Dynamic changes in right ventricular pressures during haemodialysis recorded with an implantable haemodynamic monitor

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Abstract

Background. Intermittent and chronic volume over-load contributes to the development of cardiovascular disease in patients on maintenance haemodialysis (HD). Continuous monitoring of central haemodynamic parameters may provide valuable information to improve volume control, particularly in patients with left ventricular dysfunction.

Methods. Five patients on HD, age 53–76 years, with systolic and/or diastolic dysfunction (EF 20–50%) received an implantable haemodynamic monitor (IHM) (Chronicle® model 9520, Medtronic). The IHM consists of a memory device implanted subcutaneously and a transveneous right ventricular (RV) lead carrying a pressure sensor. It continuously records heart rate, RV systolic (RVSP) and diastolic pressures (RVDP), RV dP/dt and an estimate of pulmonary artery diastolic pressure (ePAD). Continuous haemodynamic profiles were recorded in all patients.

Results. During dialysis RVSP and ePAD dropped by a mean of 39 and 50%, respectively. RVDP decreased by 6.6 mmHg. The lowest pressures occurred during the first 90 min of dialysis and were partly restored at the end of the procedure. Long-term haemodynamic monitoring unmasked severe volume overload in one patient, when dry weight was kept stable despite a decrease in lean body mass. In another patient with recurrent dyspnea after dialysis, paroxysmal atrial fibrillation, regularly occurring during dialysis, was identified as the cause of symptoms.

Conclusion. The implanted haemodynamic monitor was a sensitive indicator for changes in volume load. Continuous haemodynamic monitoring may offer a valuable tool to improve volume management in dialysis patients with left ventricular dysfunction.

Keywords: haemodialysis; haemodynamic monitoring; left ventricular dysfunction

Introduction

Cardiovascular disease is the major cause of morbidity and mortality in patients on maintenance haemodialysis (HD), accounting for up to 60% of all deaths [1–3]. Haemodynamic derangement constitutes a substantial part of the overall cardiovascular risk in dialysis patients [4]. This relates in part to the adverse effects of recurrent or chronic volume and pressure overload on the heart and the cardiovascular tree. In addition, hypertrophic or dilated cardiomyopathy is very common among patients at initiation of dialysis and seems to be aggravated after starting dialysis [5–7]. This further limits the capability of the cardiovascular system to cope with excess fluids, thus complicating optimal volume management in dialysis care.

The most commonly used method in HD to assess solute removal, ‘dry weight’, is mainly dependent on the knowledge of the body compartments’ capacity and the amount of water and sodium concentration in each compartment [8]. This method is imprecise and changes in nutritional status and lean body mass are not easily established. As a consequence, acute and chronic over- or under-hydration are common amongst dialysis patients.

Recently, haemodynamic monitoring with an implantable device has proven safe and reliable in continuously measuring cardiac filling pressures from a right ventricular sensor in patients with chronic heart failure (CHF) [9,10]. In such patients the implantable haemodynamic monitor has been proven reliable in continuously measuring right ventricular pressures compared to invasive measurements [10], in predicting volume overload before patients become symptomatic [11] and in tailoring heart failure medication [12]. Moreover, as evidenced by the recent COMPASS-HF
they can be used to decrease morbidity in heart failure patients [13]. Therefore, we hypothesized that the implantable haemodynamic monitor (IHM) would provide useful information to aid volume management in HD patients with left ventricular dysfunction. The aim of this pilot study was to describe the dynamic change of right ventricular pressures continuously recorded by an IHM during and between dialysis sessions in five chronic HD patients.

**Subjects and methods**

**Patients**

Patients included in this study were on maintenance HD, were not expected to undergo kidney transplantation within the next 6 months and had various degrees of left ventricular systolic and/or diastolic dysfunction. All patients gave their written consent to the study. The investigation conformed to the principals outlined in the Declaration of Helsinki and the local ethics committee approved the protocol.

**Implantable haemodynamic monitoring**

The Chronicle® (Model 9520; Medtronic, Inc., Minneapolis, USA) consists of an IHM with a random access memory for continuous storage of data from a pressure sensor lead (Model 4328A; Medtronic, Inc., Minneapolis, USA) positioned in the right ventricle (Figure 1). Continuous haemodynamic variables such as right ventricular systolic (RVSP), diastolic (RVDP) and estimated pulmonary artery diastolic pressure (ePAD) as well as heart rate are derived by the IHM from each cardiac cycle. The accuracy and stability of pressure measurements over time have been tested in earlier studies [9,10]. The ePAD is derived from the RV pressure waveform at maximum dP/dt, the time of pulmonary valve opening. This method was validated earlier [14]. Measured values are stored continuously as the median or median and range (6th and 94th percentiles) over each storage interval. The storage interval varies from 2 s (3.5 h) to 1 h 11 min (3 months) with several programmable steps in between. Activity counts on the IHM estimates the patient’s daily activities. The pressure sensor in the right ventricle measures absolute pressure, requiring correction for continuously varying ambient atmospheric pressures by an external pressure reference device (EPR) (Model 2955hf; Medtronic Inc, Minneapolis, USA). At each follow-up, data from the EPR are read along with data stored by the IHM. Through the use of custom software in the IHM Programmer, the absolute sensor data are corrected for changes in barometric pressure.

The normal ranges for the RVSP, RVDP and ePAD are 15–30 mmHg, 0–8 mmHg and 4–12 mmHg, respectively.

**Haemodialysis**

All patients were dialyzed three times/week in a day-care dialysis hospital. During dialysis the patients kept a half-sitting or supine position. The dialysis was performed at the same time of the day for each patient during all observations. HD was performed with bicarbonate dialysate on Gambro AK-200 (Gambro, Sweden) or Fresenius 4008 E/H (Fresenius Medical Care AG, Germany) HD machines using polysulfone (HPS; Fresenius Medical Care AG, Germany) hollow fiber dialyzers. Dialyzers were not reused.

**Study protocol**

Before start of dialysis the IHM was programmed to a storage interval of 2 s allowing 3.5 h data to be stored in the IHM. The IHM memory was interrogated once during and once right after the dialysis procedure and then reprogrammed to collect data between sessions with storage intervals 6–24 min to allow for continuous, ambulatory recordings during daily living. The individual and mean results of RVSP, RVDP and ePAD were calculated as an average of 60 s at the following time points; before initiation of dialysis, 30 and 60 min after

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**Fig. 1.** A Chronicle, implantable hemodynamic monitor with the pressure sensor lead.
initiation of dialysis, the minimum value during dialysis for each of the variables above and just after termination of dialysis. The time from start of dialysis to when the lowest value of each variable occurred was also calculated.

**Results**

**Patients**

Five patients with end-stage renal disease were implanted with the haemodynamic monitor. Baseline patient characteristics and dialysis information are given in Table 1. The medical management was tailored to the individual patient by the nephrologists in charge of the dialysis care. Prior to the study, beta-blocker therapy had been withdrawn in patient no. 1 due to frequent pressure falls during dialysis. In patient no. 2 ACE inhibitor treatment had been stopped due to low blood pressure and ASA had been withdrawn for bleeding complications. All patients had an arteriovenous fistula in the arm. At time of this study the patients had been on HD for 1–6.5 years. Two patients (nos 3 and 4) were treated with haemodiafiltration and highflux polysulfone dialysis membranes, while three patients (nos 1, 2 and 5) were on conventional HD with lowflux polysulfone membranes. The duration of dialysis ranged from 4.25 to 5 h, the average ultrafiltration volume per dialysis from 0 to 2800 ml, i.e. 0–3.8% of the dry weight.

Standard laboratory parameters were well controlled with a haemoglobin concentration ranging from 117 to 141 g/l, serum albumin from 30 to 40 g/l, standard bicarbonate from 22 to 26 mmol/l and parathyroid hormone levels from 31 to 230 ng/l.

There were no complications associated with the device or the implantation procedure. Three weeks after implant one patient (no. 2) with cystic kidney disease and a history of recurrent Gram-negative septicemia developed *Klebsiella* sepsis. Although this was not considered device related, the IHM was explanted on the patient’s demand.

**Table 1. Patient baseline characteristics**

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<td>Age/sex</td>
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<td>76/male</td>
<td>60/male</td>
<td>59/male</td>
<td>53/female</td>
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<td>Hypertensive renal disease</td>
<td>Polycystic kidney disease</td>
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<td>Chronic pyelonephritis</td>
<td>Chronic gomorulo-nephritis</td>
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<td>Etiology, cardiovascular</td>
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<td>CAD</td>
<td>CAD</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Other cardiovascular</td>
<td>Pacemaker</td>
<td>None</td>
<td>None</td>
<td>Pacemaker implantation and RF-ablation 2002</td>
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<tr>
<td>NYHA class</td>
<td>II</td>
<td>III</td>
<td>III</td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>25</td>
<td>35</td>
<td>35</td>
<td>60</td>
<td>50</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>60</td>
<td>53</td>
<td>51</td>
<td>51</td>
<td>35</td>
</tr>
<tr>
<td>LVEDD</td>
<td>1.51</td>
<td>1.41</td>
<td>1.63</td>
<td>1.46</td>
<td>2.07</td>
</tr>
<tr>
<td>PCR</td>
<td>0.84</td>
<td>1.80</td>
<td>1.34</td>
<td>1.13</td>
<td>0.82</td>
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<tr>
<td>Body weight (kg)</td>
<td>105</td>
<td>78</td>
<td>67</td>
<td>102</td>
<td>62</td>
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<tr>
<td>BMI</td>
<td>28</td>
<td>24</td>
<td>21</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>BP supine</td>
<td>125/80</td>
<td>175/75</td>
<td>130/80</td>
<td>150/80</td>
<td>160/90</td>
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<td>Cardiovascular medication</td>
<td>Warfarin</td>
<td>Diuretic Beta-blocker</td>
<td>ASA</td>
<td>Warfarin</td>
<td>ASA</td>
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<tr>
<td>ACE-inhib</td>
<td>Diuretic Nitrate Ca++ blocker</td>
<td>Diurexin</td>
<td>Beta-blocker</td>
<td>Diuretic Beta-blocker</td>
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<td>None</td>
<td>None</td>
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<tr>
<td>Dialysis schedule</td>
<td>M/W/F</td>
<td>M/W/F</td>
<td>M/W/F</td>
<td>T/T/S</td>
<td>T/T/S</td>
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</tbody>
</table>

ACE-inhib = angiotensin converting enzyme inhibitor; NYHA = New York Heart Association; LVEF = left ventricular ejection fraction; LVEDD = left ventricular end dia stolic diameter; BMI = body mass index; BP = blood pressure; $K_t/V$, [K] blood urea clearance of dialyzer (l/h) × [t] dialysis duration (h)/[V] volume of total body water (l); PCR = protein catabolic rate; M/W/F, Monday/Wednesday/Friday; T/T/S, Tuesday/Thursday/Saturday.

**Observations during haemodialysis**

Three patients had dialysis M/W/F and two on T/T/S (Table 1). Measurements representing each dialysis day of the week were performed in all patients except patient no. 2 who only had two days represented (M/W). Figure 2 shows a typical recording of continuous haemodynamic data during a dialysis session.

The individual and mean results of RVSP, RVDP and ePAD at the initiation of dialysis (baseline), after 30 and 60 min of dialysis, the minimum values of each variable and those at the end of dialysis are represented in Figure 3. The average decrease from baseline to the lowest RVSP and ePAD was 39 and 50%, respectively (Table 2). Changes in RVDP ranged from 3.4 to 10.3 mmHg between patients and averaged 6.6 mmHg in all of the patients. The lowest pressure for each variable occurred within the last 1.5 h of the dialysis procedure. After 30 min of dialysis, RVSP and ePAD had decreased 17 and 19%, respectively, almost 50% of the total decrease in RVSP and 40% of the decrease in ePAD. However, 1 h after initiation of dialysis the pressures remained stable or even slightly increased.
Fig. 2. A typical example of continuous haemodynamic recordings during a dialysis procedure in one patient. The graph shows high-resolution data with a storage interval of 5 min. —, right ventricular systolic pressure; —, estimated pulmonary artery diastolic pressure; —, right ventricular diastolic pressure.

Fig. 3. Pressure changes during dialysis procedure. Values are reported from before dialysis (pre), 30 and 60 min after start of dialysis, the lowest value during dialysis (min, only reported for pressure) and directly after discontinuation of dialysis (post). Diamond, patient no. 1; square, patient no. 2; triangle, patient no. 3; square, patient no. 4; square, patient no. 5; circle, mean. Normal values RVSP 25–30 mmHg, RVDP 0–8 mmHg, ePAD 6–12 mmHg.
Table 2. Pressure changes during the dialysis procedure [RVSP/RVDP (ePAD)]

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Pre dialysis</th>
<th>30 min dialysis</th>
<th>60 min dialysis</th>
<th>Min value</th>
<th>Post dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>27/2 (13)</td>
<td>20/—1 (9)</td>
<td>22/0 (10)</td>
<td>14/—4 (5)</td>
<td>24/0 (11)</td>
</tr>
<tr>
<td>2</td>
<td>26/3 (13)</td>
<td>21/1 (10)</td>
<td>26/3 (13)</td>
<td>17/—1 (8)</td>
<td>25/1 (11)</td>
</tr>
<tr>
<td>3</td>
<td>25/4 (11)</td>
<td>21/2 (10)</td>
<td>21/1 (9)</td>
<td>15/—2 (6)</td>
<td>19/0 (8)</td>
</tr>
<tr>
<td>4</td>
<td>34/16 (24)</td>
<td>29/12 (20)</td>
<td>30/13 (20)</td>
<td>21/7 (12)</td>
<td>30/10 (20)</td>
</tr>
<tr>
<td>5</td>
<td>31/12 (20)</td>
<td>28/8 (17)</td>
<td>26/6 (16)</td>
<td>21/2 (11)</td>
<td>24/4 (14)</td>
</tr>
<tr>
<td>Mean</td>
<td>28/7 (16)</td>
<td>24/4 (13)</td>
<td>24/4 (14)</td>
<td>18/1 (8)</td>
<td>24/3 (13)</td>
</tr>
</tbody>
</table>

compared to the 30 min levels. At the end of the dialysis session the pressure was partly restored, RVSP was then 15%, ePAD 22% and RVDP 3.4 mmHg (54%) lower than baseline.

Heart rate was not affected in patients nos 1, 2 and 3. Patient no. 4 developed atrial fibrillation towards the end of the dialysis procedure and therefore markedly increased heart rate while patient no. 5 increased the heart rate 20% during the dialysis without any indications of arrhythmia.

Case reports

One patient (no. 3) was hospitalized for 5 weeks after a fall-injury with five fractured ribs complicated by pneumonia. This caused a cachectic metabolic state with significant protein loss. However, the patient’s body weight was artificially kept constant by maintaining the dry weight at prescribed target dose. This regime resulted in considerable volume overload and progressive left ventricular dysfunction with a drop in left ventricular ejection fraction from 35 to 20%. The RVSP, ePAD and RVDP from this period are shown in Figure 4. The pressure measurements from the monitor were not available until the patient suffered from acute cardiac decompensation but they were then used to guide withdrawal of excess fluid representing a true volume overload of 6 kg.

Patient no. 4 suffered from chest discomfort and dyspnea after dialysis restricting daily activities. The heart rate counter of the IHM revealed paroxysmal atrial fibrillation regularly developing during dialysis (Figure 5). While the arrhythmia onset correlated with the intermittent re-increase of right ventricular pressures during the first third of haemodialysis, ongoing atrial fibrillation was associated with a marked pressure drop. In most cases atrial fibrillation converted spontaneously to sinus rhythm within a few hours after the end of dialysis. However, when atrial fibrillation recurred (Figure 5, Sunday morning), this caused another pressure drop underlining the detrimental haemodynamic effect of atrial fibrillation in this patient.

Discussion

The present pilot study is the first to document the haemodynamic changes during and between dialysis by means of continuous haemodynamic monitoring with an implantable device. The IHM provided a detailed description of dynamic changes in right ventricular pressures during the dialysis procedure and revealed long-term deviations in the haemodynamic state. These pilot observations indicate a potential role for the IHM to improve volume control in patients on intermittent HD.

Earlier studies in patients with chronic heart failure demonstrated that the IHM is a sensitive tool to detect changes in volume load [9–12]. Moreover, in a recent report from the randomized COMPASS-HF study, the risk of heart failure-related hospitalization was significantly reduced when the IHM was used for heart failure management [13]. Beyond the information from changes in body weight, commonly used to estimate volume state in heart failure and dialysis patients, intracardiac pressures reflect the capability of the cardiovascular system to cope with excess fluids. This is of potentially high value in the dialysis population with a high prevalence of progressive cardiovascular disease. Since volume overload is one of the main causes of hypertension, improved volume management may help to prevent its deleterious long-term effects on morbidity and mortality.

In the five study patients, left ventricular filling pressures as measured by ePAD were within the normal range at the end of dialysis, but were elevated prior to the next dialysis procedure to a level consistent with symptomatic heart failure. During dialysis all patients had a marked decrease in pressure. The RVSP dropped on average 39% and the ePAD 50%. Although neurohormonal assessment was not part of this pilot study, it is conceivable, that these marked haemodynamic changes contribute to an adverse activation of neurohormonal and sympathetic nervous systems in dialysis patients [15,16].

Notably, 40–50% of the intradialytic pressure decrease occurred within the first 30 min followed by a pressure plateau or even a slight increase in pressures. This finding is in agreement with previous reports from non-invasive haemodynamic measurements [17] and decreases in the vena cava diameter, which was steepest during the first hour of HD [18]. Leyboldt et al. [19] showed that large intradialytic decreases in systolic blood pressure were associated with intradialytic decreases in both body weight and plasma volume, pointing out that cardiac status alters the relationship between blood pressure and fluid removal during HD.
Thus the rapid initial drop in pressure during dialysis could be a function of impaired myocardial performance and a reduced contractile reserve. It could also reflect an initial quick shift of fluid from the intravascular compartment into the dialysate compartment, before the ‘refilling’ of the intravascular compartment from the extra-vascular compartment has started.

Although the aim of the present pilot study was merely descriptive, the first patient example illustrates the possible usefulness of continuous haemodynamic monitoring in optimizing dry weight. By maintaining stable dry weight a marked increase in extra-cellular fluids with concomitant reduction in lean body mass was masked until true hypervolaemia was revealed by the IHM. Thus, pressure information from the IHM may be helpful both in the revelation and correction of acute and chronic hyper- or hypovolaemia. The pressures are not only measured during HD but more importantly during the interdialytic period, which probably reflects a steady state in which there is a relative equilibrium between the various fluid compartments. Moreover, the haemodynamic information is accessible by a custom device-programmer in the HD unit or in the patient’s home using remote tele-monitoring technology. Unlike non-invasive methods such as ultrasound vena cava diameter, bioimpedance and natriuretic peptides, IHM-derived pressures are not subject to inter- and intra-observer variability and are not limited to the dialysis unit and access to expert technical support. In addition, information from continuous haemodynamic monitoring may be helpful in the management of arrhythmias common in the dialysis population.

A major point of concern is related to the invasive nature of this method in a population with increased risk of infection and bleeding. In heart failure patients side-effects by the IHM are comparable to those by single chamber pacemakers. In a report from the Medicare database on 13,000 dialysis patients receiving an index pacemaker implant, the incidence of device infection was 1–2% per year [20], indicating that infection risk is not a major deterrent to device

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Fig. 4. Long term trends of implantable haemodynamic monitor right ventricular pressure recordings data in patient no. 3. Arrows indicate rib fracture first from left, cardiac decompensation and correction of dry weight with the help of RV pressures second from left. The solid line shows a 2h median and the shaded area the 2h range.
implant. To decrease the risk of subclavian vein stenosis and peri-operative bleeding, the pressure sensor lead was always inserted in the contra-lateral side of the vascular access and care was taken not to interfere with present dialysis routes. Clearly, larger studies are needed to elucidate the risk/benefit ratio of continuous haemodynamic monitoring in dialysis patients. At present we believe that a haemodynamic sensor as an integrated part of a pacemaker or implantable defibrillator may improve volume management in those dialysis patients with a traditional indication for device treatment.

Clinical implications

The information derived from continuous haemodynamic monitoring could be useful to assist the adjustment of individual optimal dry weight and to balance the long-term volume state in order to avoid chronic over- or under-hydration in chronic haemodialysis patients. This novel approach to improved volume management is currently being evaluated in a larger prospective study.

Limitations

The present data represent findings from a pilot study in a small number of patients and does not allow for general conclusions.

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Conflict of interest statement. B. Kjellström is a full time employee at Medtronic Inc, Minneapolis, USA.

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Fig. 5. Long-term trends of implantable haemodynamic monitor heart rate right ventricular pressure recordings in patient no. 4. The patient experienced intermittent atrial fibrillation episodes in connection with the dialysis procedure. The solid line shows a daily median and the shaded area the daily range.


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