Left ventricular disorders in patients of end stage renal disease entering hemodialysis programme

SA Kale, NS Kulkarni, S Gang, A Ganju, L Shah, MM Rajapurkar
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Abstract

This prospective study includes 161 patients of end stage renal disease entering hemodialysis programme between 1-6-97 to 31-12-99. Patients were evaluated for left ventricular disease manifesting as systolic dysfunction, left ventricular hypertrophy & left ventricular dilatation on echocardiography after 4 to 12 weeks of initiating hemodialysis. Patients of ischemic heart disease, valvular heart disease & pericardial effusion were excluded. The mean age of this group of patients was 40.57 ± 11.71 years and 129 were men. Left ventricular disease was common & encountered in 105 (65.2%) patients. Only 56 (34.8%) had normal echocardiogram. We observed systolic dysfunction in 24 (14.9%), left ventricular hypertrophy in 88 (54.7%) & left ventricular dilatation in 42 (26.1%) patients. Hypertension, older age, male sex, anemia, hypoalbuminemia and hypocalcemia were found to be significantly associated with manifestations of left ventricular disorders. Patients of end stage renal disease with diabetes had higher frequency of systolic dysfunction (37.6%) as compared to non-diabetic patients (8.06%). It is concluded that left ventricular disorders are common in end stage renal disease patients entering hemodialysis programme and aggressive control of hypertension and anemia can help to prevent these disorders.

Key words: Echocardiography, left ventricular hypertrophy, hemodialysis, uremia, hypertension, anemia.

Introduction

Cardiovascular involvement in uremia is common and reported in India on autopsy¹ & clinical studies.² Echocardiographic abnormalities in small number of patients have also been reported³⁴. Left ventricular (LV) disease occurs frequently in End stage renal disease (ESRD)⁵-¹⁰ manifesting as systolic dysfunction, LV hypertrophy and LV dilatation: These disorders are associated with high risk of heart failure and death in uremic⁶,¹¹ and non uremic¹²,¹³ populations. Echocardiographic assessment of patients with ESRD is useful in evaluation of LV structure and functions, as well as in the detection of pericardial effusion and coexisting cardiac lesions in a non invasive fashion. M-mode assessment, when used in accordance with the American Society of Echocardiography recommendations¹⁴, provides a standardized method of assessing LV structure & functions. Predisposing factors to LV disease in ESRD are multiple and include hypertension, anemia, volume overload, arteriovenous fistula [AVF] flows, hyperparathyroidism, ischemic heart disease [IHD]⁶,⁸ and diabetes¹⁵. Role of malnutrition and hypoalbuminemia is unelucidated. Presence of uremic cardiomyopathy is suggested but unproven¹⁶,¹⁷. Therefore a prospective study to evaluate LV disease and risk factors for the same in ESRD patients initiating hemodialysis was undertaken.

Patients and Methods

Two hundred & ten patients of ESRD (Gr-I) entering hemodialysis programme between 1-6-97 to 31-12-99 at Muljibhai Patel Urological Hospital Nadiad, Gujarat were studied. Forty nine patients were excluded from the study because of proven IHD, pericardial effusion, severe valvular heart disorder, regional wall motion abnormality on echocardiogram and technically unsatisfactory echocardiogram. IHD was defined as prior history of coronary arteriopathy grafting surgery or coronary angioplasty, angina and evidence of myocardial infarction on electrocardiogram.

Clinical and biochemical assessment of the patients including blood pressure recordings (BP), antihypertensive therapy, erythropoietin therapy,
hemoglobin, serum creatinine, serum albumin and serum calcium levels was done. Serum parathyroid hormone levels or bone biopsy was not done. All these patients received thrice a week, four hours, hemodialysis. Weekly Kt/V was calculated to assess adequacy of dialysis after June 1998 and thus was not assessed for all patients. Blood flows across AVF were not assessed. Echocardiography (M-Mode, 2 Dimensional and Doppler) was performed the day after hemodialysis after achieving dry weight of the patient, 4 to 12 weeks of starting hemodialysis. LV end systolic diameter (LVESD), LV end diastolic diameter (LVEDD), interventricular septal thickness (IVS) and LV posterior wall thickness (PW) were noted in millimeters according to American Society of Echocardiogram recommendations on M-Mode assessment. These calculations have been validated on necropsy and in clinical studies. All these were performed by the same observer. Calculations used are as per equation 1.

Systolic dysfunction was defined as FS < 25%; LV hypertrophy as LVMi > 130 gm/m² in males & > 100 gm/m² in females; LV dilatation as LVV > 90 ml/m². Patients were divided into four groups according to echocardiographic abnormality detected.

Group I - Normal echocardiogram
Group II - Systolic dysfunction
Group III - Left ventricular hypertrophy
Group IV - Left ventricular dilatation

All the results are shown as mean ± standard deviation. Differences in mean values of various groups were analyzed using student's t test, p value of < 0.05 was considered significant. Independent associations of risk factors with LV abnormalities were calculated using multivariate logistic regression analysis.

Clinical and biochemical characteristics of 161 patients (Gr-IA) of ESRD without IHD, pericardial, valvular disease or regional wall motion abnormality on ECHO are shown in Table 1. Their mean age was 40.57 ± 11.71 years and 129 of these were men. Basic renal disease observed were chronic glomerulonephritis (43), chronic interstitial nephritis (32), diabetic nephropathy (37), hypertensive nephrosclerosis (20), reflux nephropathy (5), renal amyloidosis (3), polycystic kidney disease (3), hereditary nephritis (2) and indeterminate (16). Number of patients requiring antihypertensive therapy was 136 and receiving erythropoietin therapy was 40. Radiocephalic AVF were commonest dialysis access used (146) followed by brachiocephalic AVF (10) and temporary double lumen catheters (5).

<table>
<thead>
<tr>
<th>SNo</th>
<th>Parameter</th>
<th>Mean±SD</th>
</tr>
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<tr>
<td>1</td>
<td>Age (Years)</td>
<td>40.57±11.71</td>
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<td>2</td>
<td>Sex (M / F)</td>
<td>129 / 32</td>
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<tr>
<td>3</td>
<td>Systolic blood pressure (mmHg)</td>
<td>139.86±22.00</td>
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<td>4</td>
<td>Diastolic blood pressure (mmHg)</td>
<td>87.99±13.95</td>
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<td>5</td>
<td>Mean blood pressure (mmHg)</td>
<td>105.28±15.47</td>
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<td>6</td>
<td>Hemoglobin (gm/dl)</td>
<td>7.53±1.80</td>
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<td>7</td>
<td>Serum Creatinine (mg/dl)</td>
<td>9.59±2.68</td>
</tr>
<tr>
<td>8</td>
<td>Serum Albumin (gm/dl)</td>
<td>3.33±0.56</td>
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<td>9</td>
<td>Serum Calcium (mg/dl)</td>
<td>8.31±0.81</td>
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<tr>
<td>10</td>
<td>Fractional Shortening (%)</td>
<td>35.60±10.93</td>
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<tr>
<td>11</td>
<td>L.V.Mass Index (gm/m²)</td>
<td>144.76±47.46</td>
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<tr>
<td>12</td>
<td>L.V.Volume (ml/m²)</td>
<td>80.43±35.55</td>
</tr>
</tbody>
</table>

Table 1: Clinical, biochemical and echocardiograph characteristics of (n=161) Gr-IA ESRD patients initiating hemodialysis

\[ \text{Fractional Shortening (FS) = } \frac{\text{LVEDD} - \text{LVESD}}{\text{LVEDD}} \times 100 \]

\[ \text{Left ventricular Mass Index (LVMi) = } \frac{0.00083 \times (\text{LVEDD + IVS + PW})^3 - (\text{LVEDD})^3 + 0.6}{\text{Body Surface Area}} \]

\[ \text{Left ventricular volume (LVV) = } \frac{\text{(LVEDD)3} \times 0.001047}{\text{Body Surface Area}} \]

Equation 1
Results

Echocardiographic abnormality was detected in 105 (65.2%) patients and 56 (34.8%) had normal echocardiogram. Sixty patients had one and 45 patients had more than one echocardiographic abnormalities. Systolic dysfunction in 24 (14.9%), LV hypertrophy in 88 (54.7%) and LV dilatation in 42 (26.1%) patients was observed. Patients were divided into four groups according to their echocardiographic diagnosis as shown in Table 2. Patient with systolic dysfunction had statistically significant higher BP records (Systolic, diastolic and mean), lower serum creatinine and serum albumin when compared to patients with normal echocardiogram. They also had lower hemoglobin levels but this difference was not statistically significant. Patients with LV hypertrophy, when compared to patients with normal echocardiogram, had statistically significant, higher age, higher BP records (systolic, diastolic and mean) and lower-hemoglobin, serum albumin and serum creatinine levels. Similarly, patients with LV dilatation had significantly high BP, lower hemoglobin, serum albumin and serum calcium levels. On multivariate analysis (Table 3, 4, &5) all the three forms of LV disorders were found to be associated with higher age, mean BP, male sex, lower hemoglobin, serum creatinine, serum albumin and serum calcium levels.

Of the thirty seven diabetic ESRD patients twenty seven (72.9%) had echocardiographic abnormalities and 10 (27%) had normal echocardiograms. Sixteen patients had one, and 11 patients more than one LV disorder. Fourteen (37.8%) patients had systolic dysfunction, 17 (45.9%) LV hypertrophy and 6 (16.2%) had LV dilatation. Systolic dysfunction was observed with higher frequency in diabetic ESRD patients (37.8% VS 8.06%) and this difference was statistically significant. LV hypertrophy and LV dilatation was observed with similar frequency in diabetic and nondiabetic ESRD patients.

Discussion

Left ventricular disease manifesting as systolic dysfunction, LV hypertrophy and LV dilatation is encountered in 65% in Gr-IA and 77% in Gr-I patients of ESRD at initiation of renal replacement therapy. Prevalence of LV disorder in ESRD shown in other studies ranges from 71% to 85% 5-10. Gr-IA in the current study shows lower frequency of these disorders, the reason being prior exclusion of patients with IHD in this study, and lower age of patients included 23. Present study highlights the fact that after exclusion of patients with IHD, which is an important risk factor for development of LV disorders 8, almost two thirds of ESRD patients at initiation of therapy in Gr-IA suffered from LV disorders.

### Table 2: All patients of ESRD grouped according to echocardiographic diagnosis (n=210) Gr-I

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Gr.I (n=56)</th>
<th>Gr.II (n=24)</th>
<th>Gr.III (n=88)</th>
<th>Gr.IV (n=42)</th>
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<td></td>
<td>(Mean±SD)</td>
<td>(Mean±SD)</td>
<td>(Mean±SD)</td>
<td>(Mean±SD)</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>37.57±12.58</td>
<td>42.00±13.84</td>
<td>42.07±10.33**</td>
<td>40.12±9.88</td>
</tr>
<tr>
<td>Sex (M / F)</td>
<td>48 / 8</td>
<td>19 / 5</td>
<td>67 / 21</td>
<td>33 / 9</td>
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<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>121.64±14.72</td>
<td>145.42±22.84**</td>
<td>153.82±17.14**</td>
<td>149.29±20.17**</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>76.86±8.06</td>
<td>93.08±15.50**</td>
<td>96.84±11.41**</td>
<td>94.00±14.31**</td>
</tr>
<tr>
<td>Mean blood pressure (mmHg)</td>
<td>91.79±9.16</td>
<td>110.53±17.24**</td>
<td>115.83±11.31**</td>
<td>112.43±14.94**</td>
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<tr>
<td>Hemoglobin (gm/dl)</td>
<td>8.02±1.46</td>
<td>7.58±2.11</td>
<td>7.33±1.97*</td>
<td>6.07±1.34**</td>
</tr>
<tr>
<td>Serum Creatinine (mg/dl)</td>
<td>9.97±2.53</td>
<td>8.21±2.24**</td>
<td>9.27±2.58*</td>
<td>9.49±3.11</td>
</tr>
<tr>
<td>Serum Albumin (gm/dl)</td>
<td>3.45±0.48</td>
<td>3.13±0.42**</td>
<td>3.26±0.61*</td>
<td>3.14±0.47**</td>
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<tr>
<td>Serum Calcium (mg/dl)</td>
<td>8.36±0.80</td>
<td>8.37±0.77</td>
<td>8.27±0.80*</td>
<td>8.10±0.92*</td>
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<tr>
<td>Fractional Shortening (%)</td>
<td>38.24±8.11</td>
<td>19.82±3.25</td>
<td>35.07±12.22</td>
<td>32.32±10.45</td>
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<tr>
<td>L.V.Mass Index (gm/m^2)</td>
<td>105.26±16.83</td>
<td>151.76±43.32</td>
<td>175.80±42.02</td>
<td>174.13±54.16</td>
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<tr>
<td>L.V.Volume (ml/m^2)</td>
<td>68.21±19.33</td>
<td>91.47±44.90</td>
<td>89.59±39.59</td>
<td>126.43±32.27</td>
</tr>
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</table>

* : P<0.05 (When compared to normal group)
** : P≤0.001 (When compared to normal group)
Gr.I : Normal Echocardiogram Gr.II : Systolic Dysfunction Gr.III : LVHypertrophy Gr.IV : LV Dilatation

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Hypertension was identified as important risk factor for all three LV disorders observed in this study. Systolic, diastolic and mean BP were separately and significantly associated with LV disease. This mandates an aggressive control of hypertension in ESRD patients. Regression of LV hypertrophy with control of BP in a small number of patients has been demonstrated\textsuperscript{24, 25}. Anemia, a common accompanying feature of ESRD, is significantly associated with LV hypertrophy and LV dilatation, as observed in this study. Regression of these on correction of anemia further implicates it as an important risk factor\textsuperscript{26,27,28}. Thus correction of anemia in ESRD would help to prevent LV disease. Low serum albumin, lower blood urea, lower serum calcium have been demonstrated to be associated with echocardiographic abnormalities\textsuperscript{34}. Current study identifies hypoalbuminemia, low serum creatinine and low serum calcium to be associated with LV echocardiographic abnormalities. Role of malnutrition in development of LV disorders is largely speculative unless addressed specifically in future studies.

Parathyroid hormone levels, bone biopsy for secondary hyperparathyroidism, AVF blood flows were not assessed in this study and their role as risk factors remains unaddressed.

Diabetic ESRD, expectedly had higher frequency of LV disorders mainly as systolic dysfunction. Diabetes in CRF is predictive of LV disease\textsuperscript{7}. So despite prior exclusion of IHD, diabetic ESRD patients do have a higher burden of LV disorders as compared to non-diabetic ESRD patients. Renal transplantation has been performed in 124 of these patients, and these are under yearly follow-up with echocardiography. In future it would be interesting to note regression of LV disease after successful renal transplantation. Such benefits have been reported previously\textsuperscript{30}.

In conclusion LV disorders are frequent in-patients of ESRD entering hemodialysis programme. Older age, male sex, hypertension, anemia, hypoalbuminemia and hypocalcemia are important risk factors for these disorders. Aggressive control of hypertension and anemia can help to prevent these disorders.

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References


