Ultrafiltration Volume is Associated with Changes in Different Blood Pressure Clinical Parameters in Chronically Hemodialyzed Patients
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Citation

Abstract
Introduction: Volume overload is a main factor in development of hypertension in hemodialysis patients. In order to demonstrate impact of ultrafiltration volume on blood pressure during 15-months period in a group of patients undergoing chronic hemodialysis therapy, we conducted this study. We hypothesized that ultrafiltration volume different affects the pre-/postdialysis systolic pressure, diastolic pressure, mean arterial pressure (MAP) and pulse pressure (PP) values.

Subjects and methods: Study subjects were 23 anuric chronically hemodialyzed patients. Overall study time was 15 months. One hundred thirty six single hemodialysis treatments were processed.

Results: Ultrafiltration was negatively correlated with predialysis systolic blood pressure ($r=-0.169, p=0.025$), postdialysis systolic blood pressure ($r=-0.292, p<0.001$), postdialysis MAP ($r=-0.186, p=0.015$), predialysis PP ($r=-0.290, p<0.001$), and postdialysis PP ($r=-0.370, p<0.001$). Ultrafiltration/dry body mass (UF/W) ratio was negatively correlated with predialysis PP ($r=0.222, p=0.005$), postdialysis PP ($r=-0.340, p<0.001$), and postdialysis systolic blood pressure ($r=-0.243, p=0.002$). We found significant difference in postdialysis PP between dialyses with UF/W ratio < 0.05 and dialyses with UF/W ratio > 0.05 (63.49±20.76 vs. 56.27±16.33 mmHg, $p=0.033$).

Conclusion: The ultrafiltration volume strongly affects postdialysis PP values. Evaluation of elevated blood pressure treatment in patients undergoing chronic hemodialysis therapy must be consider in respect of postdialysis PP values, not just depending on pre/postdialysis systolic and diastolic pressure or MAP values.

INTRODUCTION
Cardiovascular disease is the leading cause of morbidity and mortality in end-stage renal disease. Hypertension is common and contributes to the high cardiovascular morbidity in patients undergoing chronic hemodialysis therapy.

The impact of ultrafiltration and volume control on hemodialysis blood pressure is well known fact. Although hypertension in the hemodialysis patient population is multifactorial, volume overload is a main factor in development of hypertension in hemodialysis patients.

Definition of hypertension in patients undergoing chronic hemodialysis therapy is still under debate. Predialysis systolic and diastolic blood pressures are of particular importance. Interdialytic ambulatory blood pressure monitoring may help to determine if the patient is in fact hypertensive. The mean arterial pressure (MAP) usually serves as expression of blood pressure in hemodialysis patients, instead solely systolic or diastolic blood pressure.

Recent recognition revealed pulse pressure (systolic minus diastolic blood pressure) as a measure reflecting the pulsatile nature of the cardiac cycle.
important correlate of mortality in patients receiving dialysis. In order to demonstrate impact of ultrafiltration volume on pre-/postdialysis blood pressure (systolic and diastolic pressure, MAP and PP values) during 15-months period in a group of patients undergoing chronic hemodialysis therapy, we conducted this study. We hypothesized that ultrafiltration volume different affects the pre-/postdialysis systolic pressure, diastolic pressure, MAP and PP values.

SUBJECTS AND METHODS
Study subjects were 23 anuric chronically hemodialyzed patients (11 males and 12 females) on three-time-per-week dialysis regime, with history of chronic hemodialysis treatment for at least one year (mean hemodialysis treatment period was 5.09±3.59 years). Fifteen subjects suffered from chronic glomerulonephritis, 5 from chronic pyelonephritis and 3 subjects had diabetic nephropathy. Clinical characteristic of the subjects are demonstrated on the table 1.

Table 1: Clinical characteristic of the subjects (n = 23) on the study beginning.

<table>
<thead>
<tr>
<th>Calcium (mmol/L)</th>
<th>2.58±0.24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphorus (mmol/L)</td>
<td>1.60±0.50</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>1258.8±318.31</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>110.3±13.59</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>25.77±5.82</td>
</tr>
<tr>
<td>Albumins (g/L)</td>
<td>39.2±5.57</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.1±0.94</td>
</tr>
<tr>
<td>LDL-cholesterol (mmol/L)</td>
<td>3.0±0.99</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/L)</td>
<td>1.28±0.44</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>2.2±0.93</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.38±3.14</td>
</tr>
</tbody>
</table>

LDL: low-density lipoproteins; HDL: high-density lipoproteins, BMI: body mass index.

Overall study time was 15 months. Outcomes were measured on the study beginning and at three months intervals; six measurements per subject were totally conducted.

Antihypertensive drugs used were ACE inhibitors (3 subjects), calcium antagonists (2 subjects) and beta blockers (2 subjects).

Primary outcome measures for every single observed hemodialysis (HD) were: systolic and diastolic blood pressure before and after hemodialysis treatment (mmHg), and ultrafiltration (L).

Secondary outcome measures were predialysis and postdialysis mean arterial pressure (MAP) calculated as (systolic +2diastolic blood pressure)/3 (mmHg), predialysis and postdialysis pulse pressure (PP) computed as (systolic-diastolic blood pressure) (mmHg), and ultrafiltration volume/ dry body mass (UF/W) ratio (L/kg).

The duration of single hemodialysis treatment was 3.5-5 hours, mean heparinisation dose was 4950±1282.17 i.u. Temperature of the dialysis bath was 35.5-36.6°C, and the dialysis bath consisted of: bicarbonate 32- 35, sodium 138-145, potassium 2, and calcium 1.25- 1.75 mmol/L. The subjects were dialyzed on low flux polysulphone dialyzers F6 and F8 (Fresenius, Bad Homburg, Germany). All subjects had Cimino fistula as blood access.

No subject dropped out from the study. During the study period, medication and dialysis conditions for the same subject were unchanged. If the prescribed conditions during dialysis treatment were changed, that dialysis session was not included in the study. Two dialysis process dropped out, so 136 dialyses were included in the investigation.

Blood pressure was measured with mercury column sphygmomanometer by a trained clinician, just before beginning of the hemodialysis treatment and just after the end of the same dialysis treatment in recumbent subject. Disappearance of bruits (Korotkoff phase V) identified diastolic blood pressure. Ultrafiltration was measured volumetrically on the dialysis machine.

The results were expressed as arithmetic mean ± standard deviation. Normality of distribution was tested with the Shapiro-Wilk's W test. Differences between two dialysis groups were calculated by Student's t tests for dependent and independent data, respectively. Correlations between variables were tested by Pearson correlation coefficients and linear regression analysis.

A p value of less than 0.05 was considered statistically significant.

RESULTS
Data from 136 single dialysis treatments were processed. Differences between predialysis vs. postdialysis systolic blood pressure, diastolic blood pressure, mean arterial
pressure (MAP), and pulse pressure (PP) with significances are demonstrated on the table 2.

**Figure 2**
Table 2: Differences between predialysis vs. postdialysis systolic blood pressure, diastolic blood pressure, mean arterial pressure, and pulse pressure with significances (p) (Student t test for dependent data).

<table>
<thead>
<tr>
<th></th>
<th>Predialysis</th>
<th>Postdialysis</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>144.9±22.9</td>
<td>134.0±27.4</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>79.4±4.3</td>
<td>72.5±4.3</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>101.2±6.7</td>
<td>93.2±6.7</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>65.3±13.0</td>
<td>60.5±13.3</td>
<td>p=0.001</td>
</tr>
</tbody>
</table>

Pearson's correlations between blood pressure parameters and ultrafiltration (UF) and ultrafiltration/dry body mass ratio (UF/W) were performed.

We found that UF was negatively correlated with predialysis systolic blood pressure (r=-0.169, p=0.025), postdialysis systolic blood pressure (r=-0.292, p<0.001), postdialysis MAP (r=-0.186, p=0.015), predialysis PP (r=-0.290, p<0.001), and postdialysis PP (r=-0.370, p<0.001). We found that UF/W ratio was negatively correlated with predialysis PP (r=0.222, p=0.005), postdialysis PP (r=-0.340, p<0.001), and postdialysis systolic blood pressure (r=-0.243, p=0.002). Linear regression plot between postdialysis pulse pressure (PP) and ultrafiltration volume per hemodialysis is depicted on the figure 1.

**Figure 3**
Figure 1: Linear regression plot between postdialysis pulse pressure (PP) and ultrafiltration per hemodialysis (HD).

We also tested differences in blood pressure parameters between two groups of dialyses: dialyses with UF/W ratio < 0.05 and dialyses with UF/W ratio > 0.05. We found significant difference between dialyses with UF/W ratio < 0.05 and dialyses with UF/W ratio > 0.05 only in postdialysis PP (63.49±20.76 vs. 56.27±16.33 mmHg, p=0.033).

**DISCUSSION**
Arterial hypertension is frequent among chronically dialyzed patients. In dialysis patients the chronic fluid overload may represent a nonphysiologic condition, which brings both arterial hypertension and hemodynamic instability.

Our data confirmed our assumption of different influence of ultrafiltration volume on blood pressure parameters in dialysis patients. Changes in the ultrafiltration volume affected mostly systolic postdialysis blood pressure and consequently, pulse pressure (PP). We demonstrate the most significant influence of ultrafiltration volume on the postdialysis PP. Dialysis blood pressure was not affected with ultrafiltration volume, neither predialysis nor postdialysis.

Prakash et al. demonstrated positive correlation of volume overload with predialysis MAP. Ozkahya et al. displayed good blood pressure control (systolic an diastolic) with ultrafiltration, after cessation of antihypertensive drugs. On the contrary, Testa et al. could not improve volume overload on systolic and diastolic blood pressure increasing in patients undergoing chronic hemodialysis therapy. Luik et al. concluded that interdialytic fluid load does not result in higher blood pressure (interdialytic blood pressure was measured with an ambulatory blood pressure monitor) in hemodialysis patients. Expansion of extracellular fluid volume is the major pathophysiologic mechanism for the development of hypertension in these patients; however, alterations in other humoral mechanisms (especially nitric oxide and endothelin 1 disbalance) also play a significant role.

Although various factors influence the pathogenesis of hypertension, volume overload is the most significant. The normalization of the patient hydration status is followed by a reduction in pressure values. Fluid removal is usually achieved by ultrafiltration to achieve a clinically derived value for “dry weight.” The achievement of an optimal dry weight is still one of the most difficult and important tasks of a dialysis clinic. Covic et al. concluded that 24-hour blood pressure and blood pressure after dialysis are better related to total body water than blood pressure before dialysis, which was however weakly related to the acute
volume overload, induced by interdialytic weight gain. In some hypertensive hemodialysis patients, blood pressure rises further during ultrafiltration. Cirit et al. concluded that the paradoxical blood pressure rise with ultrafiltration usually occurs in the presence of overhydration and cardiac dilatation and should be treated by intensified ultrafiltration. The explanation of this phenomenon remains speculative.

Finally, our findings support our assumption that amount of ultrafiltration volume affects different blood pressure clinical parameters. The ultrafiltration volume strongly affects postdialysis PP values. Treatment of arterial hypertension in dialyzed patients depends mostly on ultrafiltration volume removal and real dry weight achievement. Consequently, evaluation of elevated blood pressure treatment in patients undergoing chronic hemodialysis therapy must be considered in respect of postdialysis PP values, not just depending on pre/postdialysis systolic and diastolic pressure or MAP values.

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