

Original Article

Acute effects of haemodialysis on endothelial function and large artery elasticity

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Abstract

Background. Disturbances of functional properties of large arteries contribute to increased cardiovascular morbidity and mortality in patients with end-stage renal disease. However, it is not clear whether haemodialysis *per se* acutely affects mechanical vessel wall properties or endothelial function.

Methods. Twenty-five chronic haemodialysis patients (mean \pm standard error of the mean (SEM): age 52 ± 5 years; time on dialysis 63 ± 7 months; blood pressure $132 \pm 4/72 \pm 2$ mmHg) were studied before and immediately after a haemodialysis (HD) session using a polysulphone dialyser (ultrafiltration 1460 ± 54 ml), as well as on the following day. Blood pressure was measured with an automatic sphygmomanometer and applanation tonometry. End-diastolic diameter and distension of the brachial and carotid arteries were measured by Doppler frequency analysis of vessel wall movements in M-mode using a multigate pulsed Doppler system and aortic pulse wave velocity (PWV) by an automatic device (Complior[®]). Endothelial function was determined as brachial artery flow-mediated dilation (FMD) and compared with endothelium-independent nitroglycerine-induced dilation (NMD).

Results. FMD was $7.9 \pm 1.8\%$ in patients before HD and did not change significantly after HD or in the dialysis-free interval (6.7 ± 2.1 and $7.1 \pm 2.0\%$, respectively; NS). The same was true for NMD and PWV (12.6 ± 0.8 m/s before HD, 12.8 ± 0.8 m/s after HD, and 11.9 ± 0.7 m/s on the HD-free day). Carotid distensibility coefficients decreased significantly during HD (from $18.1 \pm 1.9 \times 10^{-3}/\text{kPa}$ to $16.7 \pm 2.2 \times 10^{-3}/\text{kPa}$, $P < 0.05$) and increased again on the HD-free day ($19.8 \pm 2.4 \times 10^{-3}/\text{kPa}$). However, when corrected for blood pressure by tonometry, isobaric carotid distensibility did not change significantly. Brachial artery

distensibility also did not show significant acute changes.

Conclusions. Haemodialysis *per se* did not have a significant effect on endothelial function or large artery mechanical vessel wall properties in patients on maintenance dialysis therapy.

Keywords: arterial distensibility; endothelial dysfunction; flow-mediated vasodilation; haemodialysis; pulse wave velocity

Introduction

Cardiovascular complications due to accelerated atherosclerosis are still the leading cause of death in patients with end-stage renal disease (ESRD) [1]. Alterations of mechanical vessel wall properties and endothelial dysfunction of large arteries are common in renal insufficiency and appear to contribute to increased cardiovascular morbidity and mortality in these patients [2–5]. Reduced arterial distensibility impairs large artery cushioning function and results in increased ventricular afterload, promoting left ventricular hypertrophy and reduced coronary perfusion. Recently, increased aortic stiffness determined by measurement of aortic pulse wave velocity has been reported to be a strong independent predictor of cardiovascular mortality in patients with ESRD [6]. However, mechanisms leading to reduced arterial distensibility in renal insufficiency are not clear. It is not known whether haemodialysis (HD) *per se* or associated chronic factors such as hyperparathyroidism or hypertension are responsible for altered arterial elastic properties [7].

Moreover, renal failure is characterized by severe impairment of endothelial function [2,4,5,8]. Endothelial dysfunction is a crucial factor in atherogenesis and an early event in the pathogenesis of arterial disease. Additionally, the endothelium plays an

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important role in the control of vascular tone of conduit arteries [9,10]. Disturbed endothelial function can result from the decreased production of endothelium-dependent endogenous vasodilators—mainly nitric oxide (NO)—and/or from a blunted response to these substances on the arterial wall. Accumulation of endogenous inhibitors of the NO synthase-like asymmetrical dimethylarginine in uraemia has been suggested to cause reduced availability of NO in renal insufficiency [11]. Clearance of these substances by haemodialysis might therefore have a beneficial effect on endothelial function. On the other hand, activation of leucocytes and platelets and oxidation of lipids during the haemodialysis procedures have been hypothesized to contribute to impairment of endothelial function [12,13]. However, data concerning the acute effect of haemodialysis on endothelial function are sparse and equivocal [14,15].

Therefore, the aim of the present study was to assess the acute effects of haemodialysis on functional vessel wall properties. In patients on maintenance haemodialysis, we measured brachial artery flow-mediated vasodilation as parameter of endothelial function, and brachial and carotid artery distensibility as well as aortic pulse wave velocity as parameters of mechanical vessel wall properties immediately before and after a haemodialysis session and on the next, dialysis-free day.

Subjects and methods

Patients

Our study was performed in accordance with protocols approved by the local ethics committee at the University of Münster. Each subject gave informed consent to participate. Patients on maintenance haemodialysis were included if coronary artery disease, heart failure, valvular heart disease or cerebral vascular disease could be excluded. Additionally, patients that had experienced episodes of dialysis-induced hypotension were not included. A total of 25 consecutive patients presenting at the dialysis centre of the University of Münster who fulfilled these criteria were included. Patients were studied before and immediately after a session of haemodialysis, and on the next dialysis-free day. Standard laboratory assays were used to determine fasting concentrations of serum creatinine, total cholesterol, triglycerides, glucose, and total calcium and phosphate levels. Table 1 shows clinical data of the patients. All patients were receiving haemodialysis three times a week by a polysulphone membrane dialyser and each session lasted 3–4 h. Four patients were smokers (mean consumption 8 ± 4 cigarettes per day). Seven patients were hypertensive (mean duration of hypertension 7 ± 4 years) and were taking ACE inhibitors ($n=4$) or a calcium antagonist combined with an ACE inhibitor ($n=3$). In six patients, diabetes mellitus was present. Two diabetic patients were also hypertensive. In all hypertensive patients, arterial hypertension was well controlled (blood pressure $<160/95$ mmHg). All antihypertensive or vasoactive drugs were paused for a minimum of 12 h before the study.

Table 1. Clinical and biochemical characteristics of 25 patients on maintenance haemodialysis treatment

| Parameter | |
|-----------------------------|----------------|
| Age (years) | 52.8 \pm 5.0 |
| Male/female | 12/13 |
| Smokers/non-smokers | 4/21 |
| BMI | 24.4 \pm 3.6 |
| Total cholesterol (mg/dl) | 204 \pm 23 |
| Total triglycerides (mg/dl) | 214 \pm 27 |
| Haemoglobin (mg/dl) | 10.3 \pm 1.0 |
| Parathyroid hormone (pg/ml) | 103 \pm 25 |
| Time on dialysis (months) | 63.3 \pm 7 |
| Ultrafiltration (ml) | 1460 \pm 54 |

Blood pressure measurements

Brachial artery blood pressure was measured using an automatic sphygmomanometer (Critikon Dinamap model 1846 SX, Tampa, FL, USA). The measurements were done at rest and the mean value of five consecutive measurements over 15 min was calculated. Additionally, carotid artery pulse waveforms were recorded using applanation tonometry (Mikro-Tip[®] Pulse Transducer, SPT 301 and Transducer Control Unit TCB-500; Millar Instruments Inc., Houston, TX, USA). The carotid artery pressure waveform was calibrated using brachial artery blood pressure. Here we assumed that mean arterial pressure does not differ between large arteries.

Vessel wall investigations

The vessel wall properties of the left common artery 2 cm below the bifurcation and of the right brachial artery 5 cm proximal of the elbow were studied in a longitudinal projection using a 7.5 MHz linear array transducer (Scanner 2000; Pie Medical Equipment B.V., Maastricht, The Netherlands) and a multigate pulsed Doppler system (Pie Medical Equipment B.V.). The arm with the arteriovenous fistula was never used for vessel wall investigations. Vessel wall movements were monitored based on low-frequency Doppler signals originating from the sample volumes coinciding with the anterior and posterior wall. The positions of the sample volumes were continuously adjusted according to the displacement of the wall. The Doppler signals in M-mode were temporarily stored and analysed by a personal computer system. The system allows the assessment of the relative change in major peripheral artery diameter as a continuous function of time, with an accuracy of $\sim 0.5\%$ [16]. With this non-invasive method the end-diastolic diameter (d (mm)) and the systolic increase of vessel diameter (distension, Δd (μm)) were measured using an electrocardiogram trigger. From these data and from the systolic and diastolic blood pressure, relative systolic increase of vessel diameter ($\Delta d \times d^{-1}$ (%)) and arterial wall distensibility coefficient ($DC = 2 \Delta d \times d^{-1} / (SBP - DBP) (10^{-3} / \text{kPa})$) were calculated. The coefficient of variation was 3.4% for the end-diastolic diameter, 7.4% for the relative systolic increase in vessel diameter and 10.8% for the distensibility coefficient ($n=25$).

Additionally, from the ascending limbs of the simultaneous continuous recordings of carotid artery pressure and wall movements, isobaric distensibility of the carotid artery

was calculated at 100 mmHg, taking a pressure window of 10 mmHg. For this purpose IGOR PRO software (WaveMetrics Inc. Lake Oswego, OR, USA) with a procedure designed by Wisstech GmbH (Sprechbach, Germany) was used.

Measurement of flow-mediated and nitroglycerin-induced vasodilation

Using the above described multigate pulsed Doppler system, end-diastolic diameter of the brachial artery was determined at five consecutive cardiac cycles and the results were averaged to a single value. The coefficient of variation using this technique is $4.5 \pm 0.7\%$ ($n=25$) for the end-diastolic diameter of the brachial artery. After three measurements at baseline were taken, a forearm cuff was inflated at 300 mmHg for 4 min at least 10 cm distal from the site of ultrasound measurement. During the last minute of cuff inflation and 1, 2, 3, 5, 7 and 10 min after cuff release, further measurements of brachial artery end-diastolic diameter were taken. Additionally, brachial artery blood flow at baseline and during the initial 15 s of reactive hyperaemia was estimated using pulsed Doppler, and the degree of reactive hyperaemia (%) of the basal blood flow was calculated. Eleven minutes after cuff release, when vessel diameter had returned to baseline values, 400 µg of glycerol trinitrate were administered sublingually and further scans of the brachial artery were taken after 1, 3 and 5 min. Flow-mediated vasodilation was calculated as the maximum absolute and relative increase in brachial artery end-diastolic diameter during reactive hyperaemia. Nitroglycerin-induced vasodilation was calculated accordingly as the maximum increase in artery diameter after sublingual application of glycerol trinitrate.

Pulse wave velocity (PWV) measurements

PVW was evaluated using the previously validated non-invasive automatic Complior device, and calculated by the transit time and the distance travelled by pulse between two recording sites: $PVW = \text{distance (m)}/\text{transit time (s)}$. The acquisition frequency of pressure waveforms was 500 Hz, obtained using two pressure transducers (TY-306, Fukuda Denshi Co., Tokyo, Japan) placed on the carotid and femoral arteries and connected to an automatic processor (Complior Colson AS, Paris, France). The concept of PVW as an indicator of aortic stiffness is based on the Bramwell-Hill formula stating that $PVW^2 = \Delta P \times V / \Delta V \times \rho$, where $\Delta P \times V / \Delta V$ is the inverse of distensibility, ΔP is the change in pressure, $\Delta V / V$ is the relative change in arterial volume and ρ is blood density [17]. All measurements were performed by the same observer. The intraobserver reproducibility coefficient was 0.92, calculated in a sample of 10 normal subjects.

Protocol

Each subject was placed in a supine position and studied first at 8:00 a.m., before the dialysis session. Following blood sampling and measurement of baseline blood pressure, we started with measurement of aortic pulse wave velocity by the Complior system. Thereafter, tonometry of the right carotid artery and measurement of distensibility of the left carotid artery for calculation of isobaric distensibility was performed as described above. After that, distensibility, and

flow-mediated and nitroglycerine-induced vasodilation of the brachial artery was studied. Immediately after the end of the dialysis session, the same protocol was repeated. The measurements at the next (dialysis-free) day were performed between 8:00 and 10:00 a.m.

Statistics

Data are expressed as mean \pm standard error of the mean (SEM). Statistical analysis was performed using the computer software SPSS (Statistical Package of Social Science, 9.0, 1999, SPSS Inc., Chicago, IL, USA). The effect of haemodialysis treatment on the measured variables was tested by repeated measures analysis of variance (ANOVA) and post-hoc comparisons (planned contrasts). Influence of arterial diameter and blood pressure was tested for by analysis of covariance. Statistical significance was assumed at $P < 0.05$.

The power of the study was calculated in cooperation with the Institute of Biomathematics, University of Münster, and was based on the main outcome parameter of flow-mediated vasodilation. It was assumed that changes in this parameter in the order of 20% of the mean were clinically relevant. Previous studies from our laboratory in different patient populations have shown that measurements of flow-mediated vasodilation and parameters of arterial distensibility have standard deviations of $< 30\%$ of the mean. To detect a change in the mean of 20% after vs before dialysis with a power of 80% and a type I error of 5%, 18 patients were needed. Therefore, it was assumed that the number of recruited patients shall be large enough to detect physiologically significant changes in vessel wall parameter.

Results

Table 2 shows blood pressure, heart rate and arterial vessel wall parameter before and after haemodialysis, and in the dialysis-free interval. Blood pressure did not change significantly with time; however, there was a mild increase in pulse pressure and heart rate after dialysis, which did not reach statistical significance (Table 2). Carotid or brachial artery diameter were also not significantly different before and after haemodialysis or in the dialysis-free interval.

Flow-mediated vasodilation was $7.9 \pm 1.8\%$ at baseline before haemodialysis and did not change significantly with dialysis or in the interval (Table 2). The same was true for nitroglycerine-induced, endothelium-independent vasodilation of the brachial artery (baseline $22 \pm 4.0\%$).

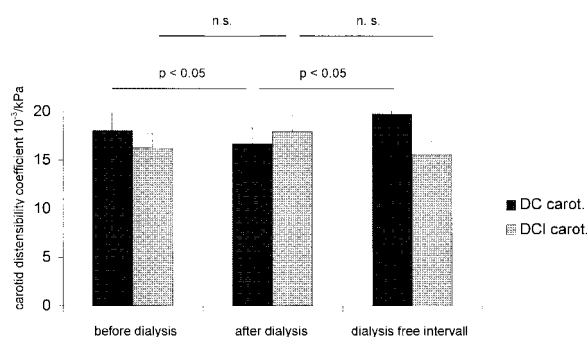
Increase in blood flow after release of the occluding forearm cuff was estimated by pulsed Doppler and was not significantly different between measurements (before HD: $421 \pm 27\%$; after HD: $411 \pm 20\%$; in interval: $425 \pm 25\%$; NS).

Aortic pulse wave velocity did also not change significantly with dialysis or in the interval (Table 2).

The carotid artery distensibility coefficient decreased significantly from $18.1 \pm 1.9 \times 10^{-3}/\text{kPa}$ before to $16.7 \pm 2.2 \times 10^{-3}/\text{kPa}$ after HD, and increased to $19.8 \pm 2.4 \times 10^{-3}/\text{kPa}$ on the next, dialysis-free, day ($P < 0.05$; Figure 1). However, when data were corrected for blood pressure changes by tonometry and

Table 2. Functional vessel wall parameter of patients on haemodialysis treatment before, immediately after and 1 day after haemodialysis (no significant changes were observed)

| Parameter | Before HD | After HD | Interval |
|--|------------|------------|------------|
| Systolic blood pressure (mmHg) | 132 ± 4 | 138 ± 4 | 130 ± 3 |
| Diastolic blood pressure (mmHg) | 72 ± 2 | 72 ± 2 | 73 ± 2 |
| Heart rate (1/min) | 87 ± 4 | 90 ± 5 | 85 ± 5 |
| Carotid artery diameter (mm) | 8.1 ± 0.7 | 8.0 ± 0.5 | 8.0 ± 0.7 |
| Carotid relative distension (%) | 7.0 ± 0.9 | 6.4 ± 0.8 | 7.3 ± 0.7 |
| Brachial artery diameter (mm) | 4.6 ± 0.2 | 4.5 ± 0.4 | 4.6 ± 0.2 |
| Brachial relative distension (%) | 5.4 ± 0.6 | 5.2 ± 0.8 | 5.1 ± 0.9 |
| Arachial distensibility coefficient ($\times 10^{-3}$ /kPa) | 13.8 ± 2.0 | 13.2 ± 2.0 | 13.8 ± 2.0 |
| Aortic pulse wave velocity (m/s) | 12.6 ± 0.7 | 12.8 ± 0.8 | 11.9 ± 0.6 |
| Flow-mediated vasodilation (%) | 7.9 ± 1.8 | 6.7 ± 2.1 | 7.1 ± 2.0 |
| Nitroglycerine dilation (%) | 22.0 ± 4.0 | 21.0 ± 4.0 | 22.0 ± 3.0 |

**Fig. 1.** Distensibility coefficient (DC) and isobaric distensibility coefficient at 100 mmHg (DCI) (corrected for blood pressure by tonometry) of the carotid artery in 25 patients before and after haemodialysis, and on the next dialysis-free day.

isobaric carotid distensibility at 100 mmHg, there was no significant difference between measurements ($16.3 \pm 1.8 \times 10^{-3}$ /kPa before and $18.8 \pm 2.0 \times 10^{-3}$ /kPa after HD, and $15.8 \pm 2.0 \times 10^{-3}$ /kPa in the dialysis-free interval; Figure 1). There were no significant changes in brachial artery distensibility coefficient ($13.8 \pm 2.0 \times 10^{-3}$ /kPa before and $13.2 \pm 2.0 \times 10^{-3}$ /kPa after HD, and $13.8 \pm 2.0 \times 10^{-3}$ /kPa in the interval).

When patients with diabetes mellitus and hypertension were excluded from the analysis, the results from the remaining 16 patients were not different to the results of the whole patient group. Moreover, subgroup analysis of the diabetic and hypertensive patients did not show different results or significant changes in vessel wall parameters after haemodialysis (Table 3).

Carotid artery distensibility but not brachial artery distensibility coefficient at baseline was negatively correlated to age ($r = -0.59$, $P < 0.05$) and time on dialysis ($r = -0.51$, $P < 0.05$). There was no correlation between flow-mediated vasodilation and brachial or carotid distensibility coefficient ($r = 0.10$ and 0.15 , respectively, NS). On analysis of covariance, arterial diameter or blood pressure did not have a significant effect on changes in arterial distensibility or flow-mediated vasodilation.

Discussion

The present study has two major findings: first, endothelial function as determined by flow-mediated vasodilation was not substantially altered acutely by the dialysis procedure; and secondly, haemodialysis *per se* does not significantly alter elastic wall properties of large arteries. No changes in brachial artery distensibility coefficient or aortic pulse wave velocity were observed. The mild and reversible reduction of the carotid artery distensibility coefficient after dialysis was attributable to a slight increase in pulse pressure and was not observed with isobaric carotid distensibility.

Although impairment of arterial distensibility and endothelial function has been repeatedly demonstrated in patients on maintenance dialysis, data concerning the impact of haemodialysis *per se* are equivocal. We report impaired brachial artery flow-mediated dilation (FMD) at baseline in our patients. In healthy volunteers we have measured brachial artery FMD between 15 and 20% [2]. The findings presented here in dialysis patients are comparable to those reported by others [4,15].

Similarly to the results of a Japanese group [15] who studied the acute effects of dialysis with a vitamin E-coated dialyser on FMD, we also did not observe a significant change in FMD after dialysis with a polysulphone dialyser. The authors suggested antioxidative properties of the vitamin E-coated membrane as a protective mechanism for endothelial function. In support of this, Targ and co-workers demonstrated recently that vitamin E-coated cellulose membranes were comparable to polysulphone membranes with respect to markers of oxidative stress; however, both were superior to standard cellulose dialysers [18]. Miyazaki and co-workers observed a significant decrease in FMD after dialysis with a standard cellulose dialyser, contrasting with the results obtained with a vitamin E-coated dialyser. Thus, it is conceivable that the dialyser membrane used is of importance. However, it was beyond the scope of the present study to compare different dialysers with respect to their effect on FMD.

Table 3. Subgroup analysis of functional vessel wall parameters before and after haemodialysis of patients with diabetes mellitus and hypertension (no significant changes or differences to the results of the groups as a whole were observed)

| Parameter | Before HD | After HD | P value |
|--|----------------|----------------|---------|
| Diabetic patients (<i>n</i> = 6) | | | |
| Brachial distensibility coefficient ($\times 10^{-3}$ /kPa) | 13.4 \pm 2.1 | 14.0 \pm 3.0 | NS |
| Isobaric carotid distensibility coefficient ($\times 10^{-3}$ /kPa) | 16.5 \pm 4.0 | 15.9 \pm 3.0 | NS |
| Aortic pulse wave velocity (m/s) | 11.8 \pm 0.4 | 12.2 \pm 0.5 | NS |
| Flow-mediated vasodilation (%) | 7.2 \pm 1.7 | 6.9 \pm 1.9 | NS |
| Hypertensive patients (<i>n</i> = 7) | | | |
| Brachial distensibility coefficient ($\times 10^{-3}$ /kPa) | 13.0 \pm 2.0 | 13.5 \pm 2.5 | NS |
| Isobaric carotid distensibility coefficient (10^{-3} /kPa) | 14.9 \pm 3.2 | 15.6 \pm 4.0 | NS |
| Aortic pulse wave velocity (m/s) | 13.4 \pm 2.1 | 13.7 \pm 2.6 | NS |
| Flow-mediated vasodilation (%) | 8.8 \pm 2.2 | 8.3 \pm 2.3 | NS |

On the other hand, an acute improvement in endothelial-dependent acetylcholine-stimulated vasodilation of hand veins has been recently demonstrated by Hand and co-workers after haemodialysis in patients with ESRD [14]. Moreover, in their experiments, impaired endothelium-dependent dilation before dialysis was also improved by administration of L-arginine, the physiological substrate of NO synthase. Since accumulation of endogenous inhibitors of NO synthase has been described in renal insufficiency [11], the authors suggested a beneficial effect of haemodialysis on endothelial function by clearance of endogenous NO synthase inhibitors. We could not confirm such a beneficial effect of haemodialysis on endothelial function in the conduit arteries investigated in our study. Differences in the vascular beds studied—veins *vs* large arteries, or in the vasodilatory stimuli, acetylcholine infusion *vs* flow-induced shear stress—may account for this discrepancy. A putative beneficial effect of clearance of NO-synthase inhibitors may be more pronounced in the venous bed than it is in the arterial system. Moreover, the issue of a possibly inhibited NO synthesis in renal failure is still being debated. Thus, a recent report showed increased systemic NO concentrations in patients with ESRD that were significantly reduced by haemodialysis, but returned again to baseline levels the day after the dialysis session [19].

Some possible confounding factors of flow-mediated vasodilation have to be addressed. First, it has been shown that baseline arterial diameter is an important determinant of endothelial-dependent vasodilation: larger arteries dilate relatively less than smaller arteries [20]. However, the end-diastolic diameter of the brachial artery was not significantly changed after the dialysis session in our study, and arterial diameter was no relevant co-variable of distensibility on statistical analysis. Secondly, differences in the degree of reactive hyperaemia may influence the degree of flow-mediated vasodilation. In the present study, the increases in blood flow during reactive hyperaemia were determined by pulsed Doppler and were comparable before and after dialysis, indicating that the degree of shear stress delivered to the brachial artery was comparable. In addition, we found no difference in

nitroglycerine-induced vasodilation, a measure of endothelium-independent vascular function.

Our results do not suggest a major acute influence of the haemodialysis session on aortic pulse wave velocity or regional distensibility of the brachial artery. However, the study presented showed a reversible and mild, however significant, reduction in carotid distensibility after haemodialysis. When distensibility was corrected for blood pressure by tonometry, and isobaric distensibility at 100 mmHg was calculated, this effect was completely blunted and carotid distensibility did not show significant acute alterations. The observed reduction in distensibility coefficient appears, therefore, to be due to the mild increase in pulse pressure and heart rate after dialysis. The observed tendency towards an increase in systolic blood pressure and heart rate after dialysis may be caused by activation of the sympathetic nervous system, which has been reported during dialysis [21]. Moreover, sympathetic activity exerts a tonic restraint on large artery distensibility, and sympathetic activation is accompanied by a reduction of arterial distensibility [22]. Activation of the renin system by ultrafiltration may also cause an acute impairment of large artery distensibility. On the other hand, volume correction may improve vascular function. Therefore, it is conceivable that a favourable 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.

ACE-inhibitor therapy can alter arterial distensibility and endothelial function. Therefore, we did perform a subgroup analysis of these patients. However, the results of the hypertensive subgroup did not differ from those of the whole population and also did not show a significant effect of haemodialysis on the parameters studied in these patients.

Chronic alterations in elasticity of conduit arteries are common in patients with ESRD. This has been confirmed in our study, the presented baseline measures of arterial elasticity being comparable to those reported by others and substantially decreased compared with healthy volunteers (personal observation). The consequences are increased systolic and decreased

diastolic blood pressure, increased left ventricular afterload, left ventricular hypertrophy and reduced coronary perfusion [3,23]. Recently, increased aortic stiffness measured as increased pulse wave velocity has been identified as an independent predictor of all-cause and mainly cardiovascular mortality in haemodialysis patients [6]. The origin of reduced elasticity of large conduit arteries in patients with ESRD is probably multifactorial. Major contributing factors are hypertension, sympathetic activation, hyperparathyroidism, lipid disorders and fluid volume overload [4,7,22,24]. Our data suggest that haemodialysis *per se* is not of major acute influence.

We conclude that haemodialysis *per se* does not acutely affect endothelial function. Existing evidence suggests that the accumulation of uraemia-related toxins, structural alterations in the arterial wall, and fluid volume overload with hypertension are the major causes of endothelial dysfunction in ESRD. However, it is conceivable that haemodialysis treatment may chronically worsen endothelial dysfunction. Moreover, acute changes in large artery elastic properties independent of changes in blood pressure are not observed during the haemodialysis session. Haemodialysis *per se* appears therefore not to contribute acutely to the impairment of functional vessel wall properties of large arteries observed in patients on maintenance dialysis treatment.

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