A single session of haemodialysis improves left ventricular synchronicity in patients with end-stage renal disease: a pilot tissue synchronization imaging study

Shirley Yumi Hayashi1,3, Astrid Seeberger3, Britta Lind2, Jacek Nowak2, Marcelo Mazza do Nascimento3, Bengt Lindholm3 and Lars-Åke Brodin1,2

1Department of Medical Engineering, School of Technology and Health, Royal Institute of Technology, 2Department of Laboratory Medicine, Division of Clinical Physiology and 3Division of Renal Medicine and Division of Baxter Novum, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Karolinska University Hospital in Huddinge, Stockholm, Sweden

Abstract

Background. Mechanical left ventricular (LV) dyssynchrony impairs cardiac function in patients with heart failure and LV hypertrophy (LVH) and may be a factor contributing to the high incidence of cardiac deaths in patients with end-stage renal disease (ESRD).

Objectives. To evaluate the possible presence of LV dyssynchrony in ESRD patients, and acute effect of haemodialysis (HD) on LV synchronicity using a tailored echocardiographic modality, tissue synchronization imaging (TSI).

Methods. In 13 clinically stable ESRD patients (7 men; 65 ± 10 years) with LVH, echocardiography data were acquired before and after a single HD session for subsequent off-line TSI analysis enabling the retrieval of regional intraventricular systolic delay data. Six basal and six midventricular LV segments were evaluated. Dyssynchrony was defined as a regional difference in time to peak systolic velocity >105 ms.

Results. Before HD, all patients had at least one dyssynchronous LV segment. The percentage of delayed segments correlated positively to LV end-diastolic diameter (r = 0.68, P < 0.05). HD induced a substantial decrease in the percentage of delayed segments from 36 ± 25% to 19 ± 14% (P < 0.01), reduced average maximal mechanical systolic LV delay from 300 ± 89 to 225 ± 116 ms (P < 0.05) and completely normalized LV synchronicity in three patients (23%).

Conclusions. LV dyssynchrony appears to be present frequently in ESRD patients with LVH. The severity of LV dyssynchrony correlates with LV end-diastolic diameter and decreases after a single session of HD suggesting a mechanistic relevance of volume overload and possibly other toxins accumulating in HD patients.

Keywords: end-stage renal disease; haemodialysis; left ventricular hypertrophy; systolic dyssynchrony; tissue synchronization imaging

Introduction

Cardiac disease is the major cause of premature deaths in haemodialysis (HD) patients, accounting for 43% of all-cause mortality [1,2], and the frequency of sudden cardiac death is almost 50% higher after the long dialysis interval [3]. A factor that may have a potential to contribute to the high incidence of cardiac deaths in end-stage renal disease (ESRD) patients is intra-left ventricular (LV) mechanical dyssynchrony, a disorder that markedly affects systolic performance, cardiac electrophysiology, regional myocardial perfusion and metabolism [4,5]. Awareness of a possible occurrence of LV dyssynchrony in ESRD patients is indeed of clinical importance since, firstly, dyssynchronously contracting left ventricle has been recognized as a significant contributor to increased morbidity and mortality in patients with congestive heart failure [6,7], and secondly, cardiac resynchronization therapy (CRT) now provides the possibilities to improve haemodynamics and systolic performance, to alleviate the symptoms and to increase the survival rate of patients with chronic heart failure [8].

Coincident with the increasing understanding of pathological significance of LV dyssynchrony, the accurate identification of LV dyssynchrony has been considerably improved by the introduction of a new diagnostic echocardiographic technique called tissue synchronization imaging (TSI) [9]. TSI provides an advanced analysis of synchronicity of myocardial motion based on the automatic detection of the time to peak systolic myocardial velocity at any discrete point within the myocardial wall.
and subsequent translation of the synchronicity data into colour-coded maps. The regions of dys synchronously contracting LV myocardium can thus be easily and quickly identified and quantified, and the obtained information allows better selection of patients for CRT and better therapeutic results [10, 11].

The occurrence of intra-LV dysynchrony has been described not only in patients with heart failure but also in individuals with LV hypertrophy (LHV) caused by pressure overload [12]. LHV has been shown to be present in 74–78% of patients on dialysis [13–15] and constitutes an independent risk factor for mortality in this patient category [16]. LHV, together with other cardiac abnormalities such as LV dilatation and arrhythmias [17, 18] that often occur in ESRD patients [4], may by themselves induce and also be worsened by LV dyssynchrony. However, a possible occurrence of LV dyssynchrony in ESRD patients without heart failure and normal QRS duration has not yet been assessed. Therefore, the aim of this study was (i) to establish whether intra-LV electromechanical disorders are present in patients with ESRD and concomitant LHV and (ii) to evaluate acute effects of HD on LV synchronicity in these patients using the TSI technique.

Materials and methods

Study population

Thirteen patients (seven men and six women), 65 ± 10 years old, with ESRD and echocardiographically verified LHV, who have been on renal replacement therapy for at least 3 months (diagnosis of renal disease on HD treatment 3.6 ± 1.6 years, range 1–6 years), were enrolled into the study. None of the patients presented any clinical evidence of infection, or clinical and/or echocardiographic signs of coronary artery disease, conduction disturbances, arrhythmias, severe valvular heart disease, congestive heart failure (New York Heart Association Classes III and IV) or pericardial disease. Patients with previous renal transplantation were excluded. The causes of renal failure were diabetes mellitus (2 patients), polycystic kidney disease (2 patients), chronic interstitial nephritis (1 patient), Wegener’s granulomatosis (1 patient), nphrotic syndrome (1 patient), nephrosclerosis (2 patients), vasculitis (1 patient), membranous nephropathy (1 patient) and unknown (2 patients). No medication was taken on the day of the study before all echocardiographic measurements were accomplished.

In order to explore any possible time-dependent spontaneous changes in LV synchronicity, in seven patients (four men and three women, 67 ± 7 years old), colour tissue velocity imaging and synchronization imaging was performed on two different occasions 7 days apart. On both occasions, the echocardiographic procedure was carried out immediately before a scheduled HD session that followed a long interval (3 days) between the sessions.

The study was performed in accordance with the Declaration of Helsinki. All subjects gave their informed consent to participate.

Haemodialysis

All patients underwent haemodialysis three times a week using polyamide (10 patients) and haemophan (3 patients) dialyzers. HD was performed for 3.0–4.5 h (QH 230–400 ml/min, Qb 500 ml/min) using bicarbonate-buffered dialysate with potassium 2 ± 0.2 mmol/l (range 2–3 mmol/l), sodium 139 ± 12 mmol/l (range 136–140 mmol/l) and bicarbonate 33 ± 2.9 mmol/l (range 25–38 mmol/l). During each dialysis session, excess fluid was removed to achieve the patient’s clinically determined ‘dry weight’ and the mean reduction of body weight was 2.7 ± 1.5 kg. Echocardiographic measurements and biochemical analysis were performed before and after the HD session that followed after the long interval (3 days) between the sessions.

Standard echocardiography

All ultrasound examinations were performed before and immediately after HD using a M3S multifrequency transducer and Vivid 7 equipment (GE Vingmed Ultrasound AS, Horten, Norway) with pre-installed EchoPacPC BT 05 software. The cardiac images during at least three consecutive cardiac cycles were acquired in parasternal long and short axis, and in apical two-, three- and four-chamber projections. All two-dimensional and Doppler variables were acquired according to the guidelines of American Society of Echocardiography. The two-dimensional variables included left ventricular end-diastolic (LVEDd) and end-systolic (LVESd) dimensions, end-diastolic and systolic interventricular septal (SWTd and SWTs, respectively) and left ventricular posterior wall posterior wall (PWTd and PWTs, respectively) thickness measured by M-mode in parasternal long-axis views. Left ventricular ejection fraction (EF) and fractional shortening (FS) were estimated by M-mode measurement. LV mass was calculated according to the Penn convention and LV mass index (LVMI) was calculated by the indexation of LV mass by height and body surface area. LV hypertrophy was diagnosed when LVMI was > 50 g/m²母 for males and > 47 g/m²母 for females [19]. The relative wall thickness (RWT) was calculated according to the formula: 

\[ \text{RWT} = \left( \frac{\text{IVS} + \text{PWT}}{\text{LVEDd}} \right) \]

In order to classify the LV geometric pattern (concentric LVH: RWT > 0.45; eccentric LVH: RWT < 0.45) [20]. Mitral inflow velocities were measured by conventional pulsed wave Doppler with the sample volume positioned at the level of the tips of mitral leaflets in apical four-chamber views.

Colour tissue velocity imaging (TVI)

TVI images from apical two-, three- and four-chamber views were recorded at the end of expiration with the subject in the left lateral position. Cineloops of three consecutive cardiac cycles were acquired with a high temporal resolution (>100 frames/s). The formatted raw data containing both grey scale and TVI information were stored on a magneto-optical disc for off-line analyses using EchopacPc software version BT 05 (GE Vingmed Ultrasound, Horten, Norway). The software permits real-time digital acquisition of the tissue velocity curve at any point in the myocardial
Fig. 1. Tissue synchronization imaging before (upper panel) and after (lower panel) a single HD session. Regional longitudinal myocardial velocities (middle panels) obtained at the sampling points placed on the opposing basal septal (yellow) and lateral (green) and midventricular septal (blue) and lateral (red) segments as shown in the left-hand panels. Time to systolic peak velocity is colour-coded and, before HD, a delay in reaching maximal systolic velocity can be clearly discerned in the lateral segments coloured red in a four-chamber view in the left upper panel, but also when inspecting systolic velocity curves in the middle upper panel. The bull’s eye image of this systolic delay is presented in the right-hand upper panel. After HD, the normalization of time to PSV in the previously dyssynchronously contracting LV region is evident in all lower panel images.

location in the stored cineloops. The myocardial velocity analysis was performed with 2 mm sampling volume from an optimal measuring position in the basal segment of inferoseptal, anteroseptal, anterior, anterolateral, inferior and inferolateral LV wall. Delineation of the isovolumic contraction and relaxation phases was achieved off-line as described by Lind et al. [21]. By mathematical processing of the velocity data, the EchopacPc software also allows the analysis of the myocardial strain rate (SR) that represents velocity of regional myocardial deformation expressed in s$^{-1}$ and, when measured at peak systole, reflects velocity of myocardial contraction. In order to calculate the longitudinal strain rate, the velocity gradients within the area of interest (12 mm) were divided by the distances between the respective measured points and averaged. The spatial offset was selected as a compromise between the acceptable signal-to-noise ratio and the longitudinal resolution.

The measured variables were myocardial isovolumic contraction velocity (IVCV), isovolumic relaxation time (IVRT), peak systolic velocity (PSV), early (E') and late (A') diastolic velocities and SR.

Tissue synchronization imaging

The tissue synchronization software processes acquired TVI data and provides automatic detection of the time to PSV at any discrete point within the myocardial wall. The obtained temporal data are translated into colour-coded maps of LV contraction synchronicity with colour coding ranges from green (earliest), yellow, orange, to red (latest) giving a detailed quantitative information about the regions of dyssynchronously contracting LV myocardium.

A colour-coded image of synchronicity of LV contraction is thus created (Figure 1).

The analysed systolic interval was set by default to start 60 ms after the beginning of electrocardiographic R wave and to end 200 ms after the closure of the aortic valve, thus including possible postsystolic contraction. Prior to the analysis, the TSI images were frozen and scrolled to the end of systole to ensure adequate positioning of regions of interest within the myocardial wall for the whole systole. Subsequently, circular regions of interest (diameter 2 mm) were placed manually on the basal and midventricular myocardium of the opposing LV walls according to a previously described 12-segment model [9] including inferoseptal, anterolateral, anterior, inferior, anteroseptal and inferolateral walls. Intraventricular mechanical dyssynchrony of a LV segment was defined according to Perry et al. [22] as the delay to PSV >105 ms compared with the shortest time to PSV among all the evaluated 12 segments. The percentage of the dyssynchronous segments as well as the standard deviation of the average values of time to PSV was calculated.
Haemodialysis improves TSI-assessed left ventricular synchronicity

Table 1. Clinical and biochemical variables before and after HD

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before haemodialysis</th>
<th>After haemodialysis</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>73 ± 16</td>
<td>71 ± 15</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>R–R interval (ms)</td>
<td>761 ± 80</td>
<td>745 ± 107</td>
<td>NS</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>142 ± 20</td>
<td>138.3 ± NS</td>
<td>18.2</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>80 ± 9</td>
<td>80 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>Haemoglobin (g/l)</td>
<td>117 ± 15</td>
<td>123 ± 14</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>26 ± 10</td>
<td>36 ± 4</td>
<td>0.001</td>
</tr>
<tr>
<td>Creatinine (µmol/l)</td>
<td>897 ± 163</td>
<td>329 ± 98</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Urea (mmol/l)</td>
<td>24 ± 5</td>
<td>7.0 ± 3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Potassium (mmol/l)</td>
<td>5.0 ± 0.5</td>
<td>3.5 ± 0.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sodium (mmol/l)</td>
<td>140.3 ± 2.9</td>
<td>140.3 ± NS</td>
<td>4.3</td>
</tr>
<tr>
<td>Calcium (mmol/l)</td>
<td>2.7 ± 0.1</td>
<td>2.6 ± 0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Phosphate (mmol/l)</td>
<td>1.7 ± 0.3</td>
<td>0.8 ± 0.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Calcium × phosphate (mmol/l)</td>
<td>4.4 ± 0.8</td>
<td>2.2 ± 0.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Parathyroid hormone (ng/l)</td>
<td>308 ± 216</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 2. Conventional echocardiography, TVI and TSI data before and after HD

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before haemodialysis</th>
<th>After haemodialysis</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF (%)</td>
<td>69 ± 9</td>
<td>70 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>FS (%)</td>
<td>40 ± 7</td>
<td>43 ± 9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LV EDD (mm)</td>
<td>47 ± 7</td>
<td>45 ± 5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>SWTD (mm)</td>
<td>14 ± 1</td>
<td>14 ± 1</td>
<td>NS</td>
</tr>
<tr>
<td>PWTd (mm)</td>
<td>14 ± 1</td>
<td>14 ± 1</td>
<td>NS</td>
</tr>
<tr>
<td>Mitral E (cm/s)</td>
<td>65 ± 50</td>
<td>45 ± 35</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mitral A (cm/s)</td>
<td>66 ± 50</td>
<td>58 ± 42</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mitral E/A</td>
<td>0.9 ± 0.2</td>
<td>0.7 ± 0.2</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial PSV (cm/s)¹</td>
<td>5.8 ± 1.1</td>
<td>6.0 ± 1.1</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial E' (cm/s)¹</td>
<td>5.9 ± 1.6</td>
<td>5.0 ± 1.3</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial A' (cm/s)¹</td>
<td>7.4 ± 1.6</td>
<td>7.7 ± 1.8</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial SR (s⁻¹)¹</td>
<td>0.8 ± 0.2</td>
<td>1.0 ± 0.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IVCV (cm²)²</td>
<td>3.3 ± 1.9</td>
<td>5.7 ± 2.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IVRT (ms)²</td>
<td>94.2 ± 24.2</td>
<td>92.5 ± NS</td>
<td>25.6</td>
</tr>
<tr>
<td>E/E'</td>
<td>13.3 ± 4.4</td>
<td>12.3 ± 4.3</td>
<td>NS</td>
</tr>
<tr>
<td>Average maximal delay (ms)</td>
<td>300 ± 25</td>
<td>225 ± 116</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Delayed segments (%)</td>
<td>36 ± 25</td>
<td>19 ± 14</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

¹Data represent average values obtained from the six left ventricular walls.

Biochemical analyses

Plasma levels of parathyroid hormone were measured before HD using commercially available electrochemical immunoassay (Eclesys PTH kit, Roche Diagnostics, Mannheim, Germany). Plasma levels of sodium, potassium, calcium, phosphate, creatinine, urea, as well as serum albumin and haemoglobin concentrations were measured before and immediately after HD using routine methods.

Statistical analysis

The data are expressed as mean ± SD and median (range). Student’s test and Wilcoxon’s signed-rank test were used when suitable for a pairwise comparison of data obtained before and after HD. The relation between echocardiographic and biochemical variables was analysed with standard linear regression and correlation techniques. A P-value of <0.05 was considered statistically significant.

Results

Clinical and biochemical data

The clinical and biochemical data before and after HD are presented in Table 1. HD resulted in a significant reduction of body weight, whereas systolic and diastolic blood pressure as well as heart rate remained unaltered. Haemoglobin and albumin concentrations increased while plasma levels of creatinine, urea, potassium, phosphate and calcium × phosphate product decreased significantly after HD. Plasma concentrations of sodium and calcium were not significantly altered.

Standard echocardiographic and TVI variables

All participating patients had normal EF and %FS, and no LV wall motion abnormalities were recorded. They all exhibited signs of concentric LVH, with a mean LVMi value after HD indexed by the height and body surface area of 73.3 ± 18.4 g/m²² and 171.5 ± 45.1 g/m², respectively, and RWT ≥ 0.45 in all cases.

The values of standard echocardiography and TVI variables before and after HD are presented in Table 2. As can be seen, HD resulted in a significant decrease of LVEDd accompanied by a significant increase in IVCV and SR values. On the other hand, EF and %FS as well as the average PSV and IVRT values did not change significantly after HD. Among the diastolic variables, a significant decrease in diastolic mitral inflow velocities (E and A) was observed after HD. Furthermore, the myocardial E' velocity values were somewhat lower after HD, but these changes did not reach the level of statistical significance.

Intra-left ventricular synchronicity

Before HD, all 13 patients presented with LV dyssynchrony (average maximal delay 300 ± 89 ms; Table 2), at least one delayed segment at basal or midwall level and SD > 34.4 [9]. The HD session resulted in complete normalization of LV synchronicity in three (23%) patients. Furthermore, HD caused a significant decrease in the average maximal systolic LV mechanical delay from 300 ± 89 ms (median 327, range: 119–390) to 225 ± 116 ms (median 265, range: 50–410), paralleled by a significant reduction in the percentage of segments with >105 ms delay from 36 ± 25% (median 33.3, range: 8.3–83.3) to 19 ± 14% (median 16.6, range: 0–50) (Figure 2). The percentage of delayed LV segments before HD was positively related to LVEDd, as shown in Figure 3.

In the control group of seven patients studied before the HD session at two different occasions 7 days apart, LV dyssynchrony was found in all individuals at the first echocardiographic examination (maximal delay 233.3 ± 85.5 ms and 29.4 ± 24.3% of delayed segments) and no significant changes in this respect were observed at the end
In the present study, the occurrence of intra-LV mechanical dyssynchrony and the effects of a single session of HD on LV synchronicity were evaluated in patients with ESRD and concomitant LVH. The obtained results clearly indicate that LV dyssynchrony indeed is present in patients with ESRD. Furthermore, both the severity and the extent of the disturbances in intraventricular synchronicity appear to relate positively to LVEDd and decrease significantly after a single HD session.

The current analysis of LV synchronicity was performed using the automated detection and quantification of regional delay in LV systole with the TSI technique [9,23,24]. Hitherto, a prolonged duration of QRS complex in the surface electrocardiogram has traditionally been employed as a marker of LV dyssynchrony. However, the accuracy of the QRS duration criteria appears to be poor, as significant mechanical dyssynchrony is usually absent in 30–58% of patients with QRS duration >120 ms [6,22,25,26], being at the same time present in 65% of individuals with QRS complex <120 ms [22]. The TSI technique is a novel echocardiographic imaging modality that analyzes myocardial tissue velocity signals and provides the timing of regional peak systolic velocities in relation to the onset of depolarization. The method has been proved to be reliable and reproducible [11,22], and its capacity to identify significant systolic dyssynchrony and thereby predict a positive response to CRT has been found to be superior to that of QRS duration criteria [11,22,23].

However, the accuracy of LV dyssynchrony identification depends not only on the choice of the diagnostic method but, to a considerable extent, also on the choice of diagnostic decision threshold. In several previous studies, cut-off values ranging from 40 to 110 ms were used to discriminate between normal and dyssynchronous LV systole [6,11,22,23]. These cut-off values were established retrospectively from the cohorts of CHF patients to yield the best sensitivity and specificity when predicting positive clinical response and reverse LV remodelling after CRT. The definition of LV dyssynchrony in the present study was based on the cut-off value proposed by Perry et al. who studied a cohort of 100 volunteers with normal LV systolic function and normal QRS duration [22]. The mean level of dyssynchrony in these individuals was found to be 47 ± 29 ms that gives the mean + 2SD value equal to 105 ms as the cutoff for a significant dyssynchrony of LV during systole.

In this context, it should be kept in mind that mechanical LV dyssynchrony can be caused not only by an abnormal electrical activation, but also by diffuse tissue injury or non-uniformity of the ventricular wall structure due to areas of scar tissue secondary to previous infarctions [7] resulting in mechanical spatio-temporal heterogeneity in dyskinetic and akinetic myocardium [27]. In order to minimize the confounding effect of such myocardial pathologies, patients with signs of conduction disturbances, coronary heart disease, previous infarctions, as well as severe valvular diseases, and congestive heart failure were excluded from the study. Even though the influence of coronary heart disease could not entirely be ruled out, the enrolled patients did not show any clinical or electrocardiographic signs of the disease, had normal ejection fraction and the conventional echocardiography screening did not reveal any regional
wall motion abnormalities. Consequently, it does not appear likely that the present results would have been affected by coronary heart disease to any significant extent.

Although the cause of the currently observed LV dysynchrony in ESRD patients is not entirely clear, the fact that LV synchronicity improved after HD and was normalized in 23% of the patients implicates at least two different mechanistic components—one stable and persistent, and the other dynamic and reversible. A myocardial abnormality that can possibly, at least partly, nourish the persistent (HD-resistant) constituent of LV dyssynchrony in ESRD patients is hypertrophy of the left ventricle, a common finding in patients with chronic kidney disease and associated with increased mortality in this patient category [14, 15, 28]. Sustained volume and pressure overload associated with the activation of the renin–angiotensin–aldosterone system and the increased release of neurotransmitters, vasodilative substances, growth factors and inflammatory mediators result in increasingly maladaptive left ventricular remodelling in ESRD patients [29]. The maladaptive LV hypertrophic response in these patients is characterized by the abundance of interstitial fibrosis [30, 31], collagen accumulation, capillary-cardiomyocyte mismatch and cardiac calcifications [17, 18, 29]. LVH has been found to be associated with LV asynchrony in patients with pressure overload and preserved renal function [12]. The maladaptive form of LVH with its abundant fibrosis and structural heterogeneity found in the uraemic environment would provide even better substrate for LV dyssynchrony. An important factor that should not be forgotten in this context is a possible calcification of myocardium and the conduction system. In fact, calcifications of soft tissues and blood vessels are highly prevalent in dialyzed patients [32] and the occurrence of myocardial calcifications may create inhomogeneity of both LV depolarization and mechanical response, hence contributing to the HD-resistant constituent of LV dyssynchrony in ESRD patients.

The HD-reversible component of LV dyssynchrony observed in the present study may have its origin in volume overload and subsequent stretching of myocardial tissue. This would change the input signal into the myocardial mechano-electrical feedback pathway, whereby alterations of myocardial load and the resulting changes in LV kinetics lead to altered expression of myocardial electrophysiology [33]. Indeed, it has been demonstrated in animal studies and experiments in humans that sustained stretching of myocardial fibres due to increased ventricular loading induces shortening of the myocardial action potential and effective refractory time, and increase in activation time and dispersion of action potential duration [33–37]. Even if the results of some studies in animals challenge any significant impact of load alterations on the outcome of the contraction–excitation interaction under normal conditions [34–37], changes in loading conditions may be of significantly greater electrophysiologic implication under pathological conditions that may distort the normal mechano-electrical feedback mechanism. In all patients in the present study, increased load was combined with LV hypertrophy. Possible structural inhomogeneities of maladaptively remodelled LV with inhomogeneously distributed myocardial strain, as well as the possible occurrence of contraction block due to stretching and increased pressure on Purkinje fibres [38], might have increased and locally differentiated the effect of mechano-electrical feedback, thus creating substrates for dysynchrony of myocardial contraction. As evidenced by decreased LVEDd and diastolic mitral velocities, and increased isovolumic contraction velocity, HD produced a significant decrease in LV load. The simultaneously improved LV synchronicity observed in 23% of the dialysed patients might then be a result of readjusted and more normalized contraction–excitation interaction.

The identification of LV synchronicity disturbances in patients with ESRD is of clinical importance since the uniformity of LV contraction is a prerequisite for effective and energetically efficient LV performance [5, 7]. Mechanical LV dyssynchrony impairs systolic performance by creating imbalance in regional stretching and shortening of myocardial fibres following abnormal stress to myocardial tissue [5, 7]. As a consequence, the kinetics of regional LV contractions is not effectively coupled to the systolic pressure build-up, but would rather cause intracavitary shift of intraventricular blood volume. Chronic dyssynchrony leads to ventricular remodelling of both early and late activated segments [39] with increasing ventricular cavity volumes and changes in LV geometry [39, 40]. In heart disease, mechanical LV dyssynchrony has marked deleterious effects on ventricular pump function leading to prolonged contraction and reduced ejection time, delayed relaxation with reduced diastolic filling time, mitral regurgitation [5, 7] and arrhythmia susceptibility [4]. Similar effects can be expected in ESRD patients and the occurrence of LV dyssynchrony in this population ought to be seen as an important risk factor and bad prognostic omen, as it is in patients with heart failure [6, 7].

In conclusion, the results of this pilot study indicate for the first time that intra-LV dyssynchrony occurs and appears to be frequent in ESRD patients with LV hypertrophy, a fact that may have prognostic implications in this patient category. The LV dyssynchrony can be transiently eliminated or significantly alleviated by a single HD session and correlates positively with the LV end-diastolic diameter, thus suggesting that volume overload and probably even other toxins accumulating in uraemia may play a role in the mechanism of LV synchronicity disturbances. Whether more frequent dialysis, as on daily basis, would reduce the dyssynchrony and thereby decrease the risk of sudden cardiac death is not known at present. The present findings certainly warrant the future studies addressing this issue.

Conflict of interest statement. Bengt Lindholm is employed by Baxter Healthcare. The authors declare that they have no competing interests.

References


Received for publication: 27.9.07
Accepted in revised form: 7.5.08