AMBULATORY ARTERIAL STIFNESS PARAMETERS PREDICT CARDIOVASCULAR AND ALL-CAUSE MORTALITY BETTER THAN OFFICE AND AMBULATORY BLOOD PRESSURE IN HEMODIALYSIS PATIENTS

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INTRODUCTION AND AIMS

Patients with end-stage renal disease have extremely high rates of cardiovascular events and mortality compared not only to general population, but also to patients with diabetes mellitus, cardiovascular disease or cancer [1]. Arterial stiffness and augmentation of the aortic blood pressure (BP) component measured in office conditions are known cardiovascular risk factors in hemodialysis patients [2]. All devices measuring arterial stiffness and central BP indexes use brachial BP for calibration of the aortic waveforms, such measurements are subject to errors inserted by pre- or post- dialysis office BP readings [3]. This study examines the prognostic significance of ambulatory brachial and central BP, ambulatory pulse wave velocity (PWV), and ambulatory heart-rate-adjusted augmentation index (AIx75) in this population.

METHODS

In this prospective cohort study, 170 hemodialysis patients underwent 48-hour ambulatory monitoring with Mobil-O-Graph NG device during a standard inter-dialytic interval and followed-up for a mean of 28.1±11.2 months. The primary end-point was a combination of all-cause death, non-fatal myocardial infarction and non-fatal stroke. Secondary end-points included: (i) all-cause mortality; (ii) cardiovascular mortality; (iii) a combined outcome of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, resuscitation after cardiac arrest, coronary revascularization or hospitalization for heart failure.

RESULTS

Baseline demographic, anthropometric, clinical and routine laboratory characteristics are presented in Table 1. During follow-up, 37 (21.8%) patients died and 46 (27.1%) had a cardiovascular event or died from cardiovascular causes (Table 2). Cumulative freedom from primary end-point was not different for quartiles of pre-dialysis SBP, 48-hour peripheral SBP and central SBP, but was progressively shorter with higher central PP, ambulatory PWV and AIx75 (Figures 1-2). Similarly, the Hazard Ratios for all-cause-mortality, cardiovascular mortality, and the combined outcome of cardiovascular events were similar for quartiles of predialysis SBP, 48-hour peripheral SBP and 48-hour central SBP, but were progressively increasing with higher quartiles of ambulatory PWV and ambulatory AIx75 (Figures 3-5). In multivariate Cox-regression analysis 48h-ambulatory-PWV was the only vascular parameter independently associated with occurrence of the primary end-point (Table 3).

Parameter	Value	Parameter		Value
N	170	N		170
Age (years)	63.76±14.32	Albumin (g/L)		40.2±3.9
Mean follow up (months)	28.09±11.16	RAAS blockers (n, %)	ARBs	32 (18.8%)
Female (n, %)	69 (40.6%)		ACEIs	12 (7.1%)
Weight (kg)	73.04±14.93		Renin Inhibitors	1 (0.6%)
Height (cm)	168.16±8.93	Aldosterone blockers (n, %)		2 (1.2%)
BMI (kg/m^2)	26.06±5.76	CCBs (n, %)		89 (52.4%)
Dialysis vintage (months)	26 (3-180)	Loop Diuretics (n, %)		65 (38.2%)
Diabetes mellitus (n, %)	54 (31.8%)	B-blockers (n, %)		87 (51.2%)
Hypertension (n, %)	141 (82.9%)	Central Active (n, %)		33 (19.4%)
Dyslipidemia (n, %)	46 (27.1%)	Erythropoietin (n, %)		134 (78.8%)
Peripheral Vascular Disease (n, %)	11 (6.5%)	Statins (n, %)		72 (42.4%)
Coronary Heart Disease (n, %)	38 (22.4%)	Pre HD SBP (mmHg)		145.2±23.09
Heart Failure (n, %)	14 (8.2%)	48h pSBP (mmHg)		133.2±17.0
Stroke History (n, %)	15 (8.8%)	48h pDBP (mmHg)		78.9±11.1
Smoking (n, %)	29 (17.1%)	48h cSBP (mmHg)		120.9±14.8
Serum Urea Nitrogen (mmol/L)	23.26±6.22	48h cDBP (mmHg)		80.4±11.27
Serum Creatinine (μmol/L)	729.5±214.0	48h pPP (mmHg)		54.3±13.2
URR (%)	68.83 (40.41-85.71)	48h cPP (mmHg)		40.5±9.5
Serum Calcium (mmol/L)	2.25±0.18	48h heart rate (bpm)		73±10
Serum Phosphate (mmol/L)	1.75±1.06	48h PWV		9.4±2.2
Parathormone (ng/L)	295.07±210.26	48h AIx(75)		26.7±7.5
Hemoglobin (g/L)	113.1±12.7	UF rate (ml/h/kg)		7.38±4.07

Table 1: Baseline demographic, anthropometric, clinical and routine laboratory characteristics of the population studied

Parameter		Value
Myocardial Infarction (n,%)	Fatal	5 (2.9%)
	Non-Fatal	7 (4.1%)
Stroke (n,%)	Fatal	4 (2.4%)
	Non-Fatal	7 (4.1%)
Sudden Death (n,%)		19 (11.2%)
Resuscitation after cardiac arrest (n,%)		2 (1.2%)
Coronary revascularization procedure (n,%)		5 (2.9%)
Hospitalization for acute decompensated heart failure (n,%)		9 (5.3%)
All-cause Death (n,%)		37 (21.8%)
Cardiovascular Death (n,%)		28 (16.5%)
All-cause Death or non-fatal MI or non-fatal Stroke (n,%)		48 (28.2%)
Cardiovascular Death or non-fatal MI or non-fatal Stroke (n,%)		39 (22.9%)
Cardiovascular death, or non-fatal MI or non-fatal Stroke or resuscitation after cardiac arrest or coronary revascularization or hospitalization for heart failure (n,%)		46 (27.1%)

Table 2: Outcomes of interest and study endpoints during follow up in the total population

Parameter	Univariate analysis			Multivariate analysis		
	Unadjusted Hazard Ratio	95% CIs	p	Adjusted Hazard Ratio	95% CIs	p
Age >75 years	3.110	1.757 to 5.503	<0.001	0.437	0.152 to 1.252	0.123
Female	1.341	0.761 to 2.363	0.310			
BMI (per kg/m^2 increase)	0.914	0.854 to 0.979	0.011	0.900	0.834 to 0.971	0.006
Dialysis Vintage (per month increase)	0.990	0.981 to 1.000	0.052	0.996	0.986 to 1.006	0.444
Diabetes	1.918	1.083 to 3.397	0.026	1.752	0.825 to 3.721	0.144
Hypertension	1.025	0.480 to 2.191	0.949			
Dyslipidemia	0.785	0.400 to 1.541	0.482			
Heart Failure	1.187	0.486 to 3.306	0.742			
Coronary Heart Disease	1.781	0.967 to 3.280	0.064	1.573	0.752 to 3.290	0.229
Peripheral Vascular Disease	1.848	0.732 to 4.669	0.194	2.428	0.723 to 8.160	0.151
History of Stroke	0.931	0.334 to 2.591	0.891			
Smoking	0.891	0.393 to 2.020	0.783			
Hemoglobin (per gr/L increase)	0.965	0.943 to 0.987	0.002	0.970	0.945 to 0.995	0.020
Serum Albumin (per gr/L increase)	0.907	0.843 to 0.976	0.009	0.947	0.871 to 1.030	0.202
Serum Parathormone (per ng/L increase)	1.000	0.998 to 1.001	0.599			
preHD SBP (per mmHg increase)	0.993	0.981 to 1.005	0.261			
48h Peripheral MAP (per mmHg increase)	0.990	0.968 to 1.013	0.402			
48h Central SBP (per mmHg increase)	0.994	0.975 to 1.013	0.531			
48h Central DBP (per mmHg increase)	0.968	0.944 to 0.993	0.012	0.976	0.941 to 1.012	0.186
48h Central PP (per mmHg increase)	1.027	0.999 to 1.055	0.058	0.951	0.901 to 1.005	0.075
48h Heart Rate (per bpm increase)	0.991	0.962 to 1.020	0.542			
48h PWV (per m/s increase)	1.410	1.225 to 1.623	<0.001	1.579	1.187 to 2.102	0.002
48h AIx(75) (per % increase)	1.046	1.009 to 1.085	0.015	0.998	0.943 to 1.055	0.940
Use of antihypertensive medications	0.608	0.303 to 1.220	0.162	0.691	0.308 to 1.547	0.368

Table 3: Univariate and multivariate Cox regression analysis for occurrence of the primary end-point (all-cause death or myocardial infarction or stroke) in the total studied population

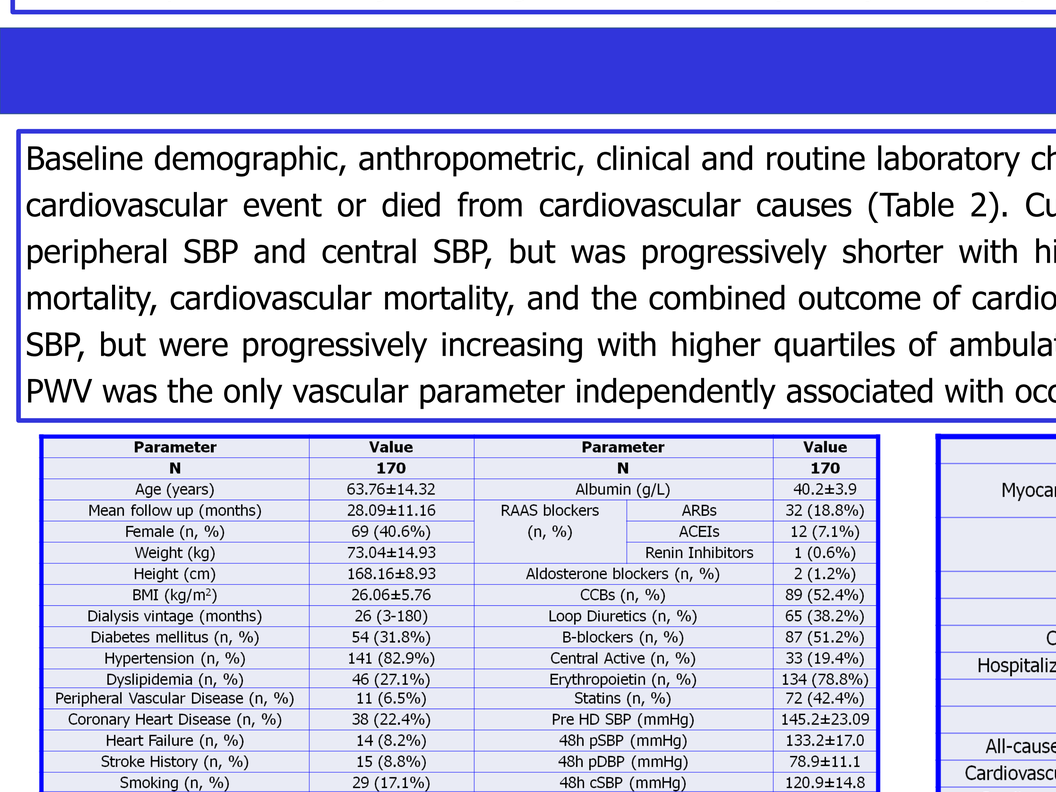
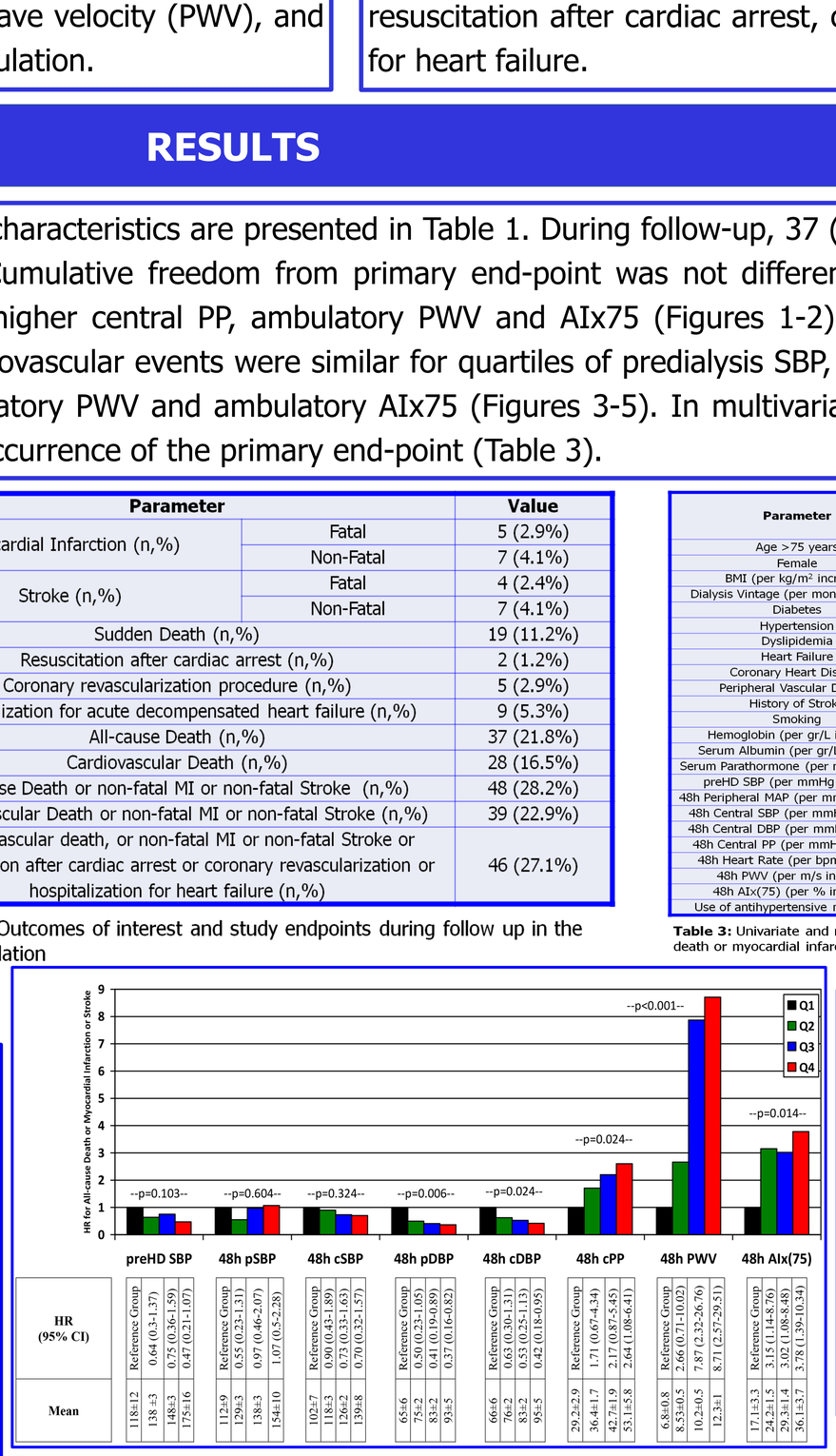
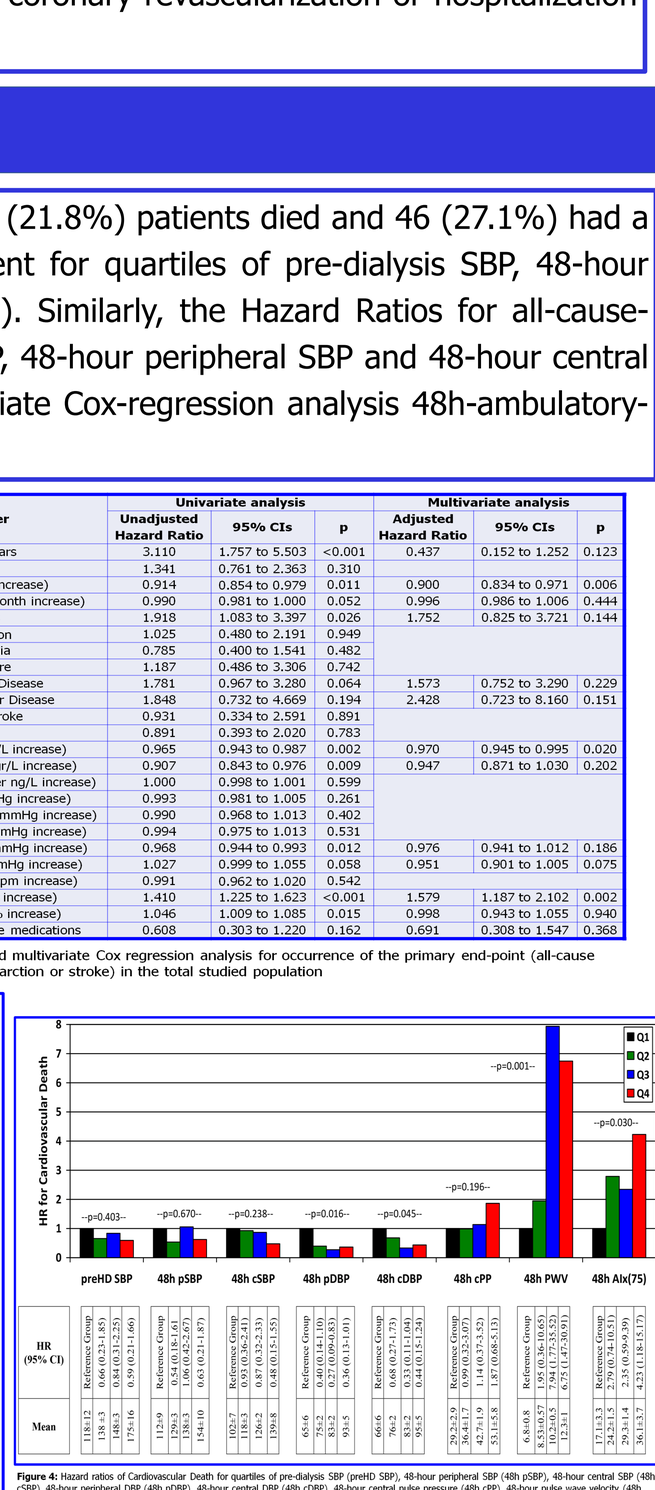


Figure 1: Kaplan Meier survival curves and Life tables for occurrence of the primary end-point (all-cause death or myocardial infarction or stroke) and (A) 48h ambulatory central systolic blood pressure (48h cSBP), (B) 48h ambulatory central diastolic blood pressure (48h cDBP) (C) 48h ambulatory central pulse pressure (48h cPP), (D) 48h ambulatory pulse wave velocity (48h PWV) and (E) 48h ambulatory heart rate–adjusted augmentation index [48h AIx(75)]



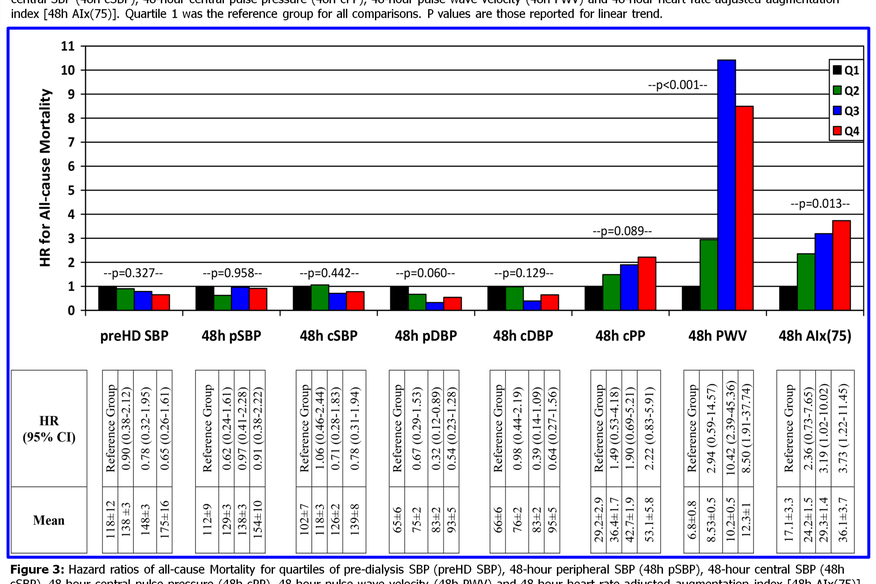
	preHD SBP	48h pSBP	48h cSBP	48h pDBP	48h cDBP	48h cPP	48h PWV	48h AIx(75)
HR (95% CI)	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group
	0.64 (0.3-1.37)	0.55 (0.23-1.31)	0.90 (0.43-1.89)	0.50 (0.23-1.05)	0.63 (0.30-1.31)	1.71 (0.67-4.34)	2.66 (0.71-10.02)	3.15 (1.14-8.76)
	0.75 (0.36-1.59)	0.97 (0.46-2.07)	0.73 (0.33-1.63)	0.41 (0.19-0.89)	0.53 (0.25-1.13)	2.17 (0.87-5.45)	7.87 (2.32-26.76)	3.02 (1.08-8.48)
	0.47 (0.21-1.07)	1.07 (0.5-2.28)	0.70 (0.32-1.57)	0.37 (0.16-0.82)	0.42 (0.18-0.95)	2.64 (1.08-6.41)	8.71 (2.57-29.51)	3.78 (1.39-10.34)
Mean	118±12	112±9	102±7	65±6	66±6	29.2±2.9	6.8±0.8	17.1±3.3
	138 ±3	129±3	118±3	75±2	76±2	36.4±1.7	8.53±0.5	24.2±1.5
	148±3	138±3	126±2	83±2	83±2	42.7±1.9	10.2±0.5	29.3±1.4
	175±16	154±10	139±8	93±5	95±5	53.1±5.8	12.3±1	36.1±3.7

Figure 2: Hazard ratios of all-cause death or myocardial infarction or stroke for quartiles of pre-dialysis SBP 48-hour peripheral SBP (48h pSBP), 48-hour central SBP (48h cSBP), 48-hour central pulse pressure (48h cPP), 48-hour pulse wave velocity (48h PWV) and 48-hour heart rate-adjusted augmentation index [48h AIx(75)]. Quartile 1 was the reference group for all comparisons. P values are those reported for linear trend.



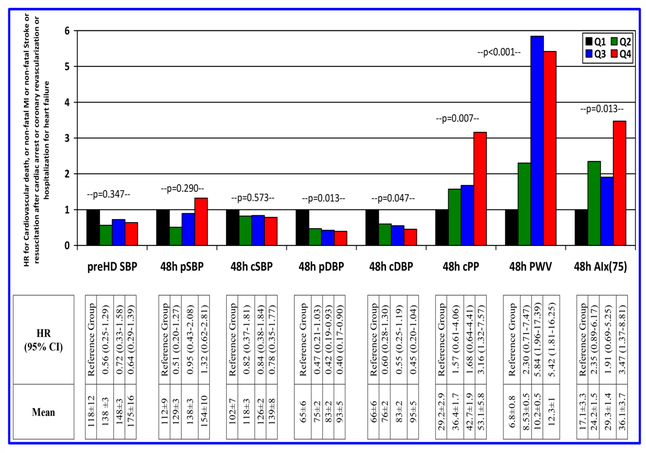
	preHD SBP	48h pSBP	48h cSBP	48h pDBP	48h cDBP	48h cPP	48h PWV	48h AIx(75)
HR (95% CI)	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group
	0.66 (0.23-1.85)	0.84 (0.31-2.25)	0.93 (0.36-2.41)	0.40 (0.14-1.10)	0.68 (0.27-1.73)	0.99 (0.32-3.07)	1.14 (0.37-3.52)	1.87 (0.68-5.13)
	0.59 (0.21-1.66)	1.06 (0.42-2.67)	0.87 (0.32-2.33)	0.32 (0.09-1.03)	0.33 (0.11-1.04)	0.44 (0.15-1.24)	1.95 (0.36-10.65)	2.35 (0.59-9.39)
	0.63 (0.21-1.87)	0.54 (0.18-1.61)	0.48 (0.15-1.55)	0.36 (0.13-1.01)	0.44 (0.15-1.24)	0.63 (0.21-1.87)	7.94 (1.77-35.52)	6.75 (1.47-30.91)
Mean	118±12	112±9	102±7	65±6	66±6	29.2±2.9	6.8±0.8	17.1±3.3
	138 ±3	129±3	118±3	75±2	76±2	36.4±1.7	8.53±0.5	24.2±1.5
	148±3	138±3	126±2	83±2	83±2	42.7±1.9	10.2±0.5	29.3±1.4
	175±16	154±10	139±8	93±5	95±5	53.1±5.8	12.3±1	36.1±3.7

Figure 4: Hazard ratios of Cardiovascular Death for quartiles of pre-dialysis SBP (preHD SBP), 48-hour peripheral SBP (48h pSBP), 48-hour central SBP (48h cSBP), 48-hour peripheral DBP (48h pDBP), 48-hour central DBP (48h cDBP), 48-hour central pulse pressure (48h cPP), 48-hour pulse wave velocity (48h PWV) and 48-hour heart rate-adjusted augmentation index (48h AIx75). Quartile 1 was the reference group for all comparisons. P values are those reported for linear trend



	preHD SBP	48h pSBP	48h cSBP	48h pDBP	48h cDBP	48h cPP	48h PWV	48h AIx(75)
HR (95% CI)	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group
	0.90 (0.38-2.12)	0.62 (0.24-1.61)	1.06 (0.46-2.44)	0.67 (0.29-1.53)	0.98 (0.44-2.19)	1.49 (0.53-4.18)	2.94 (0.59-14.57)	2.36 (0.73-7.65)
	0.78 (0.32-1.95)	0.97 (0.41-2.28)	0.71 (0.28-1.83)	0.32 (0.12-0.89)	0.39 (0.14-1.09)	1.90 (0.69-5.21)	10.42 (2.39-45.36)	3.19 (1.02-10.02)
	0.65 (0.26-1.61)	0.91 (0.38-2.22)	0.78 (0.31-1.94)	0.54 (0.23-1.28)	0.64 (0.27-1.56)	2.22 (0.83-5.91)	8.50 (1.91-37.74)	3.73 (1.22-11.45)
Mean	118±12	112±9	102±7	65±6	66±6	29.2±2.9	6.8±0.8	17.1±3.3
	138 ±3	129±3	118±3	75±2	76±2	36.4±1.7	8.53±0.5	24.2±1.5
	148±3	138±3	126±2	83±2	83±2	42.7±1.9	10.2±0.5	29.3±1.4
	175±16	154±10	139±8	93±5	95±5	53.1±5.8	12.3±1	36.1±3.7

Figure 3: Hazard ratios of all-cause Mortality for quartiles of pre-dialysis SBP (preHD SBP), 48-hour peripheral SBP (48h pSBP), 48-hour central SBP (48h cSBP), 48-hour central pulse pressure (48h cPP), 48-hour pulse wave velocity (48h PWV) and 48-hour heart rate-adjusted augmentation index [48h AIx(75)]. Quartile 1 was the reference group for all comparisons. P values are those reported for linear trend.



	preHD SBP	48h pSBP	48h cSBP	48h pDBP	48h cDBP	48h cPP	48h PWV	48h AIx(75)
HR (95% CI)	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group	Reference Group
	0.56 (0.25-1.29)	0.72 (0.33-1.58)	0.51 (0.20-1.27)	0.47 (0.21-1.03)	0.60 (0.28-1.30)	1.57 (0.61-4.06)	2.30 (0.71-7.47)	2.35 (0.89-6.17)
	0.64 (0.29-1.39)	0.64 (0.29-1.39)	0.95 (0.43-2.08)	0.42 (0.19-0.93)	0.55 (0.25-1.19)	1.68 (0.64-4.41)	5.84 (1.96-17.39)	1.91 (0.69-5.25)
			1.32 (0.62-2.81)	0.40 (0.17-0.90)	0.45 (0.20-1.04)	3.16 (1.32-7.57)	5.42 (1.81-16.25)	3.47 (1.37-8.81)
Mean	118±12	112±9	102±7	65±6	66±6	29.2±2.9	6.8±0.8	17.1±3.3
	138 ±3	129±3	118±3	75±2	76±2	36.4±1.7	8.53±0.5	24.2±1.5
	148±3	138±3	126±2	83±2	83±2	42.7±1.9	10.2±0.5	29.3±1.4
	175±16	154±10	139±8	93±5	95±5	53.1±5.8	12.3±1	36.1±3.7

Figure 5: Hazard ratios of Cardiovascular death, or non-fatal MI or non-fatal Stroke or resuscitation after cardiac arrest or coronary revascularization or hospitalization for heart failure for quartiles of pre-dialysis SBP 48-hour peripheral SBP (48h pSBP), 48-hour central SBP (48h cSBP), 48-hour peripheral DBP (48h pDBP), 48-hour central DBP (48h cDBP), 48-hour central pulse pressure (48h cPP), 48-hour pulse wave velocity (48h PWV) and 48-hour heart rate-adjusted augmentation index (48h AIx75). Quartile 1 was the reference group for all comparisons. P values are those reported for linear trend.

CONCLUSIONS

- Ambulatory PWV and ambulatory AIx75 are independently associated with the risk of cardiovascular events and mortality in this hemodialysis population, whereas office and ambulatory BP are not. These findings add to the evidence suggesting that arterial stiffness is probably the most prominent cardiovascular risk factor in hemodialysis.

REFERENCES

1. Saran R, Li Y, et al. US Renal Data System 2015 Annual Data Report: Epidemiology of Kidney Disease in the United States. Am J Kidney Dis. 2016; 67: Svii, S1-305.
2. Briet M , et al. Arterial stiffness and pulse pressure in CKD and ESRD. Kidney Int. 2012; 82: 388-400.
3. Sarafidis PA , et al. Hypertension in dialysis patients: a consensus document by the European Renal and Cardiovascular Medicine (EURECA-m) working group of the European Renal Association - European Dialysis and Transplant Association (ERA-EDTA) and the Hypertension and the Kidney working group of the European Society of Hypertension (ESH). J Hypertens. 2017; 35: 657-676.

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Dialysis - Cardiovascular complications I

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