Acute effects of haemodialysis on central venous and arterial pressure characteristics

Thalhammer, Christoph; Segerer, Stephan; Augustoni, Marlene; Jacomella, Vincenzo; Clemens, Robert K; Wüthrich, Rudolf P; Amann-Vesti, Beatrice R; Husmann, Marc

Abstract: BACKGROUND Hemodynamic stability of patients during dialysis sessions is of pivotal importance in daily practice and accurate determination of dry weight (DW) remains a challenge. Little information is available about central venous and aortic pressure during dialysis. In this pilot study we used a new non-invasive technique to describe the changes in central venous pressure (CVP) during dialysis. METHODS An ultrasound-assisted silicon-based pressure-manometer was used at the contralateral cephalic vein during haemodialysis to quantify central venous pressure. Central aortic pressure changes were assessed as aortic augmentation index (AIx) and subendocardial viability ratio (SEVR) by radial planimetry and brachial arterial blood pressure measurements. Bioimpedance was applied to measure total body water (TBW), as well as extracellular (ECW) and intracellular (ICW) water before and after HD. All measurements were performed prior during and after one and two hours on HD except for bioimpedance that was only assessed before and after dialysis. RESULTS Ten patients (5 female) were included with a median age of 72 years (23-82). Haemodialysis reduced the weight by 2.0 kg (range 0.2 - 3.9 kg), corresponding to a measured decrease in TBW of 1.9 L (36.1 L to 34.2 L, n.s.). The mean CVP showed a significant decrease (9.0 cmH2O to 0.8 cmH2O; p=0.0005) during dialysis. The major and significant drop in CVP was found during the first hour of haemodialysis (9 cmH2O to 2.8 cmH2O). Starting and stopping dialysis was reflected by a reduction of 2.6 cmH2O and a rise of 2.8 cmH2O (n.s.). AIx decreased continuously from 26.1 % to 21.0 % (n.s.). SEVR increased significantly from 126 % to 156 % (p<0.05) during HD, and decreased to 139% direct after HD (n.s.). CONCLUSIONS This is the first study that illustrates a prominent reduction of central venous pressure during the first hour of hemodialysis. Non-invasive central venous pressure measurement is feasible during hemodialysis and adds another piece in the puzzle of factors involved in hemodynamic stability.

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Acute effects of haemodialysis on central venous and arterial pressure characteristics

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Running title: Hemodynamic changes during haemodialysis
Abstract

Background:
Hemodynamic stability of patients during dialysis sessions is of pivotal importance in daily practice and accurate determination of dry weight (DW) remains a challenge. Little information is available about central venous and aortic pressure during dialysis. In this pilot study we used a new non-invasive technique to describe the changes in central venous pressure (CVP) during dialysis.

Methods: An ultrasound-assisted silicon-based pressure-manometer was used at the contralateral cephalic vein during haemodialysis to quantify central venous pressure. Central aortic pressure changes were assessed as aortic augmentation index (Alx) and subendocardial viability ratio (SEVR) by radial applanation tonometry and brachial arterial blood pressure measurements. Bioimpedance was applied to measure total body water (TBW), as well as extracellular (ECW) and intracellular (ICW) water before and after HD. All measurements were performed prior during and after one and two hours on HD except for bioimpedance that was only assessed before and after dialysis.

Results: Ten patients (5 female) were included with a median age of 72 years (23-82). Haemodialysis reduced the weight by 2.0 kg (range 0.2 – 3.9 kg), corresponding to a measured decrease in TBW of 1.9 L (36.1 L to 34.2 L, n.s.). The mean CVP showed a significant decrease (9.0 cmH\textsubscript{2}O to 0.8 cmH\textsubscript{2}O; \(p=0.0005\)) during dialysis. The major and significant drop in CVP was found during the first hour of haemodialysis (9 cmH\textsubscript{2}O to 2.8 cmH\textsubscript{2}O). Starting and stopping dialysis was reflected by a reduction of 2.6 cmH\textsubscript{2}O and a rise of 2.8 cmH\textsubscript{2}O (n.s.). Alx decreased continuously from 26.1 % to 21.0 % (n.s.). SEVR increased significantly from 126 % to 156 % (\(p<0.05\)) during HD, and decreased to 139% direct after HD (n.s.).

Conclusions: This is the first study that illustrates a prominent reduction of central venous pressure during the first hour of hemodialysis. Non-invasive central venous pressure measurement is feasible during hemodialysis and adds another piece in the puzzle of factors involved in hemodynamic stability.

Keywords
Aortic stiffness, central venous pressure, dry weight, haemodialysis
Introduction

Need for renal replacement therapy has increased significantly during the last 30 years in most parts of the world, and the incidence and prevalence of dialysis dependent patients is expected to rise further.\textsuperscript{1-3} The haemodialysis population has changed significantly, with a prominent increase in elderly, diabetic and concomitant atherosclerotic diseased patients.\textsuperscript{2} Therefore the range of tolerated fluid changes during haemodialysis in this frail patient population is small and the definition of dry-weight becomes increasingly important.\textsuperscript{4} Fluid overload results in pulmonary symptoms and left ventricular hypertrophy, whereas fluid deficiency on the other hand results in hypotension, which not only leads to severe symptoms during dialysis but also promotes heart ischemia resulting in heart failure.\textsuperscript{5} Hypotensive episodes during haemodialysis as well as overhydration are associated with increased mortality due to cardiovascular events.\textsuperscript{6, 7} The “dry-weight” is defined as the body weight to be reached at the end of dialysis.\textsuperscript{8} In daily practice nephrologists rely on the symptoms described by the patient and the clinical examination, also these subjective information do not perform well in defining fluid overload.\textsuperscript{4, 8}

Dialysis patients have a particularly high cardiovascular risk and heart failure is very common. The major causes of morbidity and mortality in patients with end-stage renal disease (ESRD) are cardiovascular diseases\textsuperscript{9}. An increased aortic stiffness is known to be a strong independent predictor of all-cause and mainly cardiovascular mortality.\textsuperscript{10, 11} In contrast to the increasing number of hemodialysis sessions performed, little information is available about central venous pressure and aortic stiffness as factors which might be involved in patient stability and might help to define "dry weight".
A novel, ultrasound based method to measure CVP non-invasively recently has been introduced.\textsuperscript{12} Peripheral venous pressure at the forearm is quantified by compression of the vein under ultrasound control. A pressure meter adapted on the ultrasound transducer records the pressure needed to compress the vein totally. This method showed an excellent correlation with CVP in two controlled studies, comparing invasive and non-invasive CVP measurement.\textsuperscript{12, 13}

We therefore used non-invasive methods to defined acute changes in central venous pressure (CVP) and central aortic pressure changes during the course of haemodialysis sessions.
Methods

Subjects and study design

This pilot study with non-invasive cardiovascular monitoring during one haemodialysis session in consecutive recruited patients was performed at a tertiary referral centre in the dialysis suite. The local ethic committee approved the study (Nr. 2010-0268/1) and all patients gave written informed consent. This pilot study was conducted in compliance with the protocol, the current version of the Declaration of Helsinki, and ICH-GCP as well as all national legal and regulatory requirements. Exclusion criteria were severe arterial hypertension or hypotension and unsuitable superficial veins of the forearm or known subclavian vein obstruction (contralateral to haemodialysis access) or cardiac arrhythmias that made pulse wave analysis impossible.

Non-invasive measurements of vascular parameters

Measurements of CVP using compression ultrasound were performed with a high-end duplex system iU22 with a 17-5 MHz linear array transducer (Philips, Best, Netherlands) by a single experienced investigator at the forearm contralateral the vascular access site. A pressure manometer (PPM0310, U. Baumann, Muensingen, Switzerland) was attached to the ultrasound transducer. The manometer consists of a translucent silicon membrane (MVQ, Angst and Pfister AG, Zurich, Switzerland) connected to a commercially available pressure meter (Bourdon Haenni AG, Jegenstorf, Switzerland) with a flexible pressure tubing. The system is described in detail elsewhere. A superficial vein at the forearm (preferentially the distal cephalic vein), clearly visible on ultrasound through the translucent manometer membrane was selected. The vein had to be easily compressible, without
postphlebitic changes locally and no overt clinical signs of proximal venous obstruction had to be present. After applying ultrasound transmission gel the transducer with the pressure meter was placed on the skin with minimal pressure. Following zero adjustment slowly increasing pressure was applied by the transducer until first complete compression of the vein. The pressure at this collapse point indicated the intravasal peripheral venous pressure. The point of measurement was below the level of the right atrium. The difference between the level of the ultrasound measurement and the position of the right atrium was documented and subtracted from the crude pressure value¹².

Bioimpedance analysis was performed before and after haemodialysis using the Body Composition Monitor BCM (Fresenius Medical Care, Bad Homburg, Germany) to assess total body water (TBW), as well as extracellular (ECW) and intracellular (ICW) water¹⁵.

Systolic (BPₓ) and diastolic blood pressure (BPₐ), heart rate (HR), CVP, AIX and subendocardial viability ratio (SEVR) as a marker of subendocardial perfusion were measured before, direct after start of HD (within five minutes), after one and two hours, and direct before and after end of haemodialysis (each within five minutes). Applanation tonometry of the radial artery was performed in the non-fistula arm with the SphygmoCor system (AtCor Medical, Sydney, Australia) by a single observer with patients in the supine position to acquire radial artery waveforms. A validated transfer function was used to generate the corresponding ascending aortic pressure waveform. Augmented pressure was defined as the difference between the second and the first systolic peak, and augmentation index (AIX) was expressed as a percentage of the pulse pressure (difference between systolic and diastolic pressure)¹⁶, ¹⁷. Subendocardial blood supply as a parameter evaluating the risk of
myocardial ischemia was expressed with the subendocardial viability ratio (SEVR), the ratio of the diastolic phase (diastolic time index) to that of the systolic phase (time tension index) as measured by the SphygmoCor system\textsuperscript{18-20}.

For statistical analysis StatView (SAS institute Inc.) was used. A \( p < 0.05 \) was referred to statistically significant. All values represent means (± standard deviation). ANOVA was used to compare the means of the measurements before, during and after HD. Fisher PLSD (Protected Least Sig. Difference) test was used to test the differences of pairwise combinations.
Results

Ten patients (5 female) were included in this feasibility study (table 1). The mean age was 61 years (range: 23-82 years). All patients underwent chronic thrice-weekly HD and were on haemodialysis for a mean of 28.4 months (range: 2-66 months). Clinically, in none of the patients a necessity of a change of the "dry weight" was expected by the nephrologist.

The changes in the measured parameters before and after HD are summarized in table 2. Systolic blood pressure decreased from 142 (± 20) to 132 (± 28) mmHg as well as the diastolic blood pressure from 66 (± 23) to 62 (± 16) mmHg. Heart rate rose from 72 (± 8) to 74 (± 15) beats/min. These changes in BP and HR were statistically not significant.

Excess water measured by bioimpedance before the start of dialysis was well controlled with a mean of +1.5 L (table 2). In only two patients the excess water exceeded 2 L. The ultrafiltration during the haemodialysis sessions reduced the mean body weight by 2.0 (range 0.2 – 3.9) kg. This was consistent with a decrease in total body water (TBW) of 1.9 L (36.1 ± 7.4 L to 34.2 ± 5.0 L, n.s.) measured by bioimpedance spectroscopy. About 2/3rd of water was from the extracellular compartment (ECW 1.1 L, from 16.4 ± 3.4 L to 15.3 ± 3.1 L, n.s.) and about 1/3rd from the intracellular water (ICW 0.8 L, from 19.7 ± 5.0 L to 18.9 ± 2.8 L, n.s.). Also well correlated with the expected reduction in water, according to body weight, the differences did not reach the level of significance.

Mean CVP showed a significant decrease during dialysis (9.0 cmH$_2$O to 0.8 cmH$_2$O; p=0.0005, Figure 1). To measure the effect of the extracorporeal blood circulation, the
CVP was measured before and immediately after the start of dialysis. Also treatment was started with the lines filled with substitute solution, the CVP showed an early drop of 2.6 cmH\textsubscript{2}O (n.s.) and a similar increase after the return of the blood to the patient with a mean increase in CVP of 2.8 cmH\textsubscript{2}O (n.s.). After one hour of dialysis the CVP was already significantly lower than the CVP before the start of dialysis (9.0 vs 2.8 cmH\textsubscript{2}O, p<0.05). Thereafter, CVP demonstrated a steady decline over the following hours with a relatively moderate delta of 1 in the second hour and 0.5 per hour during the last two hours.

AIx decreased continuously from 26.1 % to 21.0 % which did not reach the level of significance (n.s.; Figure 2). SEVR increased significantly from 126 % to 156 % (p<0.05) during HD (Figure 3), and decreased again to 139% direct after HD (n.s.).
Discussion

The present study is the first simultaneous evaluation of changes in central venous and arterial pressures using non-invasive approaches to investigate the effect of the continuous volume ultrafiltration during a four hour haemodialysis session. The novelty and primary goal of this pilot study was to demonstrate the feasibility of non-invasive evaluation of central venous pressure during dialysis. There is a scarcity of data on central venous pressure in patients during hemodialysis. The dry weight of the study population was well selected with a moderate water excess before dialysis of 1.5 L measured by bioimpedance. The ultrafiltration led to a mean decrease in body weight of 2 kg. This was associated a decrease in CVP from from 9 to 1 cmH\textsubscript{2}O. In contrast to the continuous ultrafiltration, CVP demonstrated a strong and statistically significant decrease within the first hour. With the start of the extracorporeal circuit CVP decreased rapidly. This is interesting as the lines were filed before connecting the patient. The main CVP drop was detectable during the first hour and then there was a continuous decrease during the last three hours. The prominent decrease of CVP during the first hour of dialysis needs further evaluation. It will be particularly interesting whether this decrease in CVP is associated with hemodynamic instability and whether this early drop can also be seen in overhydrated patients. The bioimpedance measurements particularly the excess water did not correlate with the absolute numbers of CVP and with the change in CVP most likely due to the low number of patients included in our feasibility study. These results will form the basis for the necessary patient number for a currently planned study.
The aortic augmentation index is a reflection of aortic stiffness and can be calculated by the wave form of a peripheral artery. In our series the AIx demonstrated a trend towards a decrease in stiffness during a four hour dialysis session. This is consistent with previously published data.\textsuperscript{21, 22} A significant (p < 0.001) decrease of AIx before dialysis from 30.6 ± 1.5 to 22.2 ± 1.8 after dialysis was demonstrated in 51 dialysis patients.\textsuperscript{21} In another study with 20 patients dialysis decreased AIX from 24.2 ± 11.3 to 15.6 ± 12.6 (p < 0.05) with a similar continuous trend in decrease within the four hours dialysis.\textsuperscript{22} The impact of volume overload on changes in aortic stiffness in patients with haemodialysis is incompletely understood. In one study arterial stiffness was independently related to the extracellular water / total body water ratio.\textsuperscript{23} Volume reduction with dialysis was significantly correlated with a decrease in Alx in nineteen patients studied before and 24 h after dialysis.\textsuperscript{24} In contrast, another study reported a high correlation of the improvement in aortic stiffness with decrease in systolic blood pressure but not with ultrafiltration volume.\textsuperscript{22} In addition to AIx, subendocardial viability ratio (SEVR) can be calculated through pulse wave analysis alike and is an interesting non-invasive measure of myocardial perfusion related to left ventricular work. For both parameters, previous studies have shown that pulse-wave analysis has a good reproducibility in patients with chronic renal failure.\textsuperscript{25, 26} There are studies on different modes of haemodialysis and their having dissimilar impacts on markers of arterial stiffness. This might have clinical impact since aortic augmentation index has been shown to be an independent predictor for cardiovascular morbidity in patients with chronic renal failure.\textsuperscript{10} During recent years new techniques have been used for the equation of “dry weight”.\textsuperscript{27-29} Particularly the role of bioimpedance spectroscopy found a lot of attention\textsuperscript{27, 30}. 

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We now demonstrate that peripheral measurement of central venous pressure is feasible during dialysis and gives additional information. This small pilot study forms the basis for the evaluation of the central venous pressure in a larger cohort of patients on hemodialysis to define the associations with dry weight and hemodynamic stability.

**Conclusions**

Fluid elimination during dialysis as reflected by the difference in weight is confirmed by bioimpedance analysis and reduction in central venous pressure. Central venous and arterial pressures show early reduction during the first hour which is accompanied by a steady improvement in subendocardial perfusion in relation to cardiac workload. Whether this new tool will help to define dry weight or preventing the early drop might reduce intradialytic hypotension needs to be evaluated in a larger population of haemodialysis patients.
References


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**: 376-82.


**Figure legends**

**Figure1:**

Course of central venous pressure (CVP) before, during and after haemodialysis

**Figure 2:**

Course of augmentation index (Alx) before, during and after haemodialysis

**Figure 3:**

Course of subendocardial viability index (SEVR) before, during and after haemodialysis
### Table 1: Basic clinical information of the study cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>10</td>
</tr>
<tr>
<td>Female/male</td>
<td>5/5</td>
</tr>
<tr>
<td>Age (years; median; range)</td>
<td>72.5 (23-82)</td>
</tr>
<tr>
<td>HD duration (months; median, range)</td>
<td>28.4 (2-66)</td>
</tr>
<tr>
<td>Height (cm; median; range)</td>
<td>163 (153-172)</td>
</tr>
<tr>
<td>Weight (kg; median; range)</td>
<td>68 (51-95)</td>
</tr>
</tbody>
</table>
Table 2: Changes in clinical and hemodynamic parameters before and after haemodialysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>before HD</th>
<th>after HD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height [cm]</td>
<td>163.5 ± 6.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight [kg]</td>
<td>68.3 ± 13.9</td>
<td>66.3 ± 13.9</td>
<td>n.s.</td>
</tr>
<tr>
<td>BMI [kg/m^2]</td>
<td>25.5 ± 4.5</td>
<td>24.7 ± 4.5</td>
<td>n.s.</td>
</tr>
<tr>
<td>TBW [L]</td>
<td>36.1 ± 7.4</td>
<td>34.2 ± 5.0</td>
<td>n.s.</td>
</tr>
<tr>
<td>ECW [L]</td>
<td>16.4 ± 3.4</td>
<td>15.3 ± 3.1</td>
<td>n.s.</td>
</tr>
<tr>
<td>ICW [L]</td>
<td>19.7 ± 5.0</td>
<td>18.9 ± 2.8</td>
<td>n.s.</td>
</tr>
<tr>
<td>BP_s [mmHg]</td>
<td>143 ± 20</td>
<td>132 ± 28</td>
<td>n.s.</td>
</tr>
<tr>
<td>BP_d [mmHg]</td>
<td>66 ± 23</td>
<td>62 ± 16</td>
<td>n.s.</td>
</tr>
<tr>
<td>Heart rate [beats/min]</td>
<td>72 ± 8</td>
<td>74 ± 15</td>
<td>n.s.</td>
</tr>
<tr>
<td>CVP [cmH_2O]</td>
<td>9.0 ± 7.2</td>
<td>3.6 ± 4.8 *</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Alx [%]</td>
<td>26.1 ± 12.2</td>
<td>21.0 ± 6.1</td>
<td>n.s.</td>
</tr>
<tr>
<td>SEVR [%]</td>
<td>126.2 ± 21.4</td>
<td>139.2 ± 31.6</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Values in mean ± standard deviation

Figures

Figure 1

Course of central venous pressure (CVP) before, during and after haemodialysis

Central venous pressure CVP [cm $H_2O$]

Time during haemodialysis

- before
- direct after
- one hour
- two hour
- before end
- after

P < 0.01
P = 0.0005
P < 0.05
Figure 2

Course of augmentation index (AIx) before, during and after haemodialysis

Time during haemodialysis

Before, direct after, one hour, two hour, before end, after
Course of subendocardial viability index (SEVR) before, during and after haemodialysis