SMGroup

SM Journal of Nephrology and Kidney Diseases

Research Article

Large Variations in Pulse Wave Velocity and Reflection Patterns occur during a Hemodialysis Session and are not Related to the Degree of Ultrafiltration

Philippe Braconnier[1]*, Corina Rotaru[2], Daniel Teta[3], Valentina Forni Ogna[1], Georges Halabi[1], Bernard Waeber[2], Michel Burnier[1], Francois Feihl[2] and Menno Pruijm[1]

[1]*Service of Nephrology and Hypertension, University Hospital of Lausanne, Switzerland*
[2]*Department of Pathophysiology, University Hospital of Lausanne, Switzerland*
[3]*Service of Nephrology, Hospital du Valais, Switzerland*

Article Information

Received date: May 16, 2018
Accepted date: May 30, 2018
Published date: Jun 04, 2018

***Corresponding author**

Philippe Braconnier, University Hospital of Lausanne, Service de Néphrologie, Rue du Bugnon 17, CH-1011 Lausanne, Switzerland, Tel: +41213141154; Fax: +41213141139; Email: philippe.braconnier@h-ne.ch

Keywords Hemodialysis; Pulse wave velocity; Augmentation index; Ultrafiltration; Arterial properties

Article DOI 10.36876/smjnkd.1014

Abstract

Arteries of end-stage renal disease patients are characterized by accelerated atherosclerosis and chronically progressive arterial stiffening. The acute effects of hemodialysis sessions on arterial properties have been less intensively studied, with contradictory results. The aim of this study was therefore to assess arterial properties throughout a hemodialysis session and to compare patients dialyzed at stable body weight with those undergoing ultrafiltration.

We measured Cartoid-Radial (CR) and Carotid-Femoral (CF) Pulse wave velocity (PWV) and the central systolic augmentation index corrected for heart rate (AIx) in 13 hemodialysis patients undergoing Ultrafiltration (UF) and 8 patients dialyzed at Stable Body Weight (SW).

No significant differences were noted between the groups for AIx, PWV and their changes. When the arterial properties of both groups were analyzed together, median cr-PWV increased slightly (from 8.6 [8.0-9.4] before to 9.8 m/sec [8.7-10.7] after hemodialysis, p=0.09), cf-PWV did not change (from 10.3 [8.8-13.1] to 10.1 m/sec [9.4-14.4], p=0.7) and AIx decreased significantly (from 28 [20.3-35] to 24.3% [19.3-31.3], p=0.02). However, large individual fluctuations occurred in arterial properties throughout hemodialysis in each group. Independently of ultrafiltration, important changes in arterial wall properties occur during hemodialysis, which may partly account for the heterogeneous hemodynamic responses observed during dialysis sessions.

Introduction

End-stage renal disease (ESRD) is associated with a high burden of mortality, mainly due to cardiovascular complications which is the leading cause of death [1,2]. Alterations in vascular properties play an important role and the process of accelerated atherosclerosis and arteriosclerosis in this patient group has been well described [3]. Atherosclerosis increases arterial stiffness, which on its turn increases Systolic Blood Pressure (SBP) during ventricular ejection and decreases diastolic pressure in the diastolic phase resulting in a high Pulse Pressure (PP) [4]. Clinical studies have demonstrated that arterial stiffness is an independent predictor of total and cardiovascular mortality in the general population and in ESRD [5,6].

Over the last two decades, several methods have been developed to measure arterial stiffness non-invasively. Pulse Wave Velocity (PWV), defined as the distance travelled by the arterial pressure wave divided by the time to travel that distance, correlates positively and linearly with arterial stiffness as expected by the Moens-Korteweg equation, and can be easily measured using different devices [7]. An increased PWV leads to the early return of reflected pressure waves from the periphery to the heart, thus increasing aortic SBP. High aortic BP increases the cardiac afterload promoting left ventricular hypertrophy [8]. Furthermore, the early wave reflection seen in arterial stiffness decreases the diastolic blood pressure leading to a decreased perfusion in the coronary arteries with a risk of cardiac ischemia [9,10].

Aortic SBP can be estimated, using the non invasive recording of the radial pulse with applanation tonometry, followed by the reconstruction of the central aortic pressure wave by means of a generalized transfer function. From the aortic pressure wave, one may calculate the Augmentation Index (AIx), which quantifies the increase in aortic SBP due to the reflected waves [7].

Several studies have shown that PWV, aortic BP and AIx are all increased in patients suffering from Chronic Kidney Disease (CKD) and ESRD [5,11].

OPEN ACCESS

ISSN: 2576-5450

In contrast, the acute effects of hemodialysis sessions on arterial properties have been studied less extensively, with contrasting results. Some groups have reported acute increases in PWV when comparing measurements made before with those measured after a Hemodialysis (HD) session [12], whereas others reported acute decreases [13,14] or no change [15-17]; Concerning AIx, most studies have reported HD induced decreases [11,17-20],yet a study by Hogas stated that this decrease did not take place in clearly hypervolemic patients [21]. It also remains unclear whether the correction of volume overload with ultrafiltration performed during a HD session has an impact on PWV or AIx. Several groups reported no correlation between the ultrafiltration volume and AIx and/or PWV [11,14,20]. However Di Iorio et al. showed that the major determinant of variations in PWV is the change in hydration status and that the ultrafiltration rate is strongly correlated with PWV changes during HD [13].

The majority of previous studies were hampered by a lack of standardization of the dialysis prescription, by the absence of validation of the pulse wave velocity measurements and/or insufficient information on possible confounders such as medication intake. Besides, few studies have assessed arterial properties during a dialysis session; most previous studies have compared PWV measured just before with those measured just after completion of a hemodialysis session. Moreover, regarding the influence of ultrafiltration on arterial stiffness patients were until now not categorized in two different comparable groups: patients dialyzed at stable body weights and patients who underwent ultrafiltration. Finally, individual changes in PWV have also not been shown in detail; in general, only mean or median PWV and Aix values were reported.

Clarifying these issues is important, since it will help to increase the understanding of the impact of hemodialysis on the cardiovascular system.

The aim of this study was therefore to assess arterial properties before, during and after a HD session performed under standardized conditions, and compare changes in arterial properties in patients dialyzed at stable body weight with those undergoing ultrafiltration.

Methods

Patients

This study was approved by the institutional ethical committee of the faculty of medicine in Lausanne, and all participating patients provided written informed consent.

The study included patients of both genders who had been on chronic dialysis for ESRD of any cause for at least three months. Participants were recruited from two centres (Lausanne University Hospital and Yverdon regional Hospital, Switzerland). Any one of the following precluded enrolment: presence of a bilateral arterio-venous fistula, frequent hypotension in the course of dialysis sessions, congestive heart failure (NYHA III-IV), atrial fibrillation, symptomatic peripheral arterial disease, and an indication for high calcium or potassium concentrations in the dialysate. Antihypertensive drugs were stopped 24h before the dialysis session.

Measurements

Brachial blood pressure: Brachial blood pressure was measured with the patient lying supine, using an oscillometric device (Mobilograph. IEM, Stolberg, Germany) and an appropriately sized cuff placed on the arm contralateral to the fistula. Measurements were taken in triplicate and the last two were averaged to obtain the final value.

Radial tonometry: The pulse waveform in the radial artery contralateral to the fistula was recorded with applanation tonometry using the SphygmoCor device (Atcor Medical, Sydney, Australia), as previously described [19]. Recordings meeting the quality criteria proposed by the manufacturer were obtained in triplicate. Using the generalized transfer function approach, as implemented in the Sphygmocor software, the radial recording was transformed into a central pulse waveform. The waveforms were calibrated using oscillometric blood pressure measured on the same arm immediately before tonometry.

From the recorded radial pulse, the central aortic pressure waveform was reconstructed by means of a generalized transfer function, as implemented in the Sphygmocor software, with the subsequent calculation of the central aortic systolic augmentation index (AIx). The AIx estimates the degree to which systolic aortic pressure is augmented by reflected waves. It is expressed in % of aortic pulse pressure. Because the AIx is influenced by heart rate, the software also provides a corrected value corrected for this confounder, i.e. and estimation for a fixed rate of 75 beats per minute.

Pulse wave velocity: Carotid-radial (cr-PWV) and carotid-femoral pulse wave velocities (cf-PWV) were evaluated in the supine position using simultaneous non-invasive recordings of the carotid, radial and femoral pulse with the Complior device and version 1.3.0j of the Complior SP software (Alam Medical, 94300 Vincennes, France) [22]. All recordings were carried out in triplicate. The carotid-to-radial and carotid to femoral distances were obtained with a ruler. The carotid-to-sternal notch distance was not subtracted.

Validation: Since pulse wave analysis is generally considered as an operator-dependent technique, all examinations were performed by the same investigator (CR). Intra-observer variability of this investigator was assessed in a group of ten healthy volunteers. All volunteers were examined twice on the same day by this investigator with at least four hours between the two examinations. Each measurement consisted of three consecutive assessments of cr-PWV, cf-PWV and AIx. The means of each series of three measurements were compared, and the differences between the first and second series calculated and expressed as the Coefficient of Variation (CV). Besides, Lin's correlation coefficients were assessed. For cr-PWV, cf-PWV and AIx the CV's were respectively 0.7%, 4.6% and 3.8%. Lin's correlation coefficients were respectively 0.82, 0.88 and 0.88 (all: p=0.001) for the same parameters, corresponding to good reproducibility.

Protocol

All examinations were carried out at the dialysis centre of Lausanne University Hospital in the course of a single HD session with an interdialytic interval of 48 hours.

Patients were divided into two groups, according to whether ultrafiltration was performed during the session (ultrafiltration group), or not (stable weight group). Patients in the stable weight group had some residual diuresis and function, enabling them to be safely dialyzed without ultrafiltration. The composition of the dialysate was standardized as follows: calcium 1.25 mEq/L, potassium 2 mEq/L, bicarbonate 28 mEq/L and temperature 36°C.

Citation: Braconnier P, Rotaru C, Teta D, Ogna VF, Halabi G, Waeber B, et al. Large Variations in Pulse Wave Velocity and Reflection Patterns occur during a Hemodialysis Session and are not Related to the Degree of Ultrafiltration. J Nephrol Kidney Dis. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smjnkd.1014

The interval between connection to and disconnection from the dialysis circuit was four hours. The following data were recorded sequentially in the hour preceding connection (T0), between 1h30 and 2h30 after connection (T2), and in the hour following disconnection (T4): brachial blood pressure, radial tonometry and pulse wave velocity, in that order. Carrying the full sequence took around 30 minutes, depending on the ease of obtaining high quality signals with the Spyhgmocor and the Complior devices.

In addition, blood samples were withdrawn at T0 and T4, from the venous side of the circuit, for routine laboratory tests.

Data analysis

Statistical analysis was conducted using STATA 12.0 (StataCorp, College Station, Texas, USA). Since the primary aim of this study was to assess changes in arterial properties throughout a hemodialysis session performed under standardized conditions, the power calculation was based on the expected intra-dialytic changes in PWV in each group. Based on a hypothetical dialysis-induced change in PWV of 10%, an alpha of 0.05 with two sided significance level, and an intra-observer standard deviation of 5% [23]., at least 8 participants were needed per group to have a power of 80%.

Descriptive statistics are presented in the form of medians and interquartile range in the two study groups, as mean±SD, or as number (percentage), as appropriate. Baseline characteristics between the two groups were compared using unpaired t-tests, Mann-Whitney's ranksum statistics, or Pearson's chi squared tests. Unless specified otherwise, statistical analysis for changes in hemodynamic parameters throughout the HD sessions was carried out with analysis of variance for repeated measures. The fixed effects in the model were the group (stable weight or ultrafiltration), the experimental time (T0 - T4), and their interaction. When the relevant F test was significant, further pair wise comparisons were carried out using Fisher's least significant difference. The alpha level of all tests was set at 0.05.

Results

Baseline characteristics

Baseline characteristics of the Stable Weight (SW) - and Ultrafiltration (UF)-groups are given in Table 1. Dialysis vintage was significantly longer in the UF group and the percentage of patients on loop diuretics significantly higher, as expected. All patients were dialyzed with an arterio-venous fistula, except one in the SW group who was dialyzed with a tunneled catheter.

Changes of hemodynamic parameters and arterial properties during hemodialysis session

Changes in laboratory parameters are shown in Table 2. Increases in hematocrite, albumin and protein occurred only in the UF group.

Hemodialysis-induced changes in hemodynamic parameters are shown in Table 3. Systolic and mean peripheral (brachial) blood pressure decreased more in the UF group than in the SW group.

Levels of cr-PWV and cf-PWV before, halfway, and after a HD session are shown graphically in Figure 1A and 1B. In both groups, there was a slight yet non-significant increase in cr-PWV throughout the dialysis session: the median cr-PWV increased from 8.0 before (T0) to 9.8 m/sec after a HD session (T4) in the SW group (p anova=0.66), versus from 8.7 to 10.2 for cr-PWV in the UF group (p anova=0.37), see Table 3. Concerning cf-PWV, no significant changes in median values were seen in the SW (from 10.3 to 10.1 m/sec, p=0.66) or the UF group (from 10.0 to 10.1, p=0.73). There was no difference in change of PWV between the two groups (p for interaction of time and dialysis type=0.97).

Overall, when the arterial properties of both groups were analyzed together, no significant change in median cr-PWV (from 8.6 (8.0-9.4) to 9.8 m/sec (8.7-10.7), p=0.09) or cf-PWV (from 10.3 (8.8-13.1) to 10.1 m/sec (9.4-14.4), p=0.7) was noted. Individual changes in PWV are shown in Figure 3A. Large variations in cr-PWV were noticed between individuals, some showing sharp increases, whereas others showed decreases or no change at all throughout a dialysis session. Similar trends were seen for cf-PWV (data not shown).

Levels of the central augmentation index adjusted for heart rate are shown graphically in Figure 2. AIx had decreased significantly halfway a HD session in both groups as compared to baseline values, but decreases noticed at the end of the HD session (T4) were not significantly lower as compared to AIx before the HD session (T0), see Table 3. These trends were not different between the groups (p for interaction and dialysis type=0.86) When changes in AIx of both groups were analyzed together, a significant decrease occurred in AIx (from 28 (20.3-35) to 24.3% (19.3-31.3), p=0.02). As for PWV, large variations in AIx were noticed between individuals (see Figure 3B).

Table 1: Baseline characteristics.

	Stable weight (n=8)	Ultrafiltration (n=13)	P
Age (years)	59 (57-61)	57 (50-72)	0.47
Gender (% female)	25	31	0.78
Body Mass Index (kg/m²)	24.2±1.4	27±1.1	0.14
Dialysis vintage (years)	2.6 (1.1-4.6)	6.5 (4.0-10.1)	*<0.05*
Cause ESRD, n (%)			
Diabetes Mellitus	2(25)	3 (23.1)	0.9
Arterial Hypertension	3 (37.5)	1 (7.8)	0.09
Glomerulonephritis	1 (12.5)	4 (30.8)	0.34
Reflux	1 (12.5)	1 (7.8)	0.71
Other	1 (12.5)	4 (30.8)	0.34
Diabetes (% yes)	25	38.4	0.53
Medication, n(%)			
RAAS-blocker	4 (50)	4 (31)	0.2
alpha-blocker	0 (0)	2 (15)	0.27
beta-blocker	2 (25)	5 (38)	0.66
calcium-antagonist	2 (25)	3 (23)	0.79
loop diuretic	8 (100)	3 (23)	*<0.05*
Midodrine	0 (0)	1 (7.7)	0.45
ESA*	8 (100)	12(92)	0.45
Ultrafiltration (liters)	0	2.6 (1.1;3.9)	*<0.05*

Note: All values expressed as mean±standard deviation, median (interquartile range) or number (percentage), as appropriate. *Erythropoiesis-stimulating agents.

Citation: Braconnier P, Rotaru C, Teta D, Ogna VF, Halabi G, Waeber B, et al. Large Variations in Pulse Wave Velocity and Reflection Patterns occur during a Hemodialysis Session and are not Related to the Degree of Ultrafiltration. J Nephrol Kidney Dis. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smjnkd.1014

Table 2: Changes in laboratory parameters occurring throughout a hemodialysis session.

	Dialysis type								
	Stable Weight				Ultrafiltration				p value for interaction of time and dialysis type
	T0		T4		T0		T4		
urea (mM)	19.4	18.0-23.5)	5	(4.6-6.1)**	21.8	(16.4-27.0)	4	(3.2-6.3)**	0.7
creatinine (µM)	659	(554-745)	217	(183-233)**	722	(596-932)	209	1(64-336)**	0.41
sodium (mM)	141	(140-143)	139	(138-140)**	140	(138-143)	139	(138-139)**	0.28
potassium (mM)	4.9	(4.1-5.4)	3.2	(3.0-3.3)**	4.9	(4.5-5.4)	3.4	(3.2-3.6)**	0.64
phosphate (mM)	1.5	(1.2-1.8)	0.6	(0.5-0.7)**	1.2	(1.0-1.4)	0.5	(0.4-0.6)**†	0.11
calciuma (mM)	2.3	(2.1-2.3)	2.2	(2.1-2.2)*	2.2	(2.1-2.3)	2.2	(2.2-2.3)*	0.009
bicarbonate (mM)	24.1	(23-24.8)	28.6	(27.6-29.5)**	23.2	(22.6-24.7)	27.6	(26.8-28.4)**	0.33
total protein (g/L)	73	(72-74.5)	70.5	(68.5-73.0)	68	(67-73.5)	78	(76.0-84.0)**††	<0.0001
albumin (g/L)	44	(41-48.0)	42.5	(40.5-44.5)	40	(38-42.0)††	45	(43.0-46.5)*	0.009
hemoglobin (g/L)	113	(109-116)	113	(108-117)	110	(102-114)	121	(116-124)**	<0.0001
hematocrit (%)	33.5	(32.5-35.5)	33	(31.5-35.0)	33	(31.0-35.5)	36	(34.0-37.0)**	<0.0001
mcv (pL)	93.5	(90.5-95.5)	92	(90-95.5)*	94	(90.0-99.0)	92	(90.0-98.0)**	0.04
mch (pg)	31.6	(30-32.0)	31.7	(30.0-32.4)	31.2	(30.0-33.3)	31.4	(30.5-32.8)	0.93
mchc (g/L)	335	(334-339)	338	(334-344)**	330	(329-332)	337	(332-339)**	0.44

Note: Laboratory data . Median with interquatile range in parentheses. *p<0.05 ** p<0.01 T4 *vs* T0. † p<0.05 †† p< 0.01 dialysis with *vs* without liquid withdrawal.

Associations between baseline arterial properties and baseline characteristics

In order to assess associations between baseline arterial properties and other baseline characteristics, univariate analyses were performed (Spearman's rank correlation). Positive associations were found between DBP and mean BP and cr-PWV as well as between age and baseline cf-PWV (Table 4). There was no significant correlation between dialysis vintage and PWV/AIx. Furthermore, we observed no significant difference in ultrafiltration volume in patients with a high PWV >12m/sec (6 patients) compared to those with a PWV ≤ 12 m/sec (15 patients) (p=0.94).

Baseline AIx was not associated with any of the other tested baseline characteristics. There were no differences in baseline PWV or AIx according to gender, smoking status, presence of diabetes, or medication intake (data not shown).

Associations between hemodialysis-induced changes in arterial properties and (changes in) baseline characteristics:

The change in PWV after 2h of HD (named 'Δ2h') was obtained by subtracting 2h PWV values from those obtained at baseline (T2-T0). In a similar way, Δ4h PWV was calculated.

We first explored associations between baseline characteristics and changes in arterial properties. Negative associations were found between Δ2h cr-PWV and age (r= -0.58, p=0.009) and between Δ4h cr-PWV and age (r= -0.60, p=0.006), corresponding to decreases in cr-PWV throughout a HD session in older patients, as compared with increases in younger patients (see Table 5 and Figure 4). No associations were found between baseline SBP or DBP and changes in PWV. Negative associations were found between Δ2h AIx and brachial DBP (r=-0.53, p=0.03) and between Δ4h AIx and brachial

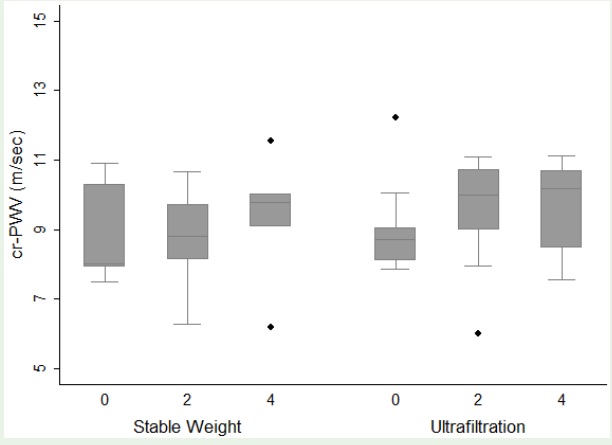

Figure 1a: Levels of cr-PWV and cf-PWV before, halfway.

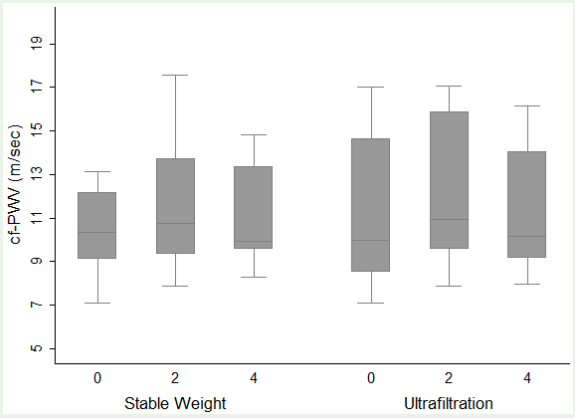

Figure 1b: Levels of cr-PWV and cf-PWV before, halfway, and after a HD session are shown graphically.

Citation: Braconnier P, Rotaru C, Teta D, Ogna VF, Halabi G, Waeber B, et al. Large Variations in Pulse Wave Velocity and Reflection Patterns occur during a Hemodialysis Session and are not Related to the Degree of Ultrafiltration. J Nephrol Kidney Dis. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smjnkd.1014

Table 3: Median (25th-75th percentile) values of hemodynamic parameters occurring during a hemodialysis session.

Protocol time	Stable weight						Ultrafiltration						p value for interaction of time and dialysis type
	T0		T2		T4		T0		T2		T4		
Heart rate (b/min)	74	(65-83)	81	(64-89)*	78	(66-92)**	70	(67-75)	72	(64-77)	74	(68-77)	<0.001
Peripheral BP (mm Hg)													
systolic	126	(112-137)	123	(111-132)	123	(112-135)	135	(112-150)	118	(112-139)*	126	(110-131)**	0.03
diastolic	81	(70-87)	75	(71-85)	73	(67-84)	73	(68-90)	76	(67-80)	73	(63-86)	0.06
mean	100	(84-106)	91	(85-104)	96	(81-101)	95	(84-112)	88	(82-102)*	88	(81-101)**	0.02
Central BP (mm Hg)													
systolic	119	(107-127)	112	(104-121)*	113	(103-124)**	117	(103-140)	110	(101-118)*	113	(105-119)**	0.06
diastolic	83	(70-88)	76	(72-86)	75	(68-86)**	73	(69-91)	77	(67-81)	73	(65-87)**	0.15
mean	100	(84-106)	91	(85-104)*	96	(81-101)**	95	(84-112)	88	(82-102)*	88	(81-101)**	0.09
Indices of wave reflexion (%)													
AIx	32.8	(23-39)	31	(19-42)*	28	(21-42)	27.7	(20-30)	19.7	(13-23)*	22.3	(18-27)	0.86
PWV Car-Rad	8	(7.9- 10.3)	8.8	(8.1- 9.7)	9.8	(9.1- 10.0)	8.7	(8.1-9.0)	10.2	(9.3-10.7)	10.2	(9.0- 10.7)	0.27
Car-Fem	10.3	(8.8-11.3)	10.7	(9.3-13.7)	10.1	(9.7-14.4)	10	(8.5-14.6)	10.9	(9.5-15.3)	10.1	(9.2-14.1)	0.97

*p<0.05 for within group comparison of T2 *vs* T0; **p<0.05 for within group comparison of T4 *vs* T0.

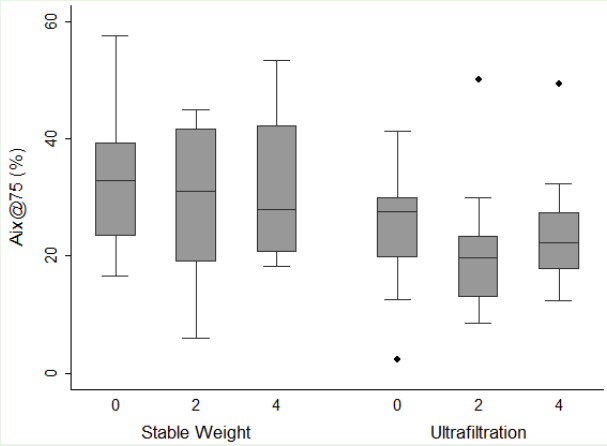

Figure 2: Levels of the central augmentation index adjusted for heart rate.

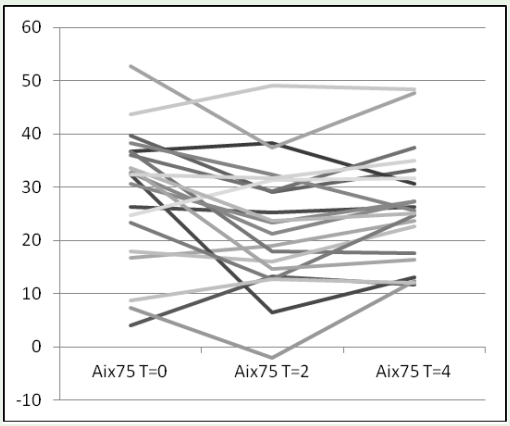

Figure 3b: significant decrease occurred in AIx.

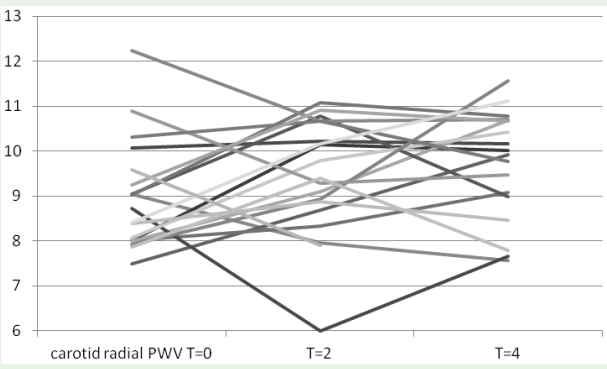

Figure 3a: large variations in AIx were noticed between individuals.

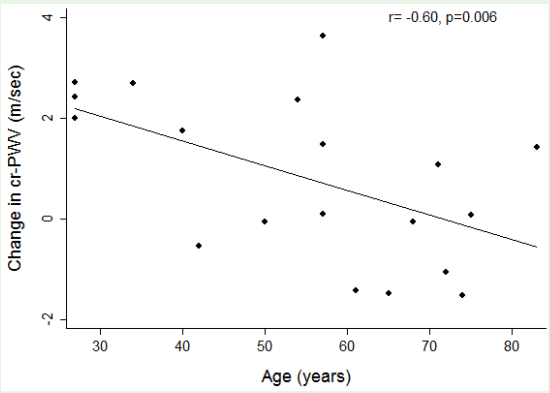

Figure 4: cr-PWV throughout a HD session in older patients, as compared with increases in younger patients.

Citation: Braconnier P, Rotaru C, Teta D, Ogna VF, Halabi G, Waeber B, et al. Large Variations in Pulse Wave Velocity and Reflection Patterns occur during a Hemodialysis Session and are not Related to the Degree of Ultrafiltration. J Nephrol Kidney Dis. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smjnkd.1014

Table 4: Univariate correlations (Spearman) between arterial properties and continuous baseline characteristics.

	cr-PWV		cf-PWV		AIx	
	r	p	r	p	r	p
Age (years)	0.3167	0.17	0.79	*0.0001*	-0.11	0.63
Brachial SBP (mmHg)	0.37	0.1	0.16	0.54	0.23	0.33
Brachial DBP (mmHg)	0.56	0.01	0.12	0.64	0.32	0.17
Mean BP (mmHg)	0.51	*0.022*	0.07	0.77	0.25	0.29
Body Mass Index (kg/m²)	-0.0797	0.73	0.34	0.17	-0.26	0.28
Dialysis vintage (months)	0.21	0.37	0.14	0.59	-0.06	0.78
Hemoglobin (g/dl)	-0.079	0.74	-0.16	0.52	-0.28	0.23
Sodium (mM)	-0.08	0.73	-0.18	0.48	0.09	0.72
Potassium (mM)	-0.22	0.3497	-0.11	0.65	0.15	0.52
Corrected calcium (mM)	0.19	0.41	0.25	0.32	0.012	0.96

Table 5: Correlations between patient characteristics, changes in hemodynamics during dialysis and changes in arterial properties.

	cr-PWV Δ2		cr-PWV Δ4		AIx Δ2		AIx Δ4	
	r	*p*	*r*	*p*	*r*	*p*	*R*	*p*
Age (years)	-0.582	*0.0089*	-0.602	*0.0064*	-0.26	0.32	-0.01	0.97
Systolic blood pressure (mmHg)	0.04	0.87	0.03	0.92	-0.29	0.26	-0.22	0.38
Diastolic blood pressure (mmHg)	-0.16	0.55	0.07	0.77	-0.53	0.028	-0.47	*0.05*
Change in SBP (Δ mmHg)	0.11	0.65	0.62	*0.004*	0.39	0.09	0.26	0.23
Change in DBP (Δ mmHg)	0.35	0.13	0.53	*0.019*	0.59	*0.006*	0.58	*0.006*
Total Ultrafiltration (ml)	na	na	-0.37	0.13	na	na	0.09	0.72

Abbreviations: r= Spearman's correlation coefficient; cr-PWV Δ2= carotid-radial pulse wave velocity measured 2 hours after initiation of hemodialysis- baseline value of cr-PWV; cr-PWV Δ4=carotid-radial pulse wave velocity after dialysis-baseline value of cr-PWV. AIxΔ2= Augmentation index adjusted for heart rate measured 2 hours after initiation of hemodialysis-baseline AIx.

DBP (r=-0.47, p=0.05): a high baseline BP resulted in large decreases in AIx.

Secondly, we examined associations between HD-induced changes in BP and changes in PWV and AIx. Large decreases in systolic or diastolic BP throughout the HD session were associated with large decreases in AIx (see Table 5 and Figure 5). No associations were found between the degree of ultrafiltration and ΔPWV or ΔAIx (Table 5).

Baseline characteristics of 'Increasers' *versus*' Non-increasers'

In order to further analyze the alterations in arterial properties, patients were divided in those who increased cr-PWV, cf-PWV and AIx during a HD session (empirically called 'increasers', n=6), and those who did not increase all three parameters ('non-increasers', n=15). A part from higher baseline diastolic and mean arterial blood pressure, and higher potassium levels in non-increasers, no other differences were seen between the two groups (see Table 6).

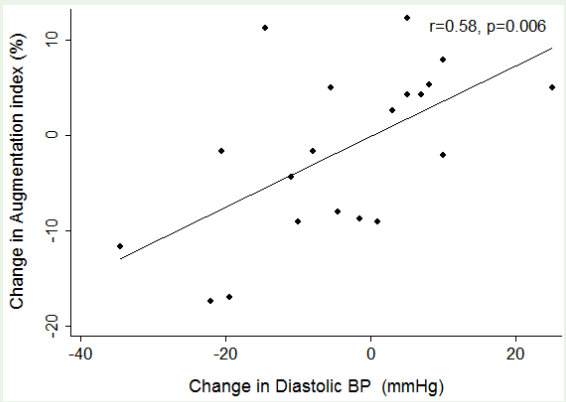

Figure 5: Large decreases in systolic or diastolic BP throughout the HD session were associated with large decreases in AIx.

Table 6: Increasers *versus* decreasers.

	Increasers (n=6)	Decreasers (n=15)	P
Age (years)	57.1	53	0.63
Body Mass Index (kg/m²)	25.2	28	0.17
Sex (% women)	50	20	0.17
Dialysis Vintage	4.7	6	0.58
Stable weight (%)	83	50	0.2
Brachial SBP (mmHg)	134.5	121.7	0.16
Brachial DBP (mmHg)	82.3	69	0.03
Brachial MAP (mmHg)	99.7	86.6	0.05
Urea (mmol/l)	22.4	18.1	0.12
Potassium (mmol/l)	5.1	4.4	0.02
Phosphate (mmol/l)	1.3	1.3	0.73
Albumine (g/dl)	44	40.7	0.43
Bicarbonate (mmol/l)	23.5	24.8	0.22

Discussion

The main findings of this study are that: 1) Ultrafiltration is not associated with systematic changes in arterial stiffness and vascular reflection properties as measured by PWV and AIx during a HD session; 2) In all individuals, large fluctuations occur in PWV and AIx throughout a HD session and 3) Higher age and brachial BP are associated with decreasing PWV and AIx during HD, yet changes are largely non-predictable.

As stated in the introduction, the acute influence of HD on PWV and AIx remains a matter of intense debate. Concerning PWV, some studies have reported increases [12], some decreases [13,14] and others including ours reported no changes [15-17]. For AIx, results have been more consistent, with most studies including ours reporting a HD-induced decrease in AIx [11,17-20],

Citation: Braconnier P, Rotaru C, Teta D, Ogna VF, Halabi G, Waeber B, et al. Large Variations in Pulse Wave Velocity and Reflection Patterns occur during a Hemodialysis Session and are not Related to the Degree of Ultrafiltration. J Nephrol Kidney Dis. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smjnkd.1014

We hypothesized that the discrepancy in results between studies might have been caused by the lack of standardization of the prescription of the dialysis session, or by the fact that ultrafiltration was not taken into account. In this study, dialysis prescription was therefore standardized and subjects were for the first time divided in two groups according to the need or absence of ultrafiltration. Nevertheless, there was no difference in HD-induced changes in PWV and/or AIx between the 'ultrafiltration' and 'stable weight' groups, nor was there a relationship between the ultrafiltration rate and alterations in PWV and/or AIx. This finding is in agreement with several groups who reported no correlation between the ultrafiltration volume and AIx and/or PWV [11,14,20]. However Di Iorio et al. found a striking parallel between hydration status and PWV which both decreased during dialysis treatment [13]. Interestingly, they noticed no significant difference in ultrafiltration between patients with high PWV (>12 m/sec) and normal PWV (<12 m/sec). Our results support this observation which suggests that the major determinant of absolute PWV in HD patients is arterial system damage rather than the hydration status. Interestingly, Power et al. reported a decrease in AIx within 20 minutes after starting HD when only minimal ultrafiltration had occurred, suggesting that other mechanisms than volume control such as pro-inflammatory effects of blood passing through the extracorporeal circuit might be involved in the hemodynamics [17].

The major finding of this study is that large intra-and inter-individual changes occur in arterial properties throughout the HD session. Previous studies have often not reported individual levels, thus somewhat masking heterogeneity of the PWV between individuals. To the best of our knowledge, only the study by Covic and colleagues described the heterogeneity in AIx between HD patients, but in this study AIx was not adjusted for heart rate and PWV was not measured [15].

In theory, PWV is a measure of intrinsically arterial stiffness and directly depends of the amount of elastic fibers and calcifications in the vascular wall [7,21]; cr-PWV provides information on the brachial and intrathoracic arteries, whereas cf-PWV provides information on the abdominal aorta and iliofemoral arteries. This parameter is less dependent of circulatory volume than the central aortic BP and the AIx. Only cf-PWV has been shown to be of predictive value for morbidity and mortality [5,24].

The AIx also depends on the amplitude and timing of the reflected wave, which in turn depends on the spatial distribution of reflection sites, PWV and particulars of ventricular ejection [22]. Indeed, Covic and colleagues ascribed the heterogeneity of AIx to different degrees of cardiac chamber dilation: those patients who did not decrease AIx had more dilated chambers at cardiac ultrasound [11].

In line with this finding, a possible explanation for the lack of effect of ultrafiltration on AIx in our study could be that fluctuations in effective circulatory volume were limited, or at least not related to the degree of ultrafiltration. The patients were possibly not on dry weight, or had adequate refilling from the interstitial tissues in response to fluid removal. Since more objective measures of fluid status such as Body Composition Monitoring, cardiac ultrasound or assessment of the diameter of the inferior vena cava were not performed in this study, we cannot confirm these hypotheses. Nevertheless, this hypothesis is supported by Hogas and colleagues who reported that clinically silent but bioimpedance-proven overhydration is associated with higher PWV, which is corrected following fluid removal [21]. At the same time, patients at true dry weight have similar PWV before and after HD.

Overall, the only factor that was positively associated with PWV and negatively with HD-induced decreases in PWV was age. This association was expected, considering the well-known relationship between aging and arterial stiffness due to loss of elastine fibers, atherosclerosis and, specifically for the ESRD population, arteriosclerosis [9]. AIx was positively associated with initial BP and negatively with changes in BP occurring throughout the dialysis session. These associations were also expected, as outlined above.

Once more, responses of the vascular system to HD differed largely between individuals. Therefore, stating that HD temporarily in-or decreases parameters of vascular stiffness is at the current state of knowledge to our opinion not possible and merely an over-simplification of the complex hemodynamics interactions that occur throughout a dialysis session.

It remains actually unknown if someone who increased his/her PWV throughout the session in this study would also do so on other sessions, as suggested by the study of Di Iorio and colleagues [12]. It is also not known whether HD patients with large fluctuations in PWV throughout the session are at higher cardiovascular risk. For example, it could be that increases in PWV are a manifestation of vascular stress; if occurring thrice weekly, this might increase the risk of adverse cardiovascular outcomes. Alterations in arterial properties should be interpreted in the light of cardiac changes occurring during HD. Mc Intyre and colleagues have convincingly demonstrated that HD is capable of inducing transient myocardial ischemia, even in patients without coronary lesions, resulting in regional wall motion abnormalities and left ventricular dysfunction, the so called 'myocardial stunning' [25]. Two-thirds of the patients in that study presented some degree of myocardial stunning, and factors that were independently associated with this phenomenon were high age, ultrafiltration volume, intradialytic BP reduction and cardiac Troponin T levels. It is tempting to suppose that PWV and central BP are also determinants of myocardial stunning, but this has, to the best of our knowledge, not been investigated so far.

In order to find answers to these questions, follow-up studies assessing simultaneously cardiac, central and peripheral arterial properties during a HD-session are necessary.

This study has several limitations. First of all, the number of participants was rather small in both groups. However, the precision of PWV was higher than expected, with a coefficient of variation of 0.7% for cr-PWV and 4.6 % for cf-PWV in the validation study, thus somehow compensating for the low number of subjects in the stable weight group. Furthermore, the variations throughout a hemodialysis session were larger than expected for cr-PWV, with hemodialysis-induced changes in PWV as large as 20%. Our study had therefore enough statistical power to assess whether changes in cr-PWV occur throughout a HD session. In contrast, our study was not powered to detect inter-group differences. The observed change in cr-PWV did not differ much between the ultrafiltration- and stable weight groups (median change in cr-PWV respectively 1.8 *vs* 1.5 m/sec). Due to the large fluctuations in PWV throughout the HD-session (SD between

1.5-1.9 m/sec), a hypothetical number of 252 patients per group should have been included to have a power of 80% to reliably reject the null-hypothesis.

A second limitation is that cardiac ultrasound was not performed, and circulating factors such as catecholamines, renin or aldosterone were not assessed. Finally, measurements were performed on a single dialysis day instead of during several sessions. The strengths of this study are the standardization of the HD prescription, the extended information on co-variables, the validation of the Sphygmocor measurement in a control group demonstrating low intra-observer variability, and the availability of data halfway the dialysis session.

Conclusion

Taken together, in this study large intra-individual and inter-individual fluctuations occurred in arterial stiffness, central aortic BP and augmentation index throughout a HD session. This heterogeneity partly explains the contrasting results reported by previous studies. It seems prudent to abandon generalizing statements reporting HD-induced increases or decreases in PWV, central aortic BP, or AIx. The direction and degree of change in mentioned parameters is so far largely unpredictable. These data underline the heterogeneous effects of HD on the cardiovascular system in different patients and future studies should clarify whether the direction and degree of changes in these vascular parameters are an expression of vascular stress and associated with increased cardiovascular risk. More research is needed to increase our understanding of hemodynamic mechanisms that take place during a HD session, in order to increase safety, patient comfort and outcome.

References

1. Foley RN, Parfrey PS, Sarnak MJ. Epidemiology of cardiovascular disease in chronic renal disease. J Am Soc Nephrol. 1998; 9: S16-23.
2. United States Renal Data System. 2016 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2016.
3. Campean V, Neureiter D, Varga I, Runk F, Reiman A, Garlichs C, et al. Atherosclerosis and vascular calcification in chronic renal failure. Kidney Blood Press Res. 2005; 28: 280-289.
4. O'Rourke MF. Principles and definitions of arterial stiffness, wave reflections and pulse pressure amplification. In: Safar ME, O'Rourke MF (eds) Handbook of Hypertension (series edts Birkenhager WH, Reid JL), Arterial Stiffness in Hypertension. Elsevier: Amsterdam, 2006; 23: 3-20.
5. Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM. Impact of aortic stiffness on survival in end-stage renal disease. Circulation. 1999; 99: 2434-2439.
6. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol. 2010; 55: 1318-1327.
7. Nichols WW. Clinical measurement of arterial stiffness obtained from noninvasive pressure waveforms. Am J Hypertens. 2005; 18: 3S-10S.
8. O'Rourke MF, Kelly RP. Wave reflections in systemic circulation and its implications in ventricular function. J Hypertens. 1993; 11: 327-337.
9. Briet M, Boutouyrie P, Laurent S, London GM. Arterial stiffness and pulse pressure in CKD and ESRD. Kidney Int. 2012; 82: 388-400.
10. Watanabe H, Ohtsuka S, Kakihana M, Sugishita Y. Coronary circulation in dogs with an experimental decrease in aortic compliance. J Am Coll Cardiol. 1993; 21: 1497-1506.
11. Covic A, Goldsmith DJ, Gusbeth-Tatomir P, Covic M. Haemodialysis acutely improves endothelium-independent vasomotor function without significantly influencing the endothelium-mediated abnormal response to a beta 2-agonist. Nephrol Dial Transplant. 2004; 19: 637-643.
12. London GM, Marchais SJ, Guerin AP. Arterial stiffness and function in end-stage renal disease. Adv Chronic Kidney Dis. 2004; 11: 202-209.
13. Di Iorio B, Nazzaro P, Cucciniello E, Bellizzi V. Influence of haemodialysis on variability of pulse wave velocity in chronic haemodialysis patients. Nephrol Dial Transplant. 2010; 25:1579-1583.
14. Öğünç H, Akdam H, Alp A, Gencer F, Akar H, Yeniçerioğlu Y. The effects of single hemodialysis session on arterial stiffness in hemodialysis patients. Hemodial Int. 2015; 19: 463-471.
15. Georgianos PI, Sarafidis PA, Karpetas A, Kosmidis D, Sioulis A, Liakopoulos V, et al. Hemodiafiltration does not have additional benefits over hemodialysis on arterial stiffness, wave reflections and central aortic pressures. Blood Purif. 2014; 37:18-26.
16. Kosch M, Levers A, Barenbrock M, et al. Acute effects of haemodialysis on endothelial function and large artery elasticity. Nephrol Dial Transplant. 2001; 16:1663-1668.
17. Power A, Charitaki E, Davenport A. Changes in Vascular Tone Occur Early During Hemodialysis Treatments Independently of Volume Reduction. Artif Organs. 2016; 40: 678-683.
18. Covic A, Goldsmith DJ, Panaghiu L, Covic M, Sedor J. Analysis of the effect of hemodialysis on peripheral and central arterial pressure waveforms. Kidney Int. 2000; 57: 2634-2643.
19. Georgianos PI, Sarafidis PA, Malindretos P, Nikolaidis P, Lasaridis AN. Hemodialysis reduces augmentation index but not aortic or brachial pulse wave velocity in dialysis-requiring patients. Am J Nephrol. 2011; 34: 407-414.
20. Mardare NG, Goldsmith DJ, Gusbeth-Tatomir P, Covic A. Intradialytic changes in reflective properties of the arterial system during a single hemodialysis session. Hemodial Int. 2005; 9: 376-382.
21. Hogas S, Ardeleanu S, Segall L, Serban DN, Serban IL, Hogas M, et al. Changes in arterial stiffness following dialysis in relation to overhydration and to endothelial function. Int Urol Nephrol. 2012; 44: 897-905.
22. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. Eur Heart J. 2006; 27: 2588-2605.
23. Pivin E, Ponte B, Pruijm M, Ackermann D, Guessous I, Ehret G, et al. Inactive Matrix Gla-Protein Is Associated With Arterial Stiffness in an Adult Population-Based Study. Hypertension. 2015; 66: 85-92.
24. Pannier B, Guerin AP, Marchais SJ et al. Stiffness of capacitive and conduit arteries: prognostic significance for end-stage renal disease patients. Hypertension 2005; 45: 592–596.
25. McIntyre CW, Burton JO, Selby NM, et al. Hemodialysis-induced cardiac dysfunction is associated with an acute reduction in global and segmental myocardial blood flow. Clin J Am Soc Nephrol 2008; 3:19-26.

Citation: Braconnier P, Rotaru C, Teta D, Ogna VF, Halabi G, Waeber B, et al. Large Variations in Pulse Wave Velocity and Reflection Patterns occur during a Hemodialysis Session and are not Related to the Degree of Ultrafiltration. J Nephrol Kidney Dis. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smjnkd.1014