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VISIT-TO VISIT SYSTOLIC BLOOD PRESSURE VARIABILITY AND OUTCOMES IN HEMODIALYSIS

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Abstract

Visit-to-visit blood pressure variation (VTV-BPV) is an independent risk factor for cardiovascular events and death in the general population. We sought to determine the association of VTV-BPV with outcomes in patients on hemodialysis, using data from a National Institutes of Health-sponsored randomized trial (the HEMO Study). We used the coefficient of variation (CV) and the average real variability (ARV) in systolic blood pressure (SBP) as metrics of VTV-BPV. 1844 of 1846 randomized subjects had at least three visits with SBP measurements and were included in the analysis. Median follow-up was 2.5 years (interquartile range [IQR] 1.3 to 4.3 years), during which time there were 869 deaths from any cause and 408 (adjudicated) cardiovascular deaths. The mean pre-dialysis SBP CV was 9.9% ± 4.6%. In unadjusted models, we found a 31% higher risk of death from any cause per 10% increase in VTV-BPV. This association was attenuated after multivariable adjustment but remained statistically significant. Similarly, we found a 28% higher risk of cardiovascular death per 10% increase in VTV-BPV, which was attenuated and no longer statistically significant in fully adjusted models. The associations among VTV-BPV, death and cardiovascular death were modified by baseline SBP. In a diverse, well-dialyzed cohort of patients on maintenance hemodialysis, VTV-BPV, assessed using metrics of variability in pre-dialysis SBP, was associated with a higher risk of all-cause mortality and a trend towards higher risk of cardiovascular mortality, particularly in patients with a lower baseline SBP.

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CONFLICTS OF INTEREST/DISCLOSURES

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Supplementary information is available at JHH's website.

Keywords

blood pressure variability; cardiovascular disease; hemodialysis; hypertension; end-stage renal disease

INTRODUCTION

Hypertension is a major modifiable risk factor for cardiovascular disease and affects over 90% of patients with end-stage renal disease (ESRD). Observational studies of over one million persons in the general population show consistent associations between higher blood pressure and higher risks of death, stroke, and coronary events[1]. However, studies in patients with ESRD have shown the highest risks of death and non-fatal cardiovascular events among patients with lower (as opposed to higher) blood pressure[2–5]. This paradox could be attributable in part to the observation that blood pressure fluctuates significantly from one day to the next[6], particularly in patients with ESRD[7,8]. This visit-to-visit blood pressure variability (VTV-BPV) relates modestly to variation in ambulatory blood pressure measurements[9] and is reproducible over time[10], suggesting that VTV-BPV is not due solely to random measurement error. Recent studies have shown VTV-BPV to be an independent risk factor for cardiovascular events and death in patients with and without kidney disease[11–17]. However, many of these studies were limited by small sample sizes or by a limited number of visits available to calculate VTV-BPV. Moreover, relatively little is known about the determinants and consequences of VTV-BPV in patients with ESRD.

We sought to examine the relation of VTV-BPV with outcomes using data from the HEMO study. The HEMO study, a randomized trial of prevalent patients on maintenance hemodialysis, contains detailed information on clinical characteristics and includes a relatively large number of baseline blood pressure measurements, allowing us to address some of the limitations of previous studies. In addition to describing the degree of VTV-BPV using two distinct metrics – coefficient of variation and average real variability – we aimed to determine clinical correlates of VTV-BPV, and to link VTV-BPV with major health events. We hypothesized that patients with more pronounced VTV-BPV would experience higher rates of all-cause and cardiovascular death.

METHODS

Study Population

Details of the HEMO study have been published previously[18,19]. Briefly, the HEMO study was a randomized clinical trial of 1846 patients receiving hemodialysis between 18 and 80 years of age from 15 U.S. centers. Subjects were enrolled between March 1995 and October 2000 and randomly assigned in a 2x2 factorial design to standard-dose or high-dose equilibrated $Kt/V_{urea,}$ and low-flux or high-flux dialyzer membranes. Subjects were excluded if they had serum albumin concentration ≤2.6 g/dL, residual urea clearance of ≥1.5 mL/min/35L of urea distribution volume, or if they were unable to achieve an equilibrated Kt/V_{urea} of more than 1.30 within 4.5 hours during two of three baseline kinetic modeling sessions. The latter criterion disqualified some prospective subjects of very large body size.

Subjects with unstable angina and/or New York Heart Association (NYHA) Class IV heart failure were also excluded.

Baseline Covariates

Trained HEMO study coordinators collected information on demographics, comorbid conditions, and selected medications. A modified Index of Coexistent Diseases (ICED) score was computed, which aggregates the presence and severity of congestive heart failure, ischemic heart disease, peripheral vascular disease, cerebral vascular disease, 15 other medical conditions and 11 physical impairments. ICED scores range from 0 to 3, with higher scores indicating increasing severity of comorbid conditions[20]. The HEMO study used a modified ICED score excluding diabetes, and accounted for this comorbid condition as a separate covariate.

Information was also available regarding several dialysis-related variables, including vintage, vascular access type, residual kidney function, target (estimated “dry”) weight, interdialytic weight gain, ultrafiltration volume, intradialytic hypotension requiring intervention, and prescribed session length. Baseline serum albumin, calcium, and phosphorus concentrations were also obtained from the clinical records.

Blood Pressure Variability

Blood pressure was measured before (“pre-dialysis”) and after (“post-dialysis”) hemodialysis in a seated position using a sphygmomanometer as per the dialysis unit routine. The devices used to measure blood pressure across participating dialysis facilities were not specified. Baseline pre- and post-dialysis systolic blood pressure (SBP) was defined as the mean of all available pre- and post-dialysis SBP measurements recorded during the pre-randomization period, which ranged from 2 to 56 days. We excluded subjects without pre-dialysis SBP determinations on at least three separate visits (N=2).

Using the mean pre-dialysis SBP from each visit prior to randomization we defined VTV-BPV as the coefficient of variation (CV= standard deviation [SD] of SBP across visits/mean SBP) for our primary analysis. We also performed a companion analysis using the average real variability (ARV), an alternative measure which takes an average of the absolute differences in blood pressure over consecutive visits. Unlike CV, ARV accounts for the order of visits during which blood pressure was measured[21].

Outcomes

Subjects were followed until death from any cause or December 2001 and censored at time of kidney transplant. We also examined death due to cardiovascular cause, censoring subjects for death due to other causes or at the study end. Cause of death was adjudicated by an Outcomes Committee using standardized criteria across centers.

Statistical Methods

We conducted two separate sets of analyses using the SBP CV and ARV as the measure of VTV-BPV. We compared baseline clinical characteristics across quintiles of VTV-BPV using general linear models or the Cochrane-Armitage trend test for trend, as appropriate.

We evaluated the association of baseline characteristics with VTV-BPV, modeled as a continuous variable, using linear regression. We used backward selection to identify predictors of VTV-BPV (in conjunction with several pre-specified factors) in multivariable-adjusted models, removing variables with p-values ≥0.1[22].

We evaluated the association of VTV-BPV modeled as a continuous variable with all-cause and cardiovascular mortality using Cox regression in a series of nested models: (1) unadjusted; (2) adjusted for age, sex, race and mean baseline pre-dialysis SBP (included as a linear and squared term); (3) fully adjusted models, including age, sex, race, mean baseline pre-dialysis SBP, mean baseline post-dialysis SBP, intradialytic hypotension, catheter use, ICED score, vintage, diabetes, heart failure, serum albumin, and the HEMO study intervention group. We chose these covariates because they were pre-specified in the HEMO study, and they differed significantly among quintiles of VTV-BPV or were significantly associated with VTV-BPV as identified above. Analyses were stratified by clinical center. We examined the possibility of non-linear associations of VTV-BPV and outcomes non-parametrically with restricted cubic splines with five knots[23]. To ease interpretation, we present results by VTV-BPV quintiles.

We explored whether mean baseline pre-dialysis SBP modified the association of VTV-BPV with outcomes by including a multiplicative interaction term. Because a significant interaction was identified, we present analyses stratified by mean baseline pre-dialysis SBP category (<140 mm Hg, 140–159 mm hg and ≥160 mm Hg).

We confirmed proportionality assumptions of the Cox regression models using Schoenfeld residuals. We considered two-tailed p-values <0.05 statistically significant. All analyses were conducted with SAS Enterprise Guide 4.3 (Cary, NC).

RESULTS

Of the original 1846 prevalent patients on hemodialysis enrolled in the HEMO study, 1844 had at least three visits with SBP measurements and were included in the present analysis. Visit-to-visit blood pressure variation was calculated using an average of 4.9 ± 1.2 (range, 3 to 13) blood pressure determinations collected over an average of 8.0 ± 4.7 (range 3 to 56) days during the baseline period. The mean pre-dialysis SBP CV was 9.9% ± 4.6%. Patients with higher VTV-BPV were generally older, more often black, and had a higher prevalence of several comorbid conditions including heart failure, hypertension, cerebrovascular disease, and diabetes mellitus (Table 1) compared to patients with lower VTV-BPV. They were also more likely to be on central adrenergic blockers (e.g., clonidine) and nitrates at baseline, and were more likely to experience intradialytic hypotension (Table 1). While most of these variables were significantly associated with VTV-BPV on univariate analysis, multivariable backward selection models identified only black race, history of heart failure, history of diabetes mellitus, lower pre-dialysis SBP, higher post-dialysis SBP, use of a dialysis catheter, and having more frequent intradialytic hypotension as significant predictors of higher VTV-BPV (Table 2).

Median follow-up was 2.5 years (interquartile range [IQR] 1.3 to 4.3 years), during which time there were 869 deaths from any cause and 408 cardiovascular deaths. Patients in the highest quintile of VTV-BPV had higher crude rates of death from any cause and a trend towards higher crude rates of cardiovascular deaths compared to patients in the lowest quintile (Figure 1). In unadjusted models, we found a 31% higher risk of death from any cause per 10% increase in VTV-BPV (Figure 2). This association was attenuated after multivariable adjustment but remained statistically significant. Similarly, we found a 28% higher risk of cardiovascular death per 10% increase in VTV-BPV, which was attenuated and no longer statistically significant in fully adjusted models (Figure 2).

Mean baseline pre-dialysis SBP significantly modified the association of VTV-BPV and outcomes. In stratified models, patients in the lowest category of pre-dialysis SBP (<140 mm Hg) had a 55% higher risk of death from any cause and 70% higher risk of cardiovascular death per 10% increase in VTV-BPV, while among patients in the two higher categories of baseline pre-dialysis SBP, there was no significant association between VTV-BPV and all-cause or cardiovascular death (Figure 3).

Average Real Variability

The mean pre-dialysis SBP ARV was 13.6 (SD 7.5) mmHg. Subjects with higher ARV were older, more often female, black, and had a higher prevalence of heart failure, other cardiovascular disease, hypertension, cerebrovascular disease, and diabetes mellitus compared to patients with lower ARV (Supplemental Table 1). Subjects with higher ARV were also more likely to use antihypertensive medications and had higher mean baseline pre- and post-dialysis SBP. Multivariable backward selection identified other cardiovascular disease, diabetes mellitus, respiratory disease, use of any antihypertensive medications, higher pre-dialysis SBP, higher post-dialysis SBP and more frequent intradialytic hypotension as significant predictors of higher ARV (Supplemental Table 2). Similar to the results with using CV as the measure of VTV-BPV, higher ARV was associated with a higher risk of death and cardiovascular death, particularly in patients with lower mean pre-dialysis SBP (Supplemental Table 3).

DISCUSSION

Our analysis of prevalent patients on maintenance hemodialysis shows that black race, a history of heart failure and diabetes mellitus, catheter use and having more frequent intradialytic hypotension are associated with higher visit-to-visit blood pressure variability (VTV-BPV), when using the coefficient of variation (CV) in systolic blood pressure (SBP) as the VTV-BPV metric. We also show that each 10% increase in VTV-BPV was associated with an 18% higher risk of death from any cause and a trend towards a higher risk of cardiovascular death, particularly in patients with lower baseline SBP. Using the average real variability (ARV) in SBP as an alternative measure of VTV-BPV yielded more modest but qualitatively similar associations.

The average pre-dialysis SBP CV in our cohort was 9.9%, markedly higher than the 6.1% reported in the general U.S. population[11], but similar to the average pre-dialysis SBP CV reported in other studies conducted in dialysis populations[7,24,25]. While the presence and

longer duration of diabetes mellitus is consistently associated with higher VTV-BPV in patients with and without significant kidney disease[24–26], other determinants of higher VTV-BPV have yet to be delineated from the available data. In non-ESRD populations, older age is associated with higher blood pressure variability[11,27–29], but this association has not been consistently seen in studies of patients with ESRD[24], including in the current analysis. The reasons for this discrepancy could stem from the observation that older patients with chronic kidney disease (CKD) (and cardiovascular disease) are more likely to die than to initiate dialysis [30]. Importantly, our analysis demonstrates an association between central venous catheter use, a potentially modifiable risk factor, and higher VTV-BPV. Whether the catheter-BPV association reflects the severity of underlying vascular disease or another aspect of ill health is unknown, but provides yet another reason to minimize catheter use.

A recent meta-analysis of randomized clinical trials showed that inter-individual blood pressure variability was higher with the use of angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, and beta-blockers and lower with the use of calcium channel blockers[31]. However, a recent Italian study of patients with CKD showed that a higher proportion of patients in the highest quartile of SBP CV used angiotensin II receptor blockers and calcium channel blockers[28]. In contrast, we found no significant differences in the baseline use of angiotensin converting enzyme inhibitors, angiotensin II receptor blockers or calcium channel blockers across quintiles of SBP CV, consistent with two prior studies of patients on hemodialysis[7,25]. Therefore, the association among the class of antihypertensive medication used and BPV remains unclear, particularly in patients on hemodialysis, and requires further prospective study.

Our finding that SBP CV is independently associated with mortality and with a trend towards cardiovascular mortality is consistent with and extends the findings from the few prior studies conducted in ESRD populations[7,8,24,25]. For example, a recent observational study of 1088 prevalent patients on hemodialysis in Italy showed that higher VTV-BPV (assessed using the CV of mean pre-dialysis SBP) was associated with a significantly higher risk of cardiovascular mortality[24]. In that study, however, it is unclear how many blood pressure measurements were available for calculation of blood pressure variability, and all patients were white race with a relatively low prevalence of diabetes mellitus (30%). Similarly, a secondary analysis of 388 participants in the Fosinopril in Dialysis (FOSIDIAL) study, a randomized trial comparing fosinopril to placebo in patients on hemodialysis with left ventricular hypertrophy[7], demonstrated an increased risk of the composite outcome of cardiovascular events or cardiovascular death associated with higher pre-dialysis SBP CV. However, that study was limited by a relatively low density of available blood pressure measurements (17 blood pressures over 24 months, or 1.4 measurements per month), and were ascertained during the same time frame as the outcomes of interest. In contrast, for the current analysis, we had access to an average of five visits with blood pressure determination, which were all ascertained prior to the observation window for outcome ascertainment.

The findings from our study and previous analysis in dialysis populations are consistent with a majority of studies in non-ESRD cohorts showing that higher VTV-BPV is independently

associated with a higher risk for adverse outcomes including death, cardiovascular events[11,12,32], and CKD[26,33]. However, a recent analysis of patients with hypertension demonstrated no association of BPV with carotid intima medial thickness or cardiovascular outcomes[29]. Another recent study of ambulatory blood pressure monitoring noted that BPV over 24 hours yielded little prognostic value after adjustment for mean SBP and covariates[27].

While our analysis has several strengths, there are also limitations. First, while several baseline blood pressure determinations were available on which to base our definitions of VTV-BPV, we did not have blood pressure information from all of the thrice weekly dialysis sessions, nor did we have blood pressure information on non-dialysis days. Consistent recording of blood pressures after the "weekend stretch" (i.e., Friday to Monday or Saturday to Tuesday), might have yielded even higher VTV-BPV. Second, although we had detailed information on baseline comorbid conditions including a history of heart failure, we did not have information on left ventricular ejection fraction or diastolic dysfunction. Third, while we had a record of baseline antihypertensive medication use, we had no information on the timing or dose of medication use and medication adherence, which are also associated with blood pressure variability[34]. Fourth, we were unable to distinguish patients with cardiorenal syndrome types 2 and 4 (in other words, whether heart failure was a contributing cause or complication of ESRD). Finally, because of exclusion criteria and the fact that HEMO was a randomized clinical trial, these subjects are not fully representative of the general hemodialysis population.

In summary, in a diverse, well-dialyzed cohort of prevalent patients on maintenance hemodialysis, VTV-BPV, assessed using metrics of variability in pre-dialysis SBP, was associated with a higher risk of all-cause mortality and a trend towards higher risk of cardiovascular mortality, particularly in patients with a lower baseline SBP. A better understanding of modifiable determinants of VTV-BPV and prospective testing of interventions that reduce VTV-BPV – in ESRD and non-ESRD hypertensive populations, will be required to establish the importance of this phenomenon.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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SUMMARY TABLE

What is known about this topic

Patients with end-stage kidney disease requiring dialysis have very high visit-to-visit blood pressure variability and are at high risk for death and cardiovascular events.

Higher visit-to-visit blood pressure variability has been independently linked to higher risks of death and cardiovascular events in studies conducted mostly in patients without chronic kidney disease.

What this study adds

- Our study is one of the few to focus on visit-to-visit blood pressure variability in patients on maintenance hemodialysis.
- Our study shows that higher visit-to-visit blood pressure variability is associated with a higher risk of death from any cause and a trend towards high risk of cardiovascular death. This association is particularly important in patients with lower baseline systolic blood pressure.
- Our results suggest that potentially modifiable risk factors such as central venous catheter use is associated with higher visit-to-visit blood pressure variability, which could be tested in future intervention trials.

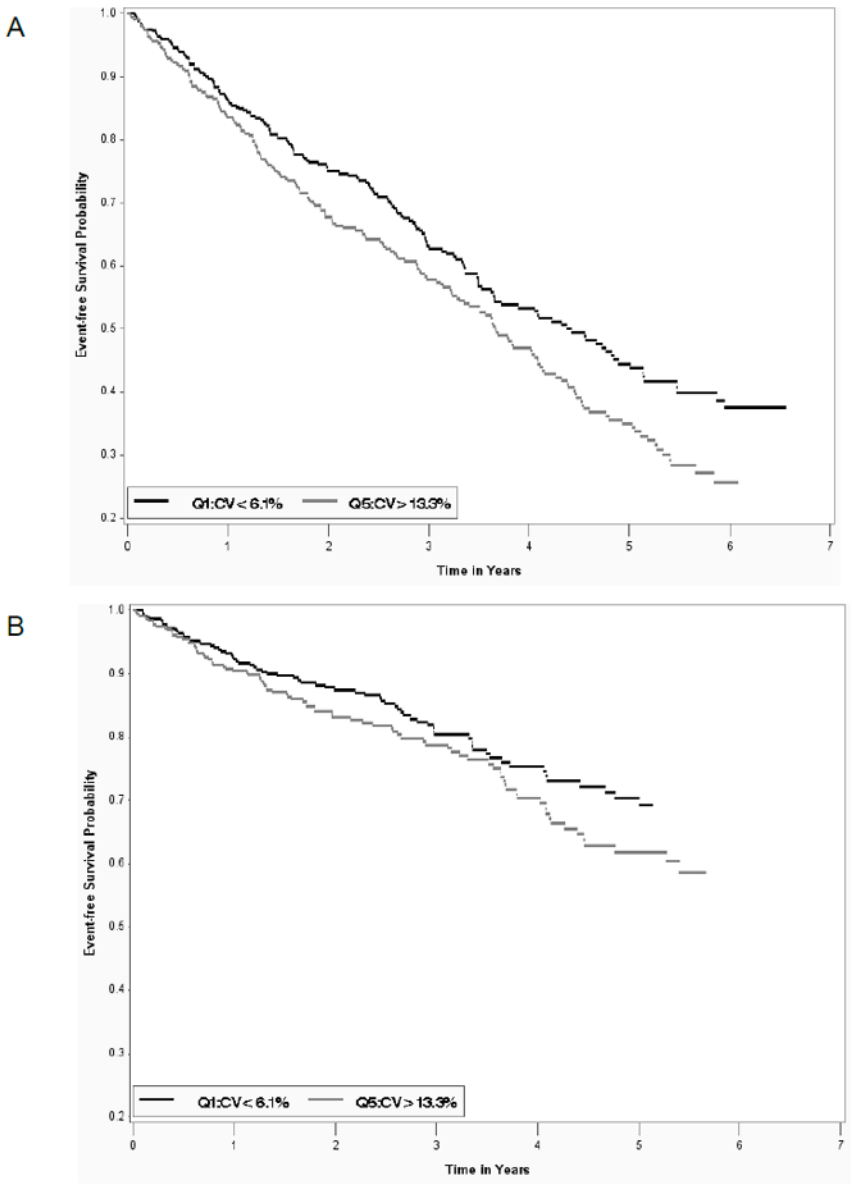

Figure 1.

Kaplan-Meier survival plots for patients in the lowest (Q1) versus highest (Q5) quintiles of visit-to-visit pre-dialysis systolic blood pressure variability for (A) death from any cause P=0.01 and (B) cardiovascular death p=0.09.

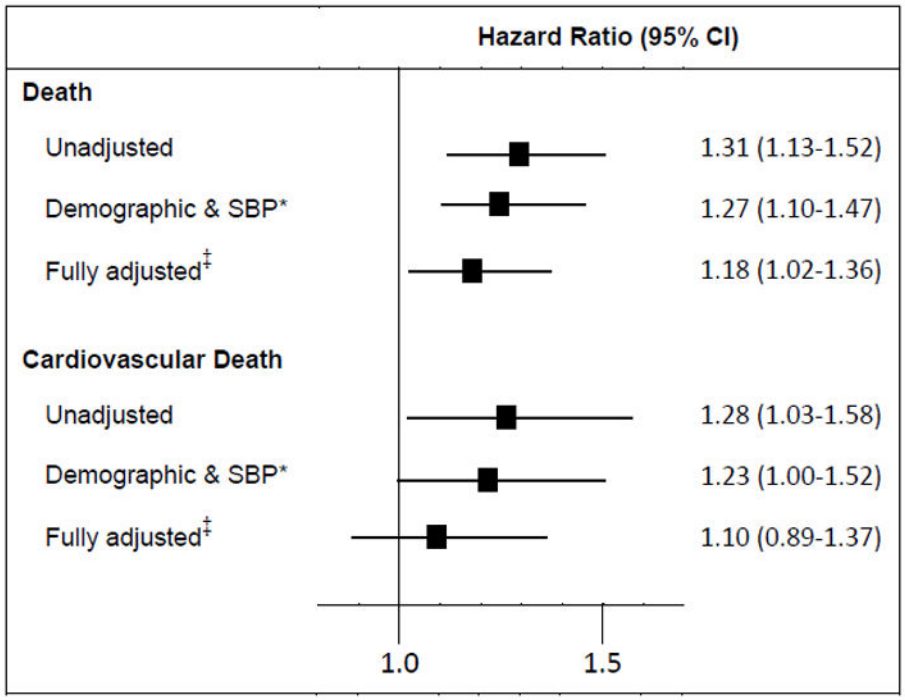

Figure 2.

Hazard ratio per 10% increase in visit-to-visit pre-dialysis systolic blood pressure coefficient of variation

*adjusted for age, sex, race, baseline mean pre-dialysis systolic blood pressure

‡ adjusted for age, sex, race, baseline mean pre-dialysis systolic blood pressure, mean baseline post-dialysis SBP, intradialytic hypotension, catheter use, ICED score, vintage, diabetes, heart failure, albumin, and intervention group.

All models stratified by clinical center.

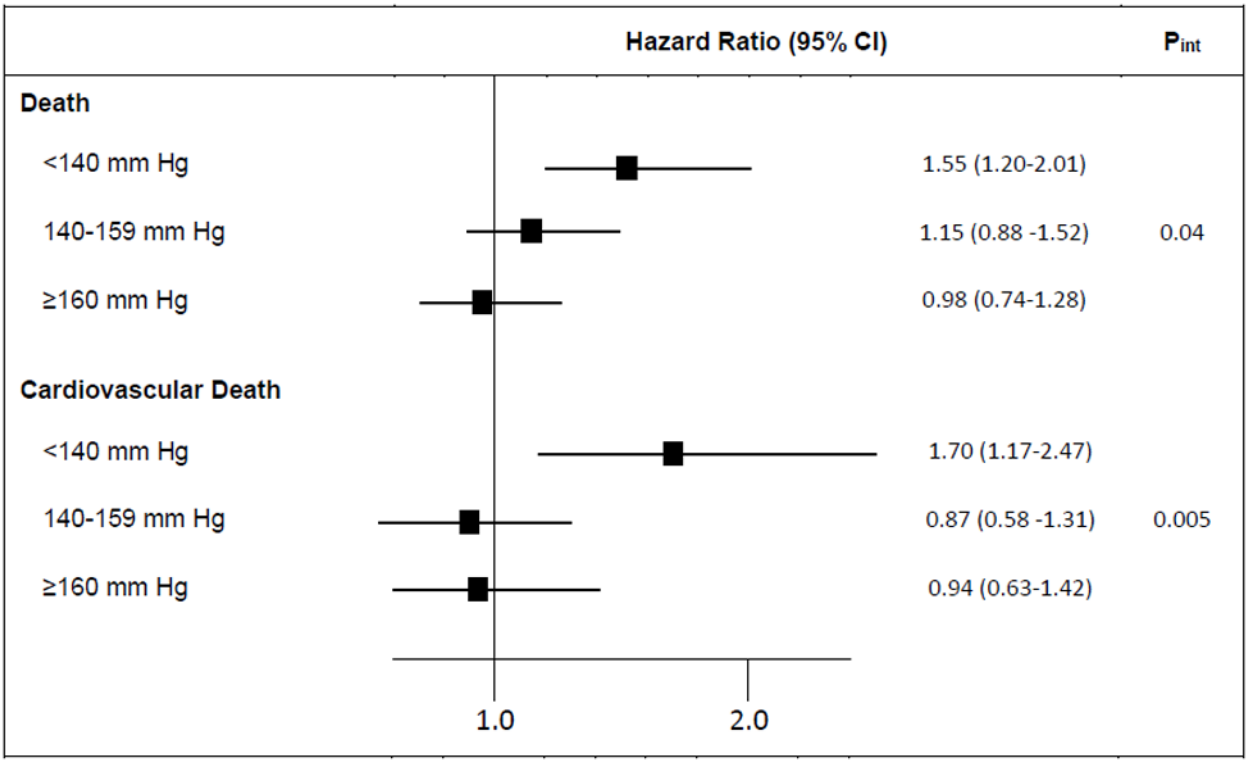

Figure 3.

Fully adjusted* hazard ratios (95% CI) per 10 % increase in visit-to-visit pre-dialysis systolic blood pressure coefficient of variation, stratified by category of pre-dialysis systolic blood pressure.

*Adjusted for age, sex, race, baseline mean pre-dialysis systolic blood pressure (including SBP squared term), mean baseline post-dialysis SBP, intradialytic hypotension, catheter use, ICED score, vintage, diabetes, heart failure, albumin, and intervention group; all models stratified by clinical center. P_{int} = p-value for interaction

Table 1

Baseline characteristics by visit-to-visit pre-dialysis systolic blood pressure quintile of coefficient of variation

	Pre-Dialysis Systolic Blood Pressure Coefficient of Variation Quintile					
	Q1 (<6.1%) N=368	**Q2 (6.1–8.0%) N=369**	**Q3 (8.0–10.3%) N=369**	**Q4 (10.4–13.3%) N=369**	**Q5 (>13.3%) N=368**	**p- trend**
Age, y, mean (SD)	57.5 (14.5)	56.1 (14.4)	57.9 (13.9)	57.2 (13.9)	59.5 (13.4)	0.02
Female	56.6	53.4	55.3	55.0	60.7	0.23
Black race	56.4	63.1	61.5	68.6	63.7	0.01
Married	42.3	40.9	37.4	35.5	38.2	0.09
Education <12 years	36.6	37.4	34.4	39.0	43.1	0.07
Currently working	9.2	10.0	10.6	8.9	6.2	0.13
Cause of ESRD						
Diabetes	33.9	35.0	34.4	39.0	43.4	
Hypertension	28.7	31.7	32.3	34.2	32.0	
Glomerulonephritis	15.5	14.6	16.0	10.8	11.9	0.02
Other	22.0	18.7	17.3	16.0	12.7	
Ill in week before enrollment	23.0	23.0	24.4	26.6	21.4	0.97
Body mass index (kg/m^2)	25.2 (5.2)	25.8 (5.2)	25.3 (4.9)	25.5 (5.2)	25.4 (5.7)	0.87
Comorbid Conditions						
Ischemic heart disease	36.9	37.1	43.6	37.7	41.2	0.25
Heart failure	36.9	36.9	38.5	40.7	45.5	0.01
Arrhythmias	30.4	31.2	30.9	29.8	32.3	0.75
Other cardiovascular disease	62.6	59.6	62.6	61.0	69.1	0.07
Hypertension	94.3	95.4	96.2	97.0	97.3	0.02
Cerebrovascular disease	15.7	18.2	20.9	21.1	21.4	0.03
Peripheral vascular disease	23.9	27.1	25.2	24.1	28.2	0.43
Diabetes mellitus	40.1	42.0	42.0	47.7	51.0	<0.01
Respiratory disease	15.7	14.4	15.2	13.6	18.2	0.49
Musculoskeletal disease	41.2	45.5	43.6	44.2	44.7	0.49
Non-vascular nervous system disease	36.6	36.0	33.3	39.3	40.7	0.15

	Pre-Dialysis Systolic Blood Pressure Coefficient of Variation Quintile					
	Q1 (<6.1%) N=368	**Q2 (6.1–8.0%) N=369**	**Q3 (8.0–10.3%) N=369**	**Q4 (10.4–13.3%) N=369**	**Q5 (>13.3%) N=368**	**p- trend**
Gastrointestinal disease	32.5	36.3	37.1	38.8	39.0	0.05
Hepatic disease	17.1	16.0	19.0	19.8	15.5	0.93
Urinary tract disease	9.5	7.9	7.1	6.8	6.0	0.06
Malignancy	7.3	6.2	12.2	8.9	10.0	0.08
Ophthalmological disease	28.2	25.8	26.6	30.1	33.6	0.04
Hematological disease	4.9	3.0	3.3	4.6	4.6	0.74
On transplant list	21.1	19.2	22.0	19.5	16.0	0.12
History of smoking	46.3	49.9	49.1	51.8	51.5	0.14
History of drug abuse	7.6	8.9	6.5	9.5	6.5	0.72
History of alcohol abuse	13.6	16.5	14.1	19.6	16.5	0.14
ICED Score						
0–1	38.3	36.0	36.3	32.5	35.0	
2	30.2	32.3	32.87	32.3	29.0	0.70
3	31.5	31.7	30.9	35.2	36.0	
Labs						
Albumin (g/dL), mean (SD)	3.6 (0.4)	3.6 (0.4)	3.6 (0.4)	3.6 (0.4)	3.6 (0.4)	0.08
Calcium (mg/dL), mean (SD)	9.3 (1.0)	9.3 (1.0)	9.3 (0.9)	9.2 (1.0)	9.3 (1.0)	0.35
Phosphorus (mg/dL), mean (SD)	5.8 (2.0)	5.9 (2.0)	5.8 (1.8)	5.8 (1.8)	5.7 (1.7)	0.35
Medications						
ACEI or ARB	26.8	22.8	22.2	30.9	28.2	0.13
Beta blocker	28.7	24.1	33.6	33.3	30.1	0.11
Calcium channel blocker	49.6	49.9	45.8	49.1	52.0	0.62
Minoxidil	1.1	0.5	2.7	1.9	2.4	0.06
Central adrenergic blockers	3.3	1.6	2.4	4.3	5.2	0.03
Nitrates	14.4	17.1	17.3	16.3	20.9	0.05
Alpha blockers	6.5	4.1	7.6	8.4	7.3	0.15
# of antihypertensive classes						
0	32.3	31.2	29.0	25.8	27.9	

	Pre-Dialysis Systolic Blood Pressure Coefficient of Variation Quintile					
	Q1 (<6.1%) N=368	**Q2 (6.1–8.0%) N=369**	**Q3 (8.0–10.3%) N=369**	**Q4 (10.4–13.3%) N=369**	**Q5 (>13.3%) N=368**	**p- trend**
1	38.8	43.9	39.8	43.6	37.1	0.11
2	23.0	21.7	24.7	23.6	26.0	
3+	6.0	3.3	6.5	7.1	8.9	
Erythropoietin	92.7	89.7	90.0	91.1	89.4	0.28
Aspirin	29.3	27.1	29.0	26.8	27.6	0.63
Coumadin	7.1	9.2	8.9	10.3	10.6	0.09
Vitamin D	51.0	58.3	50.4	55.6	56.9	0.26
Dialysis-Related Variables						
Vintage, years, median (IQR)	2.1 (0.9–4.4)	2.4 (1.0–4.9)	2.1 (1.0–3.9)	2.2 (1.0–5.1)	2.1 (0.9–4.6)	0.46
Access type						
Fistula	36.3	37.1	32.5	32.8	32.5	
Graft	58.5	57.5	59.9	60.7	58.8	0.49
Catheter	5.2	5.4	7.6	6.5	8.7	
Residual renal function adjusted to Watson V (ml/min per 35L)	0.2 (0.4)	0.3 (0.6)	0.2 (0.4)	0.2 (0.4)	0.2 (0.4)	0.28
Dry weight (Kg)	67.9 (14.1)	70.8 (15.5)	68.2 (14.0)	69.4 (14.0)	68.3 (15.4)	0.81
Ultrafiltration (Kg)	2.9 (1.0)	3.0 (1.0)	2.9 (1.0)	3.0 (1.0)	2.8 (1.1)	0.77
Kg over dry weight at start of dialysis	3.1 (1.4)	3.1 (1.5)	3.2 (1.5)	3.2 (1.4)	3.1 (1.5)	0.87
Pre-dialysis systolic blood pressure (mm Hg)	152 (21)	150 (20)	152 (21)	152 (20)	151 (19)	0.75
Pre-dialysis diastolic blood pressure (mm Hg)	81 (11)	81 (11)	81 (12)	82 (12)	80 (11)	0.41
Post-dialysis systolic blood pressure (mm Hg)	137 (19)	137 (20)	138 (22)	137 (20)	139 (20)	0.26
Post-dialysis diastolic blood pressure (mm Hg)	74 (11)	75 (11)	75 (11)	74 (11)	74 (12)	0.91
≥ 1 episode intradialytic hypotension	44.4	46.9	49.1	48.8	54.7	0.01
Kt/v	1.6 (0.2)	1.6 (0.2)	1.6 (0.2)	1.6 (0.2)	1.6 (0.2)	0.36
Prescribed time, minutes	217 (23)	221 (23)	216 (24)	217 (22)	217 (23)	0.32
≥1 session with shortened time	10.9	15.5	13.0	14.4	9.8	0.5
Randomization group						
High dose	45.8	49.3	53.7	50.4	50.1	0.24
High flux membrane	48.5	52.9	47.2	48.2	52.6	0.67

All values are % or mean (SD) unless otherwise noted. SD = standard deviation; IQR = interquartile range

Table 2

Selected variables and their associations with visit-to-visit pre-dialysis systolic blood pressure coefficient of variation. Variables selected for inclusion in multivariable-adjusted model using backward selection.

	Univariate			Multivariable		
Variable	**β**	**Standard error**	**p**	**β**	**Standard error**	**p**
Age	0.20	0.08	0.01	-	-	-
Female	0.41	0.22	0.06	-	-	-
Black race	0.46	0.22	0.04	0.46	0.22	0.04
Comorbid Conditions						
Heart failure	0.61	0.22	0.01	0.50	0.22	0.02
Other cardiovascular disease	0.49	0.22	0.03	-	-	-
Hypertension	1.04	0.55	0.06	-	-	-
Cerebrovascular disease	0.50	0.27	0.07	-	-	-
Diabetes mellitus	0.63	0.22	<0.01	0.50	0.23	0.03
Ophthalmological disease	0.45	0.24	0.06	-	-	-
Baseline Medications						
Minoxidil	1.73	0.82	0.03	-	-	-
Adrenergic blockers	1.18	0.59	0.05	-	-	-
# of hypertensive medication classes	0.30	0.12	0.01	-	-	-
Dialysis-related variables						
Uses catheter	1.00	0.43	0.02	0.92	0.43	0.03
Pre-dialysis systolic blood pressure	−0.006	0.0053	0.2	−0.02	0.0074	0.002
Post-dialysis systolic blood pressure	0.004	0.005	0.4	0.02	0.0076	0.004
≥1 episode of intradialytic hypotension	0.62	0.21	0.004	0.70	0.23	0.002
Prescribed Rx time (per min)	−0.01	0.00	0.07	−	-	-
Albumin (per 0.1 g/dL)	−6.31	2.97	0.03	-	-	-

Note: mean pre-dialysis SBP CV was 9.9% (SD=4.6%)