

# Acute effects of ultrafiltration on aortic mechanical properties determined by measurement of pulse wave velocity and pulse propagation time in hemodialysis patients

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## ABSTRACT

**Objective:** The effects of acute hemodialysis session on pulse wave velocity are conflicting. The aim of the current study was to assess the acute effects of ultrafiltration on the aortic mechanical properties using carotid-femoral (aortic) pulse wave velocity and pulse propagation time.

**Methods:** A total of 26 (12 women, 14 men) consecutive patients on maintenance hemodialysis (mean dialysis duration: 40.7±25.6 (4-70) months) and 29 healthy subjects (13 women, 16 men) were included in this study. Baseline blood pressure, carotid-femoral (aortic) pulse wave velocity, and pulse propagation time were measured using a Complior Colson device (Createch Industrie, France) before and immediately after the end of the dialysis session.

**Results:** While systolic blood pressure, diastolic blood pressure, mean blood pressure, pulse pressure, and pulse wave velocity were significantly higher in patients on hemodialysis than in healthy subjects, pulse propagation time was significantly higher in healthy subjects. Although body weight, systolic blood pressure, diastolic blood pressure, mean blood pressure, pulse pressure, and pulse wave velocity were significantly decreased, heart rate and pulse propagation time were significantly increased after ultrafiltration. There was a significant positive correlation between pulse wave velocity and age, body height, waist circumference, systolic blood pressure, diastolic blood pressure, mean blood pressure, pulse pressure, and heart rate.

**Conclusion:** Although hemodialysis treatment may chronically worsen aortic mechanical properties, ultrafiltration during hemodialysis may significantly improve aortic pulse wave velocity, which is inversely related to aortic distensibility and pulse propagation time.

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**Keywords:** ultrafiltration, hemodialysis, aortic mechanical properties, pulse wave velocity, pulse propagation time

## Introduction

Cardiovascular complications, such as accelerated atherosclerosis and heart failure, are important causes of death in patients with hemodialysis, which is the generally used renal replacement therapy (1). Dialysis works on the principles of the diffusion of solutes, including urea, potassium, and phosphorus, and ultrafiltration of fluid across a semi-permeable membrane. In addition to end-stage renal disease, ultrafiltration has recently become an alternative strategy to diuretic therapy for the treatment of patients with decompensated heart failure (2). Alterations of large arterial mechanical properties, such as decreased aortic compliance and/or distensibility, assessed by

arterial pulse wave velocity, are common in hemodialysis patients and appear to contribute to increased cardiovascular morbidity and mortality (3-6). Reduced arterial elasticity may impair large artery cushioning function and results in increased left ventricular afterload and reduced coronary artery perfusion (7). However, it is not clear whether ultrafiltration acutely affects large arterial mechanical properties. Therefore, the aim of the current study was to assess the acute effects of ultrafiltration on aortic mechanical properties. We measured carotid-femoral (aortic) pulse wave velocity and pulse propagation time, which is inversely related to pulse wave velocity, as parameters of aortic mechanical properties, in patients on hemodialysis just before and after hemodialysis with an ultrafiltration session.

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## Methods

### Patient population and study protocol

A total of 26 consecutive patients on maintenance hemodialysis (mean dialysis duration:  $40.7 \pm 25.6$  (4-70) months) and 29 healthy subjects were included in this study. Patients who were treated with conventional hemodialysis received 4 hours of treatment thrice weekly with a target blood pump speed of 300 mL/min and dialysate flow rate of 500 mL/min. It was used the arteriovenous fistula during the dialysis period. Dry weight was considered optimal when patients remained without symptoms of dyspnea, orthopnea, or edema during the interdialytic period. All dialysis treatments used Fresenius 4008 machines (Fresenius Medical Care, Germany), polysulphone membranes, and bicarbonate-buffered dialysate [Fresenius Medical Care SK-F 213 (PGS 22)]. A standard calcium bath was used and adjusted as clinically indicated. Patients' diets were liberalized, and phosphate binders were used. Also, intravenous erythropoietin and iron supplementation and anti-hypertensive agents, including angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, beta-blockers or calcium channel blockers, were adjusted as clinically indicated. Eleven patients (6 men, 5 women) were hypertensive and were taking angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, beta-blockers, or calcium channel blockers.

The study exclusion criteria thus included previous myocardial infarction, peripheral arterial disease, cerebrovascular disease, valvular heart disease, history of dialysis-induced hypotension, atrial fibrillation, and 2<sup>nd</sup>-3<sup>rd</sup> degree atrioventricular block. Because of technical limitations (8), we did not measure arterial pulse wave velocity at a body height <120 cm, body weight <30 kg, and body mass index >35 kg/m<sup>2</sup>. None of the patients had a smoking or alcohol intake history. All subjects gave their consent for inclusion in the study, and the local ethical committee approved it. The investigation conforms to the principles outlined in the Declaration of Helsinki.

Each patient was placed in a supine position and studied first at 8:00 AM, before the dialysis session. Pulse wave velocity was measured before and after the dialysis session on the first dialysis day. Following measurement of baseline blood pressure, we evaluated carotid-femoral (aortic) pulse wave velocity and pulse propagation time using a Complior Colson device (Createx Industrie, France) (8). The same protocol was repeated immediately after the end of the dialysis session.

### Body weight, body height, and waist-hip ratio measurements

Body weight (kg) and body height (m) were calculated using bascule and metric measures, respectively. The circumference of waist and the circumference of the hip were calculated by a tape line.

### Measurement of body temperature

Body temperature was measured with an axillary mercury thermometer.

### Blood pressure measurement

The arterial blood pressure of the subjects was measured by the same clinician. The subjects were in supine position and had rested at least 20 minutes before the measurement. The blood pressure was measured using a mercury sphygmomanometer with a cuff appropriate to the arm circumference (Korotkoff phase I for systolic blood pressure and V for diastolic blood pressure). Blood pressure measurements were performed twice for each subject, and their mean was used for the statistical analysis.

Pulse pressure = systolic blood pressure - diastolic blood pressure

Mean blood pressure = (systolic blood pressure + 2 X diastolic blood pressure)/3

### Aortic pulse wave velocity and pulse propagation time measurement

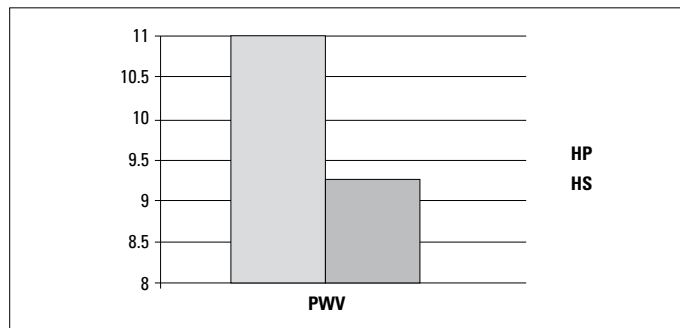
Arterial pulse wave velocity and pulse propagation time were measured using the automatic Complior Colson (France) device; the technical characteristics of this device have been described, and the estimated inter- and intraobserver repeatability coefficient values are reported to be >0.9 (8). Pulse wave velocity is calculated from measurements of pulse transit time and the distance traveled by the pulse between two recording sites (the right femoral and common carotid arteries): pulse wave velocity = distance (meters) / transit time (seconds). Different techniques can be used for the measurement of pulse wave velocity, such as Doppler and pressure (8). In this study, we used the TY-306 pressure transducer (Fukuda Co); this transducer has a large frequency bandwidth, from less than 0.1 Hz to more than 100 Hz, which largely covers the principal frequency harmonics of the pressure wave at different heart rates and thus allows its application for pulse wave velocity measurement. For automatic measurement of pulse wave velocity, pressure waveforms are digitized at different rates according to the distance between the recording sites; the sampling acquisition frequency is 500 Hz for carotid-femoral pulse wave velocity. The two pressure waveforms are stored in a recirculating memory buffer, half of which is displayed at any given time. During preprocessing analysis, the gain of each waveform was adjusted to obtain an equal signal for the two waveforms. During pulse wave velocity measurements, after pulse waveforms of sufficient quality were recorded, the digitization process was initiated by the operator, and automatic calculation of the time delay between two upstrokes was started. The measurement was repeated over 10 different cardiac cycles, and the mean value was used for the final analysis.

### Statistical analysis

Statistics were obtained using the ready-to-use software SPSS (version 8.0, SPSS Inc, Chicago, IL, USA). All of the values are expressed as means  $\pm$  SD. The Kolmogorov-Smirnov test was used to test the normality of distribution of continuous

**Table 1. Anthropometric and hemodynamic values in hemodialysis patient and healthy subjects**

	Hemodialysis patient	Healthy subjects	P
Age, years	39.8±15.4	36.5±9.7	0.36
Weight, kg	65.03±10.77	70.13±11.78	0.10
Height, m	165.73±9.78	165.51±7.03	0.92
Waist circumference, cm	84.26±7.97	87.82±10.23	0.15
Hip circumference, cm	95.15±5.51	97.24±5.51	0.16
Systolic blood pressure, mm Hg	141.34±20.66	113.62±12.09	<0.001
Diastolic blood pressure, mm Hg	82.50±14.64	72.75±7.62	0.004
Mean blood pressure, mm Hg	101.84±16.33	86.03±7.33	<0.001
Pulse pressure, mm Hg	58.84±9.62	40.17±10.64	<0.001
Heart rate, beat/min	81.50±8.91	76.34±10.15	0.05
Pulse wave velocity, m/s	10.99±3.08	9.27±1.45	0.01
Pulse propagation time, s	57.22±12.67	66.96±8.93	0.002

**Figure 1. The results of pulse wave velocity differences between hemodialysis patients and healthy subjects**

HP - hemodialysis patients; HS - healthy subjects; PWV - pulse wave velocity (m/s)

variables. Student t-test was used to examine the differences between hemodialysis patients and healthy subjects. The t-test for paired data was used to examine the differences between the pre- and post-dialysis periods. Relations between pulse wave velocity and other variables, including anthropometric and hemodynamic parameters, were calculated using Pearson's correlation tests and multivariate tests. A  $p < 0.05$  was considered significant.

## Results

The study was composed of 26 hemodialysis patients (female: 12, male: 14, mean age: 39.8±15.4) and 29 healthy individuals (female: 13, male: 16; mean age: 36.5±9.7). There was no significant difference between the groups in terms of age, weight, height, waist circumference, hip circumference, heart rate, and pulse wave velocity (Table 1). While systolic blood pressure, diastolic blood pressure, mean blood pressure, pulse pressure, and pulse wave velocity (Fig. 1) were significantly

**Table 2. Changing parameters in pre- and post-dialysis period**

	Pre-dialysis period	Post-dialysis period	P
Weight, kg	65.03±10.77	63.15±10.93	<0.001
Systolic blood pressure, mm Hg	141.34±20.66	122.50±14.64	<0.001
Diastolic blood pressure, mm Hg	82.50±14.64	75.76±9.66	0.001
Mean blood pressure, mm Hg	101.84±16.33	90.88±10.72	<0.001
Pulse pressure, mm Hg	58.84±9.62	47.11±8.26	<0.001
Heart rate, beat/min	81.50±8.91	89.53±10.16	<0.001
Pulse wave velocity, m/s	11.21±3.11	10.48±2.58	0.02
Pulse propagation time, s	55.61±11.80	58.97±12.36	0.04

**Table 3. Correlation between pulse wave velocity and anthropometric and hemodynamic parameters**

Pulse wave velocity (m/s)	P	r
Age, years	<0.001	0.48
Dialysis duration, month	0.57	0.21
Weight, kg	0.16	0.18
Height, m	0.02	0.29
Waist circumference, cm	0.02	0.30
Hip circumference, cm	0.28	0.14
Systolic blood pressure, mm Hg	0.001	0.43
Diastolic blood pressure, mm Hg	0.008	0.35
Mean blood pressure, mm Hg	0.002	0.41
Pulse pressure, mm Hg	0.009	0.35
Heart rate, beat/min	0.01	0.33
Pulse propagation time, s	<0.001	-0.87

higher in patients with hemodialysis than in healthy subjects, pulse propagation time was significantly higher in healthy subjects (Table 1). Although body weight (mean body weight loss 1.88±1.27 kg), systolic blood pressure, diastolic blood pressure, mean blood pressure, pulse pressure, and pulse wave velocity were significantly decreased, heart rate and pulse propagation time were significantly increased after ultrafiltration (Table 2). Although we found a significant positive correlation between pulse wave velocity and age, body height, waist circumference, systolic blood pressure, diastolic blood pressure, mean blood pressure, pulse pressure, and heart rate, we found a significant negative correlation between pulse wave velocity and pulse propagation time (Table 3). In the multivariate analysis, waist circumference was an independent predictor of pulse wave velocity (model;  $F=2.180$ ,  $p=0.011$ ; for waist circumference  $F=4.645$ ,  $p=0.046$ ). Five patients (2 men, 3 women) had a history of type II diabetes mellitus. Four diabetic patients were also hypertensive. All antihypertensive drugs were withheld for a minimum of 12 hours before the study.

## Discussion

In this study, we found that body weight, systolic blood pressure, diastolic blood pressure, mean blood pressure, pulse pressure, and pulse wave velocity were significantly decreased and that heart rate and pulse propagation time were significantly increased after ultrafiltration in hemodialysis patients. Blood pressure, including systolic, diastolic, mean and pulse pressure, and pulse wave velocity were significantly higher in hemodialysis patients. Also, we found a significant positive correlation between pulse wave velocity and age, body height, waist circumference, systolic blood pressure, diastolic blood pressure, mean blood pressure, pulse pressure, and heart rate.

Arterial pulse wave velocity and pulse propagation time play an important clinical role in defining patients under high cardiovascular risk, such as coronary artery disease and chronic dialysis patients (9-12). Arterial pulse wave velocity is inversely correlated with pulse propagation time, depending on age, heart rate, and variation in blood pressure level, such as systolic blood pressure and pulse pressure (8, 13), as shown in our study. Pulse wave velocity becomes higher at advanced age and high blood pressure and lower at low blood pressure through mechanical changes in arterial wall stretching, resulting in a change in the contribution of elastin and collagen fibers to the elastic modulus (14). The effect of heart rate on pulse wave velocity was shown in human and animal studies (15, 16). Heart rate changes with atrial pacing are able to influence arterial distensibility (15, 16). Because the viscous component of the elastic wall is highly frequency-dependent, it can be expected that higher heart rates are associated with reduced arterial elasticity (17). Increased waist circumference and body mass index, which are traditional cardiovascular risk factors, might adversely affect cardiovascular conditions through hyperlipidemia, insulin resistance, and inflammation, and they might also exert adverse effects on the arterial system by increasing pulse wave velocity (18).

Pulse propagation time refers to the time it takes for a pulse wave to travel between two arterial sites, such as the carotid artery and femoral artery (19). The velocity at which this arterial pressure wave travels is directly proportional to blood pressure. An acute rise in blood pressure causes vascular tone to increase, and hence, the arterial wall becomes stiffer, causing the pulse propagation time to shorten. Conversely, when blood pressure falls, vascular tone decreases and pulse propagation time increases (19). Generally, there are two systems used for measuring the pulse propagation time (20). One of these techniques includes an arterial tonometer that records pressure waveforms. Pulse propagation time is measured from the foot of the carotid waveform to that of the femoral waveform using sequential recordings referenced to electrocardiography. The other technique, which was used in the current study, is the Complior system, in which carotid artery and femoral artery waveforms are recorded simultaneously using mechanotransducers, and the timing is referenced to the point of maximum systolic upstroke.

Pulse wave velocity and/or arterial stiffness is well known as a predictive risk factor for cardiovascular events in patients on hemodialysis (3-6, 12, 21). However, the effect of acute hemodialysis on pulse wave velocity is conflicting. Some authors found no effect of hemodialysis on pulse wave velocity (22, 23), while other authors described a significant increase of pulse wave velocity or decreased arterial distensibility (20). An increase in heart rate after dialysis may be caused by activation of the sympathetic nervous system (24, 25). Sympathetic system activity exerts a tonic restraint on large artery distensibility, and sympathetic activation is accompanied by a reduction of arterial elasticity (26). Activation of the renin system by ultrafiltration may also lead to acute impairment of large artery distensibility (25). Kosch et al. (25) demonstrated that volume correction during the dialysis period may improve vascular function. Therefore, it is conceivable that a favorable effect on the vascular function tests of volume correction is offset by the simultaneous stimulation of the renin system and/or the sympathetic nervous system, resulting in the absence of an overall effect. Soubassi et al. (27) showed that aortic distensibility, evaluated by M-mode echocardiography, in the parasternal long-axis view in patients with end-stage renal disease is significantly lower than in normal subjects, and it is significantly improved after hemodialysis. Hydration status and its frequent changes appear to be the major determinants of both pulse wave velocity and changes in pulse wave velocity in hemodialysis patients, and these changes are independent of blood pressure (28, 29). Also, thermal changes during dialysis strongly influence intradialytic hemodynamics (30). Small increases in body temperature might affect the blood pressure response during dialysis. Furthermore, keeping the body temperature stable ameliorates left ventricular dysfunction. In order to eliminate the effects of temperature, we performed isothermic dialysis in this study. Another essential point that should be considered is that measures of arterial stiffness, such as pulse wave velocity, are also influenced by changes in serum ionized calcium levels in dialysis patients (21). LeBeouf et al. (31) found an association between relative changes in ionized calcium and an increase in postdialytic aortic pulse wave velocity, independent of blood pressure changes, using dialysate calcium concentrations closer to physiological concentrations. So, this should be kept in mind when interpreting our findings.

## Study limitations

Several limitations are present in our study. The sample size of subjects was relatively small. Furthermore, the changes of cardiovascular diseases markers were obtained before and after only one hemodialysis session. Several measurements could be more persuasive and definitive. Because of technical limitations (8), we did not measure arterial pulse wave velocity at a body height <120 cm, body weight <30 kg, and body mass index >35 kg/m<sup>2</sup>. Therefore, the results of this study will need confirmation in larger studies.



## Conclusion

Although chronic hemodialysis treatment may have worse aortic mechanical properties, ultrafiltration during hemodialysis may significantly improve aortic pulse wave velocity, which is inversely related to aortic distensibility and pulse propagation time.

**Conflict of interest:** None declared.

**Peer-review:** Externally peer-reviewed.

**Authorship contributions:** Concept - B.Ş.Y., A.Ş.; Design - B.Ş.Y., A.Ş.; Supervision - M.Y., B.Ş.Y.; Resource - N.B.A., H.K.; Materials - G.A., İ.A.; Data collection &/or processing - H.K., G.A.; Analysis &/or interpretation - B.Ş.Y., N.B.A.; Literature search - A.Ş., H.K.; Writing - İ.A., M.Y.; Critical review - İ.A., M.Y.

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