHg)[1]	156 (±26.2)	154 (±22.5)	0.8
Post-Dialysis Systolic Blood Pressure (mmHg)[1]	129 (±18.3)	148 (±24.0)	0.003
Change in Systolic Blood Pressure (mmHg)[1]	−26.4 (±33.1)	−6.08 (±37.1)	0.05
Lowest Systolic Blood Pressure During Dialysis (mmHg)[1]	108 (±17.4)	119 (±20.2)	0.05
Ultrafiltration Rate (mL/hr/kg)[1]	9.26 (±3.5)	9.52 (±4.1)	0.8
Pre Dialysis Endothelin-1 (pg/mL)[1]	5.10 (±1.6)	4.97 (±2.0)	0.9
Post Dialysis Endothelin-1 (pg/mL)[1]	5.59 (±1.8)	5.98 (±2.9)	0.6
Delta Endothelin-1 (pg/mL)[1]	0.49 (±1.5)	1.00 (±2.3)	0.4
Flow Mediated Dilation (%)	1.67 (±1.3)	1.03 (±0.7)	0.04
Pulse Wave Velocity (m/s)	11.9 (±4.7)	11.8 (±3.1)	0.9
Percentage of Interdialytic Weight Gain (during period of ambulatory blood pressure measurement)	3.27 (±1.4)	3.42 (±1.2)	0.7

[1]Refers to single hemodialysis treatment immediately prior to initiation of ambulatory blood pressure measurements; There were 4 missing endothelin-1 levels in controls and 2 missing endothelin 1 levels in intradialytic hypertension patients; There were 2 patients with intradialytic hypertension with missing pulse wave velocity measurements

Table 3

Univariate Analyses of Variables on Systolic Blood Pressure Slope During Hours 1–24 Post Dialysis

	Controls (n=24)		Intradialytic Hypertension (n=25)	
Variable	**Coefficient**	**p-value**	**Coefficient**	**p-value**
Change in Systolic Blood Pressure[1]	−0.01	0.002	−0.006	0.1
Change in Systolic Blood Pressure[2]	−0.003	0.4	−0.002	0.5
Diabetes Mellitus	−0.4	0.1	0.33	0.2
Age	−0.02	0.2	−0.005	0.6
Female Gender	−0.2	0.4	0.4	0.05
African American Race	0.5	0.02	−0.1	0.5
Current or Prior Tobacco Use	−0.2	0.5	−0.2	0.4
Flow Mediated Vasodilation	−0.07	0.4	0.008	0.9
Pulse Wave Velocity	−0.02	0.1	0.007	0.8
Number of Antihypertensives	0.005	0.9	0.02	0.8
Percentage of Interdialytic Weight Gain	0.02	0.9	−0.04	0.6
Delta Endothelin-1	0.07	0.4	−0.04	0.3
2nd Shift (vs. 1st shift)	0.2	0.4	0.2	0.4
3rd Shift (vs. 1st shift)	0.2	0.6	0.03	0.9
Ultrafiltration Rate (mL/hr/kg)	0.05	0.3	−0.05	0.4
Dialysate-Serum Sodium Gradient (mEq/L)	0.02	0.7	−0.03	0.6

[1] from pre to post Hemodialysis (averaged during screening);

[2] from pre to post Hemodialysis (single treatment prior to ambulatory Blood Pressure)