Development, Prevention, and Potential Reversal of Left Ventricular Hypertrophy in Chronic Kidney Disease

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Abstract. Although a high prevalence of left ventricular (LV) hypertrophy is recognized with increasing severity of chronic kidney disease (CKD), previously neither its progression nor its potential for prevention or reversal has been addressed adequately in this population group. A nested analysis of a 2-yr study involving 155 patients with stage 3/4 CKD, examining effects of hemoglobin change (range, 90 to 130 g/L) on LV mass in patients with (n = 46; 30%) and without (n = 105; 70%) initial LV hypertrophy, is reported. At baseline, the group with LV hypertrophy was older (P < 0.01), had higher BP (P < 0.01), had greater LV wall and cavity dimensions (P < 0.001), and had more prevalent use of antihypertensive agents (P < 0.001) but a lower hemoglobin concentration (P < 0.05) and GFR (P < 0.01). A total of 117 patients were available for assessment at 2 yr. Importantly, 57 (68%) with initial normal LV indices showed no appreciable change with time; however, 27 (32%) developed LV hypertrophy, with growth in both wall and cavity dimensions (P < 0.001). In contrast, 23 (50%) of those with initial LV hypertrophy maintained elevated LV indices, whereas 10 (22%) regressed, through wall but not cavity reduction, to within normal LV indices. Predisposing factors to maintaining or achieving normal LV mass dimensions included relative youth (P < 0.05), a lower pulse pressure (P < 0.05), and a higher GFR (P < 0.05) but not hemoglobin concentration or parathyroid hormone levels. These findings suggest that even at a relatively advanced stage of renal dysfunction, control of BP and volume, together with regulated metabolic and clinical indices, may contribute to the prevention or even reversal of LV hypertrophy in a substantial proportion of patients.

Left ventricular (LV) hypertrophy is recognized as a potent risk factor for cardiovascular death in dialysis patients (1,2). It is also known to be prevalent in patients with chronic kidney disease (CKD) before commencing dialysis (3,4) and has been linked to progressive renal dysfunction and anemia in cross-sectional and prospective observational studies (5,6). Few studies, however, have examined the long-term evolution and/or prevention of LV hypertrophy in patients with advanced CKD (7,8), and no large interventional study has examined the specific and related effects of such factors as kidney function, age, gender, diabetes, hyperparathyroidism, BP, and anemia. Furthermore, it is not known whether such determinants of change in LV mass in the CKD population are reversible or the mechanisms by which such changes can be achieved. Given the recent recognition of the high prevalence of CKD in the community (9) and the excessive mortality associated with LV hypertrophy (10), a better understanding of its pathophysiology and of potential treatment strategies is needed.

This nested analysis of patients enrolled in a randomized control trial designed to examine the effect of anemia prevention on LV mass in a population of stage 3 and 4 CKD (K-DOQI guidelines), the Australian Pre-dialysis (SLIMHEART) Study (11), describes the prevalence of LV geometrical patterns and their changes over 2 yr and the factors that seem to influence these changes. On intention-to-treat analysis, the randomized controlled trial failed to demonstrate an effect of anemia correction on LV mass, possibly as a result of an insubstantial fall in hemoglobin in the control group. However, the rigorous nature of the study did establish a population of CKD patients who had relatively homogeneous hemoglobin levels and were exposed to common treatment protocols and in whom serial echocardiographic data were obtained. We report here the results of this nested analysis, based on the presence or absence of LV hypertrophy at baseline, which examines the change and determinants of change in LV mass in patients with advanced CKD.

Materials and Methods

The principal study was an open-label, randomized, prospective, multicenter trial conducted in Australia and New Zealand. A detailed protocol is described elsewhere (11); however, in brief, patients were randomized into two groups, A and B. Group A patients were administered epoetin-α therapy to maintain a hemoglobin concentration
between 120 and 130 g/L for 2 yr. Epoetin-α was initiated in group B patients when the hemoglobin fell to <90 g/L, although only eight patients required treatment during the study period.

The primary end point for the principal study was the change in LV mass index over 2 yr, determined by 2D and M mode echocardiography. Echocardiograms were performed at screening and 2 yr after randomization (range, 21 to 26 mo). LV hypertrophy was defined by an LV mass index >125 g/m² (men) or >100 g/m² (women) (12–14). Each site performed its own echocardiogram by a trained, full-time technician, using the same ultrasound machine for each study. Each technician was obliged to undergo a full day of procedure standardization training directed by a core laboratory that analyzed all studies. After initial blinded reading by a skilled sonographer, subsequent blinded verification (with correction of measurements if necessary) was performed by an experienced echocardiologist. Variability in measurements was not formally compared between individual centers, but each patient served as his or her own control. Patients were excluded when echocardiographic measurements were judged insufficiently clear or not reproducible.

Explanatory variables included gender, the presence of diabetes, use of angiotensin-converting enzyme (ACE) inhibitors, and the use of other antihypertensive agents (angiotensin II receptor antagonists were not used). BP (systolic and diastolic), hemoglobin, creatinine, iron studies, and albumin were measured every 2 mo on average. Pulse pressure and mean arterial pressure, derived from BP measurements, were also used in the analysis. The GFR was calculated by either chromium EDTA (Cr-EDTA) or technetium DTPA (Tc-DTPA) clearance at the beginning and end of the study, and parathyroid hormone levels were measured at three time points: entry, 12 mo, and 24 mo.

Study Population

All patients were under the care of a nephrologist, were aged between 18 and 75 yr, had shown a historical decline in hemoglobin within the 12 mo before enrollment, and had reached a hemoglobin concentration between 110 and 130 g/L (men) or 100 and 120 g/L (women). Patients were also required to have an estimated creatinine clearance (based on the Cockcroft-Gault equation (15)) between 15 and 50 ml/min (stages 3 and 4 CKD). Patients with unstable or poorly controlled angina, severe congestive cardiac failure (New York Heart Association grade III or IV), severe chronic respiratory disease or symptomatic peripheral vascular disease, or a previously created arteriovenous fistula were excluded from study entry.

Of the 151 technically assessable initial echocardiograms performed, 34 patients did not complete a 2-yr follow-up and hence were not included for this analysis. Dropout was due to patient- or physician-initiated withdrawal (n = 16), poor echocardiographic data (n = 7), noncompliance (n = 4), adverse events (n = 3), and other causes (n = 4), leaving 117 patients available for final evaluation.

End Points for Nested Analysis

For purposes of the nested analysis, it was determined that the change in LV mass index from baseline and development or regression of LV hypertrophy were the primary end points. The cohort patient groups from the primary study, therefore, were reconfigured on the basis of the presence or absence of LV hypertrophy at study entry rather than of randomization treatment assignment. Within these two categories, it was possible to follow the changes in LV mass index over 2 yr to determine which patients progressed, which regressed, and which maintained their initial LV geometry. The subgroups thus created formed the basis for the determinants of change in LV mass in this study population.

Statistical Analyses

Using the SPSS 11.0 statistical package (www.SPSS.com), statistical analysis included, when appropriate, t test, χ², ANOVA, and stepwise linear regression. The Pearson correlation coefficient was used for initial correlation results. An a value of 0.05 was regarded as statistically significant, and values are expressed as mean ± SD unless otherwise indicated. All mean 2-yr variable estimates were calculated from an arithmetic mean of individual patient results according to the number of tests performed.

Results

Time-Related Changes after Initial Echocardiogram

Initial echocardiograms demonstrated that 46 (30%) patients had LV hypertrophy and 105 (70%) had a normal mass index. Initial demographic, clinical, and laboratory data, described elsewhere (9), are also presented for completion in Table 1 according to initial LV mass index. Figure 1 shows the subsequent complex interplay of changes in LV mass over 2 yr. Thirteen (28%) of those with initial LV hypertrophy and 21 (20%) of those with initially normal LV indices did not complete analysis at 2-yr follow-up, leaving 33 and 84 patients, respectively, available for analysis. Twenty three (50%) of those with initial LV hypertrophy maintained elevated LV mass indices, whereas 10 (22%) demonstrated normalization of myocardial mass. Of those with normal initial LV indices, 27 (26%) developed de novo LV hypertrophy or ≥30% increase in LV mass index. This latter estimate formed a convenient and convincing demarcation between patients with stable LV mass (growth over 2 yr <18%; mean, −3 g/m² ± 12) and progressive LV growth (mean, 41 g/m² ± 12).

Initial Echocardiographic Comparisons

At baseline, there were statistically significant differences between patients with a normal LV mass index (n = 105) and those with LV hypertrophy (n = 46). The latter were older, used antihypertensive agents other than ACE inhibitors more frequently, had higher systolic and pulse pressures, had lower hemoglobin concentrations, had a lower GFR, and had larger LV wall and cavity dimensions (Tables 1 and 2). No significant differences, however, were found between the groups for gender, presence of diabetes, use of ACE inhibitors, diastolic or mean BP levels, serum creatinine, albumin, or parathyroid hormone levels. Mean 2-yr changes in LV mass index in these groups from the initial assessment were small, although the range was large (normal LV mass index: 7 g/m², range –31 to 75, n = 84; LV hypertrophy: −4 g/m², range –56 to 32, n = 33).

Subgroup Analysis

Patients with sustained LV hypertrophy (n = 23) when compared with those with sustained normal LV mass index (n = 57) were older (P = 0.001) and, over 2 yr, used more antihypertensive agents other than ACE inhibitors (P < 0.001), had a higher systolic and pulse pressure (P < 0.01), and had a
lower GFR ($P < 0.01$) (Table 3). These differences were also largely apparent at the end of the study (Table 4). Echocardiographic differences were evident for both wall (interventricular septum [IVS] and posterior wall thickness [PWT]) and chamber (LV end-systolic and end-diastolic diameters [LVESD and LVEDD] and volumes [LVESV and LVEDV]) dimensions (Figure 2, Tables 3 and 5). Those who developed LV hypertrophy over 2 yr ($n = 27$) differed at entry from those who maintained a normal LV mass index ($n = 57$) only in that they were older (Table 1). Significant differences, however, were found in the 2-yr mean systolic pressure, pulse pressure, and GFR ($P < 0.05$) but not hemoglobin concentration, parathyroid hormone levels, or the presence of diabetes (Figure 2, Table 3). On echocardiographic assessment, significant differences over 2 yr were found in both wall (IVS and PWT), and chamber (LVEDD and LVEDV) dimensions (Figure 2, Table 3).

Comparison between those who maintained LV hypertrophy ($n = 23$) and those who regressed to normal LV mass ($n = 10$) demonstrated similar initial clinical parameters but did show a significant difference in mean pulse pressure over 2 yr ($P < 0.05$). For echocardiographic determinants of LV mass, significant differences between the two groups over 2 yr were found in wall (IVS and PWT) but not in cavity dimensions (Figure 2, Tables 3 and 5).

Patients whose LV mass regressed to normal levels ($n = 10$) were also compared with those who developed LV hypertrophy ($n = 27$). No differences were identified in initial, mean, or final clinical parameters (Table 3). Significant differences during the study, however, were identified in echocardiographic chamber (LVEDD, $P < 0.05$; LVEDV, $P < 0.01$) and wall (PWT and IVS, $P < 0.001$) dimensions over 2 yr (Figure 2,
Table 2. Echocardiographic parameters at the beginning and end of the study for patients with and without LV hypertrophy at study entry and at study end

<table>
<thead>
<tr>
<th>Study Commencement</th>
<th>Study End</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal LV Mass (n = 105)</td>
<td>LV Hypertrophy (n = 46)</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>93 ± 16</td>
</tr>
<tr>
<td>PWT (mm)</td>
<td>9.3 ± 1.3</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>50 ± 4</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>31 ± 4</td>
</tr>
<tr>
<td>LVEDV (ml)</td>
<td>114 ± 28</td>
</tr>
<tr>
<td>r/th ratio</td>
<td>2.7 ± 0.4</td>
</tr>
</tbody>
</table>

<sup>a</sup> Values given are means ± SD. Comparisons were performed between opposing groups at same time points. PWT, posterior wall thickness; ED and SD/V, end-diastolic and systolic diameter/volume; r/th ratio, chamber radius to wall thickness ratio.

<sup>b</sup> Retrospective analysis.

<sup>c</sup> P < 0.05.

<sup>d</sup> P < 0.01.

<sup>e</sup> P < 0.001.

Table 3. Mean values or changes in values over 2 years for groups with and without LV hypertrophy at study entry, according to observed changes in LV mass at study end.<sup>a</sup> Comparisons were performed between subgroups with and without initial LV hypertrophy.

<table>
<thead>
<tr>
<th>Initial Normal LV Mass</th>
<th>Initial LV Hypertrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at entry (yr)</td>
<td>47 ± 14</td>
</tr>
<tr>
<td>2-yr mean systolic BP</td>
<td>134 ± 12</td>
</tr>
<tr>
<td>2-yr mean PP</td>
<td>54 ± 12</td>
</tr>
<tr>
<td>2-yr mean GFR</td>
<td>26 ± 11</td>
</tr>
<tr>
<td>2-yr mean hemoglobin</td>
<td>118 ± 8</td>
</tr>
<tr>
<td>ΔLV mass index (g/m²)</td>
<td>-3 ± 11</td>
</tr>
<tr>
<td>ΔPWT (mm)</td>
<td>0.3 ± 1.4</td>
</tr>
<tr>
<td>ΔLVEDD (mm)</td>
<td>-2.2 ± 4.2</td>
</tr>
<tr>
<td>ΔLVEDV (ml)</td>
<td>-7 ± 26</td>
</tr>
<tr>
<td>Δr/th ratio</td>
<td>-0.2 ± 0.5</td>
</tr>
</tbody>
</table>

<sup>a</sup> Values given are mean ± SD. IVS, interventricular septum; PP, pulse pressure.

Tables 3 and 5). The ratio of LVEDD/2 (chamber radius) to PWT (r/th ratio) was also different between these groups at study commencement (2.5 ± 0.3 versus 2.8 ± 0.5; P < 0.05), as was the change in r/th ratio during the study (Table 3), which seemed to relate to changes in both wall and chamber dimensions (Figure 2).

**Correlations**

Correlations were performed both overall and between patients with and without initial LV hypertrophy in an attempt to identify possible explanations for changes in LV mass.

**Overall.** No correlation was identified between either final LV mass index or the change in mass index with any initial clinical or laboratory values (n = 117). Correlations, however, were identified between the change in LV mass index and mean 2-yr systolic BP levels, age (r = 0.331, n = 117, P = 0.007), the use of ACE inhibitors (r = -0.198, n = 117, P = 0.028), and the 2-yr mean GFR (r = -0.223, n = 103, P = 0.023). Mean hemoglobin concentration over 2 yr also correlated closely with mean GFR (r = 0.325, n = 103, P < 0.001), although few conclusions pertaining to this result can be drawn given that patients in each group were treated with epoetin-α to maintain hemoglobin levels.

**LV Hypertrophy (n = 33).** Significant correlations were found between 2-yr changes in LV mass index and 2-yr mean systolic BP (r = 0.373, n = 33, P = 0.033), GFR at baseline (r = -0.373, n = 32, P = 0.035), and 2-yr mean GFR (-0.619, n = 25, P = 0.001). Echocardiographically, the
expected correlation was observed between 2-yr change in LV mass index and wall thickness (PWT, r = 0.645, n = 32, P < 0.001) but, interesting, not in chamber diameter. Linear regression analysis of clinical parameters showed an independent correlation between the change in LV mass index and the 2-yr mean GFR (β = −0.568, P = 0.003).

**Normal LV Mass Index (n = 84).** Significant correlations were identified between 2-yr changes in LV mass index and age (r = 0.240, n = 84, P = 0.028), 2-yr mean urea levels (r = 0.279, n = 83, P = 0.011), and hemoglobin concentration at study end (r = −0.247, n = 82, P = 0.025). Echocardiographic correlations (P < 0.001) were observed in this group between changes in LV mass index and both PWT and LVEDD. Linear regression analysis of clinical parameters identified an independent correlation between 2-yr changes in LV mass index and each of the above parameters: age (β = 0.229, P = 0.03), urea levels (β = 0.225, P = 0.036), and end-study hemoglobin (β = −0.212, P = 0.048).

**Discussion**

This nested analysis of a randomized, controlled trial adds to our understanding of the pathophysiology of changes in LV mass in patients who have advanced CKD but do not yet require dialysis. Although LV hypertrophy is well established as a potent risk factor for increased mortality in dialysis patients (stage 5 CKD) (1,3,10), its relevance to hard outcomes in patients before dialysis (KDOQI stages 3 and 4 CKD) is not as well defined. One recent study using transplant patients as a model for CKD (16) suggested that it was at least as significant a risk factor for mortality as ischemic heart disease; however, as all patients had been exposed to dialysis before transplantation, the extrapolation to patients who have not dialyzed is problematic. In dialysis patients, a reduction in the degree of LV hypertrophy can be achieved by appropriate fluid and BP control and by treatment of anemia (8). Reversion to normal LV mass, however, is usually unsuccessful not only because of the prevailing combination of known hemodynamic and other risk factors but also because of an accepted irreversibility of disease processes (17). In contrast, substantial reductions in LV mass, often to normal dimensions, were found over 2 yr in a recent study of hypertensive patients without kidney failure using an angiotensin receptor antagonist or atenolol (18). It is known that the community prevalence of CKD is high but often unrecognized (9), so it is likely that patients will continue to present with relatively advanced kidney disease and a corresponding high incidence of LV hypertrophy. It therefore is important to determine (1) whether in advanced CKD, LV hypertrophy can be ameliorated; (2) which specific factors may be responsible for its development; and (3) to recognize those that are amenable to intervention.

In the current study of patients with stage 3 or 4 CKD and assessable echocardiograms, 30% of the patients were found to have LV hypertrophy at outset. The prevalence is lower than previously described for this level of CKD, which may well relate to the inherent selection of patients for this cohort compared with the unslected nature of previous observational

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**Table 4.** Comparison of variables at study entry, analyzed retrospectively for patients who, by study end, had either retained their initial LV indices or, alternatively, demonstrated substantial LV growth (normal initial LV mass) or regression (initial LV hypertrophy) \(^{a}\)

<table>
<thead>
<tr>
<th></th>
<th>Study Commencement (^{b})</th>
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<tbody>
<tr>
<td></td>
<td>Initial Normal LV Mass (n = 105)</td>
</tr>
<tr>
<td></td>
<td>Sustained Normal LV Mass (n = 57)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>47 ± 14</td>
</tr>
<tr>
<td>Gender (m, f)</td>
<td>24, 31</td>
</tr>
<tr>
<td>Use of ACEi (n [%])</td>
<td>45, (79)</td>
</tr>
<tr>
<td>Use of OAHAT (n [%])</td>
<td>12, (21)</td>
</tr>
<tr>
<td>Diabetes (n [%])</td>
<td>9, (16)</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>134 ± 15</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>79 ± 9</td>
</tr>
<tr>
<td>PP</td>
<td>54 ± 13</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>114 ± 8</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>40 ± 3</td>
</tr>
<tr>
<td>PTH (pmol/L)</td>
<td>14 ± 13</td>
</tr>
<tr>
<td>Creatinine (mmol/L)</td>
<td>0.26 ± 0.10</td>
</tr>
<tr>
<td>GFR (ml/min per 1.73 m(^{2}))</td>
<td>29 ± 14</td>
</tr>
<tr>
<td>LV mass index (g/m(^{2}))</td>
<td>94 ± 16</td>
</tr>
</tbody>
</table>

\(^{a}\) Values are means ± SD.

\(^{b}\) Retrospective analysis.

\(^{c}\) P < 0.05.
studies (4,5). Factors that were found to contribute to the initial presence of LV hypertrophy, however, are consistent with those described in other reports (2–6) and include age, elevated systolic BP and pulse pressure, anemia, and a lower GFR.

Patients in this study were randomized to different target hemoglobin levels, and no other treatment differences were prescribed. However, as demonstrated, apart from an initial small difference between groups in hemoglobin, the concentration over 2 yr was remarkably consistent in each group. The correlation between the change in LV mass and final hemoglobin concentration in patients with initial normal LV indices supports previous studies indicating that avoidance of progressive anemia may prevent the development and progression of LV hypertrophy in these patients (6). It is interesting that the presence of diabetes or use of ACE inhibitors also did not seem to influence LV mass in any group, suggesting that their primary effects may be mediated through routine determinants of LV mass, although the numbers available for analysis of such data in this study are relatively small and further collaborative findings clearly are required for more definitive interpretation.

Important in this cohort, the sole factor that seemed to predict normalization of LV mass in patients who had LV hypertrophy at study entry was a lower pulse pressure. Although other variables were not correlated with a reduction in LV mass, the degree of both anemia and hyperparathyroidism were modest and, importantly, stable in nearly all patients, and albumin levels were normal. In particular, an important component of the primary study (11) was to avoid progressive anemia, thus limiting the effects of this variable and hence results attributable to it. The findings do indicate, however, that aggressive, conservative management of routine clinical and metabolic indices in at least some patients with advanced CKD and LV hypertrophy may enable normalization (with a reduction in mass of up to 45%) of LV mass over 2 yr. Certainly, the data are supportive of continued aggressive BP management even at late stages of CKD. These findings are consistent with other prospective studies in both dialysis (7) and predialysis patients with advanced adult polycystic kidney disease (19). Unlike the study by Schrier et al. (19), we were unable to define a role for the use of ACE inhibitors on LV mass beyond BP control. The limited numbers in each of these studies, together with the diversity and severity of diseases responsible for CKD in the current study, may at least partially account for this difference.

It is possible that the results presented simply display a regression to the mean phenomenon. We believe that this is not the case. First, there was a tight correlation between the observed changes and known determinants of LV hypertrophy across the population as a whole. Such specific correlations would have been unlikely if changes were simply representative of a regression to the mean. Second, distinct subgroups with clear demarcations were found within the described initial groups rather than a general drift toward the mean. Third, mean changes from within the initial groups were small in comparison with the range demonstrated, further supporting two divergent populations consistent with the groups described.

This study suggests that the twin processes of an increase in LV cavity and wall thickness are involved in the development of LV hypertrophy, which occur as a function of volume and pressure overload, respectively. It was of note that an increase in both chamber size and wall thickness contributed to LV growth in patients with normal LV indices at study commencement, whereas regression in LV mass was more closely linked with a reduction in wall thickness. Volume overload is recognized as a potent factor in the development of LV hypertrophy and hypertension in dialysis patients (20,21) and could, in conjunction with a falling GFR, account for the changes observed in patients with a normal LV mass initially. In contrast, reduced aortic compliance is suggested as the primary factor

![Figure 2. Changes and comparisons between subgroups demonstrating relationship between (mean) changes in chamber and wall dimensions over 2 yr. Groups are as indicated, and significant differences are shown. LVH, left ventricular hypertrophy; LVEDV, left ventricular end-diastolic volume; PWT, posterior wall thickness; PP, pulse pressure; LVMI, left ventricular mass index. Values are expressed as mean ± SEM. *P < 0.05; **P < 0.01; †P < 0.001; NS, not significant.](Image)
Table 5. Echocardiographic parameters at study entry analyzed retrospectively for patients who, by study end, had either retained their initial LV indices or, alternatively, demonstrated substantial LV growth (normal initial LV mass) or regression (initial LV hypertrophy)\textsuperscript{a}

\begin{tabular}{|l|c|c|c|c|}
\hline
 & Initial and Sustained Normal LV Mass & Initial Normal LV Mass, Developed LV Growth/ & Initial and Sustained LV Hypertrophy & Initial LV Hypertrophy, Normalized LV Mass \\
 & \textit{(n = 57)} & Hypertrophy \textit{(n = 27)} & \textit{(n = 23)} & \textit{(n = 10)} \\
\hline
LV mass index (g/m\textsuperscript{2}) & 94 ± 16 & 90 ± 19 & 127 ± 17 & 124 ± 17 \\
PWT (mm) & 9.3 ± 1.2 & 9.0 ± 1.5 & 10.5 ± 1.4 & 10.6 ± 1.3 \\
LVEDD (mm) & 49 ± 4 & 50 ± 4 & 54 ± 4 & 53 ± 5 \\
LVESD (mm) & 30 ± 4 & 31 ± 5 & 34 ± 4 & 33 ± 5 \\
LVEDV (ml) & 110 ± 25 & 115 ± 29 & 128 ± 31 & 140 ± 37 \\
\textit{r/th} ratio & 2.7 ± 0.4 & 2.8 ± 0.5 & 2.6 ± 0.5 & 2.5 ± 0.3 \\
\hline
\end{tabular}

\textsuperscript{a} Values are means ± SD.
\textsuperscript{b} Retrospective analysis.

affecting growth or regression, respectively, of LV mass in patients with established hypertrophy. Clearly, the interdependence and synergistic effects of volume and pressure overload become evident as renal function declines and structural changes develop. The effects of age may further contribute to disease progression through both an increase in large vessel stiffness and a reduced GFR with its tendency to volume expansion. Other factors, such as anemia and severe hyperparathyroidism, likely also exert discrete effects that are not apparent in this study and should be managed appropriately.

In summary, the results demonstrated in this article suggest that even in advanced CKD, many patients can maintain normal LV indices with appropriate management. In addition, even at relatively advanced levels of renal impairment, LV hypertrophy seems to be reversible in some patients with appropriate supportive intervention, although whether this is reflected in a reduced mortality is unknown. In patients with CKD and normal heart size, however, the elderly, those with systolic hypertension, and those with more advanced dysfunction seem to be at increased risk for developing LV hypertrophy de novo.

Acknowledgments

This study was enabled by financial support from Janssen-Cilag Australia. We are indebted to the research nurses at the respective institutions, the echocardiographic technicians, and the patients for their participation.


\textsuperscript{*} Principal Investigators.

References


Access to UpToDate on-line is available for additional clinical information at http://www.jasn.org/