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Acute effect of hemodialysis on arterial elasticity

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Background/aim: Reduced arterial elasticity is an independent predictor of cardiovascular mortality in patients with end-stage renal disease (ESRD). Hemodialysis (HD) treatment per se can bring additional risk factors for vascular disease. Our study was designed to determine whether a single hemodialysis session leads to an acute alteration in parameters of arterial elasticity in ESRD.

Materials and methods: In this study, 58 patients undergoing chronic hemodialysis and 29 healthy controls were enrolled. Large artery elasticity index (LAEI) and the small artery elasticity index (SAEI) were measured by applanation tonometry. The acute effect of a hemodialysis session on arterial elasticity indices was assessed by comparison of prehemodialysis and posthemodialysis determinations.

Results: At baseline, LAEI did not differ significantly in patients compared with controls. In contrast, the SAEI was significantly lower in patients (4.1 ± 2.6 mL/mmHg × 100) than in healthy individuals (8.9 ± 3.4 mL/mmHg × 100, $P < 0.05$). In patients with ESRD, no significant changes in LAEI was observed after HD, but SAEI deteriorated significantly (from 4.1 ± 2.6 mL/mmHg × 100 to 3.4 ± 2.3, $P < 0.05$).

Conclusion: We conclude that ESRD patients face a significant reduction in SAEI, which is exacerbated by a dialysis procedure.

Key words: Arterial elasticity, hemodialysis, applanation tonometry

1. Introduction

The mortality rate of patients with end-stage renal disease (ESRD) treated by hemodialysis (HD) is 15- to 20-fold higher than that of the general population (1,2). Cardiovascular events are the dominant cause of death in patients with ESRD, and the high prevalence of established traditional risk factors for atherosclerosis in this clinical population undoubtedly contributes to the accelerated rate of vascular disease (3–5). However, hemodialysis treatment per se can be detrimental to the vessel wall because of the acute hemodynamic changes in arterial pressure, blood volume, sympathovagal balance, and electrolytes (4,6). In HD patients, both atherosclerosis (mainly affecting the intima of the arteries) and arteriosclerosis (affecting predominantly the media of large- and middle-sized arteries diffusely) are highly prevalent (7,8). Arteriosclerosis is characterized by reduced arterial elasticity and can be caused by a variety of mechanisms including chronic microinflammation, increased mechanical stress by hypertension, sympathetic overactivity, arterial calcification, chronic volume overload, formation of advanced glycation end products, oxidative stress, and abnormalities of the nitric oxide system (9,10) .

Reduced arterial elasticity is an independent predictor of cardiovascular mortality and is commonly encountered in patients with ESRD (11–13). Shoji et al. recently showed that reduced arterial compliance predicts cardiovascular mortality in ESRD patients on HD independent of arterial thickness, suggesting that stiffness and thickness of the arterial wall may play a distinct role in the pathogenesis of cardiovascular complications in this clinical population (14). The aim of the present study was to examine the acute effects of a single hemodialysis session on large and small arterial elasticity indices (LAEI and SAEI, respectively). The analysis of LAEI and SAEI allows an evaluation of the elasticity of the large conduit arteries and the small microcirculatory arteries that may be both linked to an increased vascular risk (15,16).

2. Materials and methods

The investigation conformed to the principles outlined in the Declaration of Helsinki. The study was approved by the Uludağ University ethics committee and all participants gave informed consent.

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2.1. Study design and participants

Fifty-eight HD patients (30 males and 28 females, mean age 41.6 ± 13.1 years, mean HD duration 73.7 ± 51.8 months) with a history of ESRD, in the absence of any clinical or laboratory documentation of atherosclerotic disease or systemic pathologies such as active infection, inflammatory disease, or malignancy were included in this study. Etiologies for ESRD were primary hypertension in 15, chronic glomerulonephritis in 10, diabetes mellitus in 4, polycystic kidney disease in 2, nephrolithiasis in 11, and other causes in 16 patients.

The patients were given hemodialysis treatment for 210–240 min, three times a week, using high biocompatibility membranes. Dialytic fluid included 1.5 mmol/L calcium, 2.0 mmol/L potassium, and 140 mmol/L sodium. Clinical signs of overhydration were not present; namely, no patient showed lower limb edema, dyspnea, uncontrolled hypertension, or signs of fluid overload at chest X-ray examination. The use of cardiac drugs was recorded in all participants. Calcium antagonists were used in 11 patients, angiotensin-converting enzyme inhibitors in 6 patients, angiotensin II receptor blockers in 5 patients, beta-adrenergic blockers in 13 cases, diuretics in 4 patients, insulin in 4 patients, aspirin in 15 patients, and statins in 8 patients. Fifty-four patients were receiving erythropoietin. Twenty-nine individuals (20 males and 9 females of mean age 43.1 ± 12.2 years) proven to be healthy and free from any signs of chronic disease after careful clinical and laboratory examination were included in the study as the control group. Control subjects had a mean serum creatinine 1.0 ± 0.4 mg/dL and were considered to be normotensive on the basis of blood pressure measurements (mean systolic blood pressure 118 ± 10 mmHg and mean diastolic pressure 76 ± 3 mmHg). Age was analyzed as a continuous variable. Body mass index (BMI) was calculated by taking the weight in kilograms over the height in meters squared. Serum samples were measured for lipid variables using commercially available kits on a Hitachi 7350 Autoanalyzer (Hitachi Ltd., Tokyo, Japan).

2.2. Measurements of arterial elasticity

Patients were evaluated 30 min before the initiation of the dialysis session. All measurements of arterial elasticity were performed on the radial artery using the noninvasive technique of arterial applanation tonometry. The PulseWave Sensor HDI (Hypertension Diagnostics, Eagan, MN, USA) was used to determine LAEI and SAEI. After 10 min of rest, an upper arm blood pressure cuff was placed on one arm while the opposite wrist was immobilized with a stabilizer to minimize the movement of the tonometric sensor placed over the radial artery. Once optimal arterial waveforms and a stable baseline were achieved, the waveforms were recorded at 200 Hz for 30 s. An automated software program calculated small and large artery elasticity indices (SAEI and LAEI, respectively) from the digitized waveforms. The average of three replicates for each participant was used for data analyses. Applanation tonometry is based on the principle that when the curved surface of a rounded pressure-containing chamber (in this case, an artery) is partially flattened, pressures are normalized and a sensor placed on the flattened surface can record the pressure in the chamber (15,16). This technique, which analyzes the signal-averaged radial artery waveform based on a modified Windkessel model, correlates well with other methods that measure hemodynamic parameters in humans (17). The Windkessel model leads to two measures, namely LAEI, pertaining to the pool of large arteries, and SAEI, pertaining to the pool of small arteries. The LAEI is derived primarily from the exponential decay of the diastolic waveform; this is assumed to be a capacitive function that resides primarily in the larger arteries. The SAEI is derived primarily from the oscillations (or reflections) that produce a decaying sinusoidal wave superimposed on the exponential decay. After the completion of the dialysis session all the above measurements were repeated.

2.3. Data analysis

Continuous variables are presented as means ± standard deviations. Categorical variables are reported as counts and compared using the chi-square test. Differences between subjects with and without ESRD were evaluated by unpaired t-test. Within-group comparisons were performed using the paired Student t-test. Simple linear regression analysis was used to assess whether changes in SAEI were independent of potential confounders, including age, sex, BMI, blood pressure values, urea, creatinine, and serum electrolytes. All statistical analyses were performed using SPSS 17.0 (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was regarded as significant.

3. Results

The baseline characteristics of patients and controls are given in Table 1. The two study groups did not differ significantly from each other with respect to age, sex, BMI, and triglycerides. When compared with the control group, HD patients had a statistically lower SAEI, while no significant difference was observed in the LAEI between the groups.

How HD acutely affects clinical, biochemical, and arterial elasticity indices is summarized in Table 2. In patients with ESRD, no significant changes in LAEI were observed after a single HD session (Figure 1), but SAEI deteriorated significantly (from 4.1 ± 2.6 mL/mmHg × 100 to 3.4 ± 2.3 mL/mmHg × 100, $P < 0.05$, Figure 2).

During hemodialysis session a minimum of 2000 mL, maximum of 4200 mL, and average of 2863 ± 602 mL

Table 1. General characteristics of patients and controls.

	ESRD patients (n = 58)	Controls (n = 29)	P-value
Age (years)	41.6 ± 13.1	43.1 ± 12.2	0.14
Sex (males/females)	30/28	20/9	0.19
Body mass index (kg/m^2)	24.4 ± 4.5	25.2 ± 3.8	0.18
Total cholesterol (mg/dL)	202 ± 51	170 ± 37	<0.01
HDL cholesterol (mg/dL)	45 ± 9	39 ± 8	<0.05
Triglycerides (mg/dL)	160 ± 69	152 ± 51	0.65
Urea (mg/dL)	142 ± 35	34 ± 12	<0.001
Creatinine (mg/dL)	9.8 ± 1.9	1.0 ± 0.4	<0.001
LAEI (mL/mmHg × 10)	12.1 ± 6.9	14.6 ± 6.8	0.52
SAEI (mL/mmHg × 100)	4.1 ± 2.6	8.9 ± 3.4	<0.05

Table 2. Characteristics of patients with ESRD before and after hemodialysis (HD) treatment (mean ± SD).

	Before HD	After HD	P-value
Body mass index (kg)	24.4 ± 4.5	23.2 ± 4.4	<0.001
Weight (kg)	63.5 ± 13.1	60.8 ± 12.8	<0.001
Heart rate (beat/min)	77 ± 11	80 ± 11	0.018
Systolic blood pressure (mmHg)	145 ± 33	127 ± 28	<0.001
Diastolic blood pressure (mmHg)	84 ± 18	77 ± 16	<0.001
Pulse pressure (mmHg)	60 ± 19	49 ± 15	<0.001
Stroke volume, mL	75.5 ± 26.3	62.1 ± 20.6	<0.001
Cardiac output, L/min	5.7 ± 2.1	5.0 ± 1.8	<0.001
Urea (mg/dL)	142 ± 35	37 ± 14	<0.001
Creatinine (mg/dL)	9.8 ± 1.9	3.4 ± 1.0	<0.001
Serum sodium (mEq/L)	140 ± 2.2	138 ± 2.0	<0.001
Serum potassium (mEq/L)	5.0 ± 0.6	5.0 ± 0.6	<0.001
Serum phosphorus (mg/dL)	5.4 ± 1.3	3.8 ± 0.9	<0.001
Serum calcium (mg/dL)	8.9 ± 0.7	10.4 ± 0.8	<0.001
LAEI (mL/mmHg × 10)	12.1 ± 6.9	12.2 ± 5.4	0.87
SAEI (mL/mmHg × 100)	4.1 ± 2.6	3.4 ± 2.6	<0.05

of fluid was removed by ultrafiltration. No statistically significant association was found between changes in SAEI measurements and changes in ultrafiltration volume (P = 0.89), BMI (P = 0.209), heart rate (P = 0.957), pulse pressure (P = 0.104), stroke volume (P = 0.792), cardiac output (P = 0.556), urea (P = 0.578), creatinine (P = 0.312), sodium (P = 0.165), potassium (P = 0.89), phosphorus (P = 0.613), and calcium (P = 0.988) levels at the end of hemodialysis session.

4. Discussion

The present investigation was performed to analyze whether a single dialysis procedure induces a change in arterial elasticity in chronic HD patients. There are three main results of our study that deserve consideration. First, we found that baseline SAEI but not LAEI is significantly reduced in ESRD patients undergoing chronic hemodialysis. Second, we found that a single dialysis session contributes to a significant impairment in the elasticity of the small arteries, but not of the large conduit arteries. Finally, we found that the reductions in SAEI following a single HD session were not associated with changes in ultrafiltration volume, BMI, heart rate, pulse pressure, stroke volume, cardiac output, urea, creatinine, and electrolytes levels following hemodialysis.

Pulse contour analysis provides an assessment of compliance or elasticity of the large conduit arteries, which predominantly influence the exponential decay of diastolic

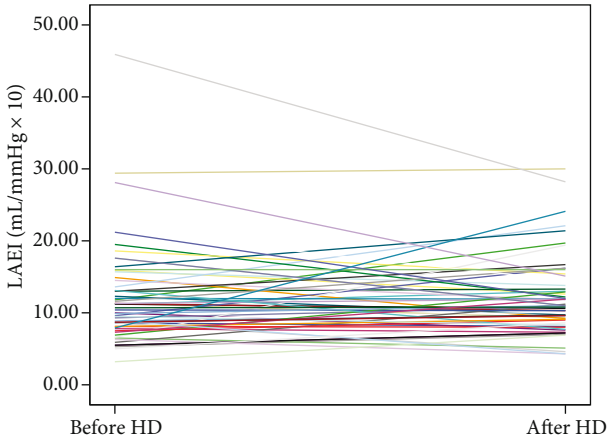

Figure 1. Prehemodialysis and posthemodialysis LAEI values in 58 patients with ESRD.

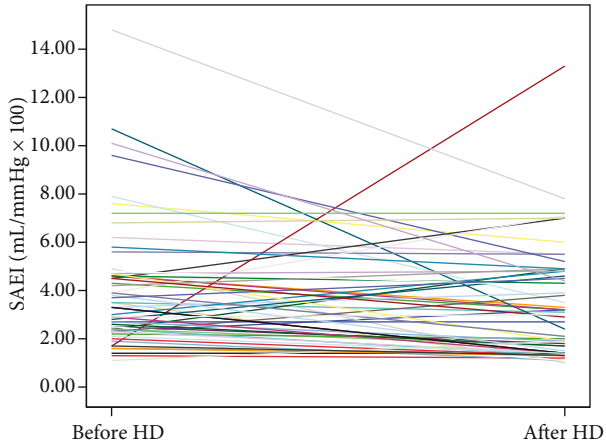

Figure 2. Prehemodialysis and posthemodialysis SAEI values in 58 patients with ESRD.

pressure, and the small artery elasticity, which influences the oscillations or reflections recorded during diastole (18). Our data suggest that LAEI is not markedly altered in patients with ESRD, whereas SAEI is selectively impaired and negatively influenced by HD. In a pilot study of 10 ESRD patients undergoing HD, Cohen and Townsend (19) showed a significant decrease in small vessel compliance during hemodialysis treatment, while no significant change was observed in large vessel compliance. Gadegbeku et al. (17) similarly observed a significant reduction in small artery compliance following HD, whereas large artery elasticity was unaffected. The capacitance mainly resides in the larger arteries (LAEI), which are particularly sensitive to aging, and the reflectance mainly resides in the branching points of the smaller vessels (SAEI), which have been shown to be particularly sensitive to the atherosclerosis (18). The potential explanation for the discrepancy between the large and small artery elasticity alterations identified by pulse wave analysis may be related to structure and function of the arteries examined. In our study, the age between the HD and control group was comparable. Because age is the major determinant of proximal large artery elasticity, it is not surprising that the LAEI is not reduced in patients with HD compared to control subjects.

Our findings are in keeping with the published results (17,19) and expand the previous studies by showing that such changes in SAEI were independent of hemodialysis-induced modifications in ultrafiltration volume, BMI, blood pressure, heart rate, pulse pressure, stroke volume, cardiac output, urea, creatinine, and serum electrolytes. A significant reduction in SAEI has been observed in patients at risk for coronary heart disease and independently predict risk for cardiovascular events (20). The decline of arterial compliance following a single HD session, with greater effects on small rather than large arteries, may have reflected an adverse effect of dialysis on endothelium-dependent vascular tone.

Endothelial dysfunction has been associated with a reduction in SAEI (21), and hemodialysis can induce this phenomenon through multiple mechanisms that include increased reactive oxygen species production, induction of adhesion molecules, and stimulation of the production of proinflammatory mediators (22–24). Besides endothelial dysfunction, functional and/or structural changes are likely to be determinants of small artery elasticity as well (25,26). However, further studies are required to fully define the link between endothelial function and the reduction in small artery compliance in HD patients.

Several study limitations should be considered in the interpretation of our results. First, our results share the limitations of observational studies. As we did not perform a clinical follow-up of the present cohort, we evaluated associations, not prediction or causation. Future prospective studies are warranted to clarify whether these changes in SAEI have prognostic implications for HD patients. Another limitation is that the pulse contour analysis as used in our study is a noninvasive measure of large and small arterial elasticity, and an invasive measure would be more precise. We recognize that the most widespread noninvasive technique to assess endothelial function is flow-mediated dilation (FMD). However, FMD is time-consuming, the equipment is very expensive, and it requires an experienced examiner (15). Other techniques available to evaluate arterial elasticity are ultrasound measurement, magnetic resonance imaging, and indirect measures such as pulse pressure.

In conclusion, our study showed an immediate association between HD and an impairment in SAEI in patients with ESRD. Further studies are needed to clarify whether treatment to improve arterial stiffness can reduce cardiovascular outcomes in patients undergoing HD.

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