ACE inhibitors captopril and enalapril induce regression of left ventricular hypertrophy in hypertensive patients with chronic renal failure

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Abstract

Background. Left ventricular hypertrophy is frequently noted in patients with moderate to severe chronic renal failure not requiring dialysis. Recently, several studies have shown reversal of myocardial hypertrophy in end-stage renal disease with long-term pharmacological control of blood pressure, but it is unclear whether left ventricular mass regresses or normalizes with antihypertensive treatment of patients with earlier stages of chronic renal failure.

Methods. Seventy-two undialysed patients with chronic renal failure, chronic mild-to-moderate hypertension, and left ventricular hypertrophy were randomly assigned in a prospective study to either the captopril (n = 36) or enalapril group (n = 36). Blood pressure measurements, echocardiographic and Doppler parameters were evaluated before treatment and at 6 and 12 months of therapy.

Results. During follow-up, six patients developed side-effects including dry cough, taste disturbances, skin rash and gastric intolerance. In the captopril group there was a decrease in mean left ventricular mass index by 12% after 6 months of treatment, which decreased by 20% after 12 months treatment. For enalapril, the average reduction of myocardial mass after 6 months treatment was 14% and after 12 months treatment, the decrease was 19%. In both treatment groups there was significant improvement of left ventricular filling dynamics. No deterioration of left ventricular systolic function was observed.

Conclusions. Our results confirm that antihypertensive monotherapy with the ACE inhibitors, captopril and enalapril, in patients with chronic renal failure results in regression of left ventricular mass index associated with a significant improvement in the diastolic function of the left ventricle without a demonstrable deterioration in left ventricular systolic performance.

Key words: ACE inhibition; blood pressure control; chronic renal failure; diastolic function; left ventricular hypertrophy

Introduction

Cardiovascular disease is the leading cause of death in end-stage renal failure, representing 43–52% of overall mortality [1–3]. Indeed, cardiovascular mortality in patients on renal replacement therapy is 10–20 times more common than in the general population [4–7]. Left ventricular hypertrophy is an independent factor related to overall mortality in uraemic patients [8–11].

In non-uraemic hypertensive patients with left ventricular hypertrophy, prolonged restoration of normal loading conditions with most classes of antihypertensive drugs, excluding direct vasodilators and diuretics, leads to significant decrease in left ventricular muscle mass index and left ventricular wall thickness and to improvement of left ventricular systolic and diastolic function [12,13]. Regression of left ventricular hypertrophy in end-stage renal disease has been demonstrated after treatment with recombinant human erythropoietin [14,15] and after renal transplantation [5,16]. Although recently, several experimental and clinical studies have shown reversal of myocardial hypertrophy in end-stage renal disease with long-term vigorous pharmacological control of blood pressure [17–20], it is unclear whether left ventricular mass and left ventricular filling dynamics are improved by antihypertensive treatment of patients with earlier stages of chronic renal failure. Moreover, the impact of regression of left ventricular hypertrophy on systolic function in this population remains controversial. Previous studies have reported no consistent improvement in left ventricular systolic function in treated patients with essential hypertension and end-stage renal failure, despite a significant reduction in left ventricular mass [12,13,18].

We investigated whether long-term antihypertensive treatment with captopril and enalapril decreases left ventricular mass and improves left ventricular systolic...
function and left ventricular filling dynamics in patients with chronic renal insufficiency and left ventricular hypertrophy.

Subjects and methods

Patient population

Seventy-two patients (34 men and 38 women, mean age 43.7 years, range 24–61 years) with moderate to severe chronic renal failure not requiring dialysis (mean serum creatinine 0.49 mmol/l, range 0.32 to 0.54 mmol/l) were enrolled in the study. Renal failure was due to primary glomerulonephritis (46 patients with mesangiocapillary glomerulonephritis) and 26 patients with mesangiocapillary glomerulonephritis. Enrolled patients had a chronic mild to moderate hypertension (defined as a resting sitting diastolic blood pressure between 95 and 116 mmHg in the untreated state), and had not been taking antihypertensive or other cardiovascular drugs for at least 3 months before the study.

Patients were included only if they met echocardiographically defined criteria for left ventricular hypertrophy (in men ≥134 g/m² and in women ≥110 g/m², as described below). Exclusion criteria included significant valvular or coronary heart disease, cardiac arrhythmia or conduction defects, or technically uninterpretable two-dimensional echocardiogram. None of the patients had echocardiographic regional wall motion abnormalities or a left ventricular shortening fraction less than 25%. Other secondary causes of hypertension were ruled out by clinical examination and routine biological tests. Enrolled patients gave written informed consent for study participation; both the study protocol and the consent form were approved by the Institutional Review Board.

Study design

The 72 recruited patients were randomly assigned to one of two treatment groups: group A (n = 36) were given captopril and group B (n = 36) enalapril. The study design consisted of three phases: a single-blind placebo phase, a 6- to 8- week phase of drug titration and a 12-month maintenance phase. A complete medical history was obtained and a physical examination, complete blood count, urinalysis, routine serum chemistry analysis, electrocardiogram, echocardiographic and Doppler examinations and thoracic radiographs were performed. All blood pressure readings were made by the same investigator, who used the same calibrated mercury sphygmomanometer throughout the study.

During the placebo phase, eligible patients received one placebo tablet per day for 1–2 weeks. Patients with a sitting diastolic blood pressure of 95–116 mmHg after the placebo phase were eligible for further participation in the study.

During the titration phase, the initial doses of captopril and enalapril were 6.25 and 2.5 mg/day respectively [21]. The dosage was increased every 2 weeks by 6.25 or 2.5 mg increments, respectively, until 'goal' BP, defined as a sitting diastolic BP of <90 mmHg or a reduction in diastolic BP of ≥13 mmHg compared to the pretreatment and baseline measurements, was achieved. Patients who did not achieve the 'goal' BP during titration phase were dropped from the study.

Patients who achieved the 'goal' blood pressure at the end of the titration phase were then evaluated at the 6th and 12th months of treatment. Evaluation during the maintenance phase was similar to baseline evaluation and included serial measurements of blood pressure, heart rate (electrocardiogram), complete blood count tests, urinalysis, routine serum chemistry analysis, and echocardiographic and Doppler parameters.

Echocardiographic and Doppler measurements

Echocardiographic studies were obtained before treatment and at 6th and 12th months after the individual doses of studied drugs were reached.

M-mode echocardiographic examination was performed with two-dimensional monitoring using ATL Ultramark-9 duplex echocardiograph (Advanced Technologies Laboratories, Bellevue, WA, USA) with a 2.5-MHz transducer. Left ventricular internal dimensions, interventricular septal thickness and posterior wall thickness were measured according to the recommendations of the American Society of Echocardiography by the same observer (I.A.L.) who was blinded to the patients’ clinical status, treatment assignment, and phase of study. Each parameter value was averaged over three cardiac cycles. Left ventricular mass was estimated by the Devereux-modified American Society of Echocardiography cube formula and was divided by the body surface area to derive the left ventricular mass index [22].

Left ventricular systolic function was assessed by examining the left ventricular shortening fraction derived from the standard equation. Left ventricular diastolic filling parameters were estimated with pulsed Doppler examinations to obtain peak velocity of early (E) and late diastolic filling (A), and the ratio (E/A) of early to late diastolic flow velocity was calculated.

Statistical analysis

Results are expressed as means ± SD. Comparisons of parameters of cardiac structure and function at baseline with those during treatment were performed by one-way analysis of variance with repeated measurements. Comparisons of studied parameters between A and B groups were performed by using Student’s t test for unpaired observations. Simple linear regression analysis was performed to correlate changes in left ventricular mass with changes in left ventricular shortening fraction or in diastolic filling parameters during treatment. A P value less than 0.05 was considered significant [23].

Results

Characteristics of the study population on entry

There was no significant difference between the two groups at baseline (Table 1). There was a slight difference between the two groups with respect to left ventricular mass index, which did not reach statistical significance.

Treatment tolerance

All patients with chronic renal failure completed the placebo phase and 72 patients were included in the study; 'goal' blood pressure during titration phase was not achieved in 14 patients. Six of 58 (10.3%) patients included in the maintenance phase of study developed side-effects during the follow-up period. Four patients
ACE inhibitors in chronic renal failure

Table 1. Baseline clinical and echocardiographic characteristics of the two patient groups

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43 ± 10</td>
<td>44 ± 12</td>
</tr>
<tr>
<td></td>
<td>(24–61)</td>
<td>(25–59)</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>13:15</td>
<td>10:12</td>
</tr>
<tr>
<td>Blood pressure (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>174 ± 18</td>
<td>182 ± 24</td>
</tr>
<tr>
<td></td>
<td>(138–218)</td>
<td>(142–222)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>107 ± 6</td>
<td>106 ± 8</td>
</tr>
<tr>
<td></td>
<td>(98–116)</td>
<td>(86–116)</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>78 ± 7</td>
<td>76 ± 13</td>
</tr>
<tr>
<td></td>
<td>(64–88)</td>
<td>(56–102)</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.7 ± 0.11</td>
<td>1.8 ± 0.16</td>
</tr>
<tr>
<td></td>
<td>(1.5–2)</td>
<td>(1.5–2.2)</td>
</tr>
<tr>
<td>Left ventricular mass index</td>
<td>147 ± 24</td>
<td>154 ± 34</td>
</tr>
<tr>
<td>(g/m²)</td>
<td>(112–189)</td>
<td>(112–222)</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SD (range).

In group A and two patients in group B reported adverse effects and were withdrawn prematurely after a mean of 26 ± 19 days. The reasons in both groups included dry cough (n=2), taste disturbances (n=1), skin rash (n=2), and gastric intolerance (n=1). Two patients were withdrawn because they were incompetent and it was impossible to regularly evaluated these patients. None of the patients developed further significant impairment of renal function and significant hyperkalaemia during the follow-up period. The mean age of the 50 patients completing the study was 44 ± 10 years (range, 24–60 years) and there were 23 men and 27 women.

Twenty-eight patients received 23 ± 8 mg of captopril (range 6.25–31.25 mg, median dose 25 mg) and 22 patients received 10 ± 2 mg of enalapril (range 5–12.5 mg, median dose 10 mg) during 12 months.

Effect of treatment on haemodynamic parameters and laboratory data

Both captopril and enalapril induced a significant decrease (P<0.05) in the systolic and diastolic blood pressure values after the end of the titration phase, which remained unchanged during maintenance therapy (Tables 2, 3). For captopril, the average reductions were 12.7 and 14.2% in systolic and diastolic blood pressure respectively. In the enalapril group, systolic and diastolic blood pressure was reduced by 11.9 and 12.3% respectively. There was no significant difference between the two groups.

In patients receiving captopril or enalapril there were no significant changes in heart rate from the baseline levels (78 ± 7 and 76 ± 13 beats/min respectively) to those after 6 and 12 months of treatment (77 ± 9, and 78 ± 6 beats/min in group A and 76 ± 9, and 75 ± 9 beats/min in group B respectively). There were no significant changes in creatinine and haemoglobin levels from the initial values in both groups during treatment (Tables 2, 3).

Effect of treatment on cardiac structure

In both groups left ventricular end-diastolic dimensions significantly decreased after the 6 months treatment. These dimensions continued to decrease in the enalapril patients after 12 months therapy, and remained unchanged in the captopril group (between 6 and 12 months) (Tables 2, 3).

After 6 months of treatment with captopril, there was a 7% decrease in interventricular septal thickness, as well as a 12% decrease in left ventricular mass index (all P<0.05). At 12 months, there was a further decrease in left ventricular mass index to 20%, and a 19% decrease in interventricular septal thickness (P<0.05 compared with pretreatment values).

For enalapril, the average reduction after 6 months treatment was 9% for interventricular septal thickness and 14% for left ventricular mass index (all P<0.05). After 12 months of treatment interventricular septal thickness had decreased by 18% and left ventricular mass index by 19% (P<0.05 compared with pretreatment values).

There was no significant difference between the two groups in terms of left ventricular dimensions, wall thickness and left ventricular mass index after 6 and 12 months treatment. The decrement in left ventricular hypertrophy was not correlated with the reduction in the systolic and diastolic blood pressure (for group A values were r=0.29 and 0.32; for group B values were r=0.24 and 0.30 respectively, all P>0.05).

Effect of treatment on left ventricular diastolic function

Left ventricular peak early inflow velocity and ratio of early to late inflow velocities increased at 6 months compared with baseline values in patients in both groups (Tables 2, 3). Conversely, peak late inflow velocity decreased during treatment in both treatment groups. These overall changes after 6 months of treatment were significant for peak early and peak late inflow velocity and ratio of early to late inflow velocities (all P<0.05). In both groups at 12 months, there was further improvement in left ventricle dynamics, evidenced by enhanced early filling with diminished late filling velocities.

There were only slight differences in left ventricular filling dynamics between patients receiving captopril and enalapril after both 6 and 12 months of treatment, which did not reach significant values. The improvement in the ratio of early to late inflow velocities during treatment in both groups was not correlated with the regression of left ventricular mass index (for group A r=0.33; for group B r=0.36 respectively, all P>0.05).

Effect of treatment on left ventricular systolic function

Left ventricular shortening fraction was unchanged in the captopril group as well as in enalapril group after 6 months, but significantly increased after 12 months of therapy over baseline levels (Tables 2, 3). These overall changes in left ventricular shortening fraction...
Table 2. M-mode echocardiographic measurements, Doppler parameters of left ventricular filling, and laboratory data before and during treatment of patients in group A

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>6 months treatment</th>
<th>12 months treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systolic BP (mmHg)</strong></td>
<td>174 ± 18</td>
<td>150 ± 14*</td>
<td>146 ± 13*</td>
</tr>
<tr>
<td><strong>Diastolic BP (mmHg)</strong></td>
<td>107 ± 6</td>
<td>93 ± 6*</td>
<td>91 ± 6*</td>
</tr>
<tr>
<td><strong>Heart rate (beats/min)</strong></td>
<td>78 ± 7</td>
<td>77 ± 9</td>
<td>78 ± 8</td>
</tr>
<tr>
<td><strong>Haemoglobin (g/l)</strong></td>
<td>90 ± 11</td>
<td>89 ± 10</td>
<td>89 ± 14</td>
</tr>
<tr>
<td><strong>Creatinine (mmol/l)</strong></td>
<td>0.48 ± 0.07</td>
<td>0.48 ± 0.10</td>
<td>0.49 ± 0.11</td>
</tr>
<tr>
<td><strong>IVS thickness (cm)</strong></td>
<td>1.4 ± 0.2</td>
<td>1.2 ± 0.2*</td>
<td>1.1 ± 0.2* **</td>
</tr>
<tr>
<td><strong>LVEDD (cm)</strong></td>
<td>1.4 ± 0.2</td>
<td>1.4 ± 0.2</td>
<td>1.4 ± 0.2</td>
</tr>
<tr>
<td><strong>LVMI (g/m²)</strong></td>
<td>5 ± 0.7</td>
<td>4.9 ± 0.7*</td>
<td>4.9 ± 0.6*</td>
</tr>
<tr>
<td><strong>LVF (%)</strong></td>
<td>34 ± 6</td>
<td>34 ± 7</td>
<td>37 ± 6*</td>
</tr>
<tr>
<td><strong>E (cm/s)</strong></td>
<td>54 ± 9</td>
<td>59 ± 8*</td>
<td>64 ± 8* **</td>
</tr>
<tr>
<td><strong>A (cm/s)</strong></td>
<td>66 ± 9</td>
<td>62 ± 8*</td>
<td>59 ± 8* **</td>
</tr>
<tr>
<td><strong>E/A</strong></td>
<td>0.8 ± 0.2</td>
<td>0.9 ± 0.1*</td>
<td>1.1 ± 0.2* **</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SD.
Abbreviations: BP, blood pressure; IVS, interventricular septum; LVEDD, left ventricular end-diastolic diameter; LVMI, left ventricular mass index; LVSF, left ventricular shortening fraction; E, peak early filling velocity; A, peak late filling velocity; E/A, ratio of peak early filling velocity to peak late filling velocity.

*P < 0.05 compared to baseline; **P < 0.05 compared to patients at 6 months treatment.

Table 3. M-mode echocardiographic measurements, Doppler parameters of left ventricular filling, and laboratory data before and during treatment of patients in group B

<table>
<thead>
<tr>
<th></th>
<th>Group B</th>
<th>6 months treatment</th>
<th>12 months treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systolic BP (mmHg)</strong></td>
<td>182 ± 24</td>
<td>149 ± 17*</td>
<td>143 ± 13*</td>
</tr>
<tr>
<td><strong>Diastolic BP (mmHg)</strong></td>
<td>106 ± 8</td>
<td>94 ± 7*</td>
<td>92 ± 6*</td>
</tr>
<tr>
<td><strong>Heart rate (beats/min)</strong></td>
<td>76 ± 13</td>
<td>76 ± 9</td>
<td>75 ± 9</td>
</tr>
<tr>
<td><strong>Haemoglobin (g/l)</strong></td>
<td>89 ± 10</td>
<td>89 ± 11</td>
<td>88 ± 12</td>
</tr>
<tr>
<td><strong>Creatinine (mmol/l)</strong></td>
<td>0.49 ± 0.06</td>
<td>0.49 ± 0.10</td>
<td>0.50 ± 0.10</td>
</tr>
<tr>
<td><strong>IVS thickness (cm)</strong></td>
<td>1.4 ± 0.2</td>
<td>1.3 ± 0.2*</td>
<td>1.2 ± 0.2* **</td>
</tr>
<tr>
<td><strong>LVEDD (cm)</strong></td>
<td>5.2 ± 0.7</td>
<td>5.0 ± 0.5*</td>
<td>4.8 ± 0.6* **</td>
</tr>
<tr>
<td><strong>LVMI (g/m²)</strong></td>
<td>154 ± 34</td>
<td>135 ± 30*</td>
<td>121 ± 26* **</td>
</tr>
<tr>
<td><strong>LVF (%)</strong></td>
<td>34 ± 6</td>
<td>35 ± 6</td>
<td>39 ± 6*</td>
</tr>
<tr>
<td><strong>E (cm/s)</strong></td>
<td>55 ± 10</td>
<td>60 ± 9*</td>
<td>64 ± 9* **</td>
</tr>
<tr>
<td><strong>A (cm/s)</strong></td>
<td>69 ± 7</td>
<td>65 ± 7*</td>
<td>62 ± 8* **</td>
</tr>
<tr>
<td><strong>E/A</strong></td>
<td>0.8 ± 0.2</td>
<td>0.9 ± 0.1*</td>
<td>1.0 ± 0.1* **</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SD.
Abbreviations are as in Table 2.

*P < 0.05 compared to baseline; **P < 0.05 compared to patients at 6 months treatment.

during treatment were statistically significant in both drugs (P < 0.05). There was a slight and insignificant difference in values of left ventricular shortening fraction between the groups of patients. There was no linear relationship between regression of left ventricular hypertrophy and overall changes in shortening fraction (for group A r = 0.36; for group B r = 0.34 respectively, all P > 0.05).

**Discussion**

**Regression of left ventricular hypertrophy**

Antihypertensive treatment with captopril or enalapril was compared in patients with chronic renal failure. ACE inhibitors have been shown to be the most effective in terms of regression of left ventricular muscle mass in essential hypertension [24]. Previous studies in experimental animals and human subjects on cardio-protective and cardioreparative properties of these agents suggest that they would be useful in preventing and reversing the myocardial structural changes in left ventricular hypertrophy [25–27].

Left ventricular hypertrophy is frequently noted in patients with moderate to severe chronic renal failure not requiring dialysis. Greaves et al. [28] have observed that of 38 undialysed patients with chronic renal failure, 63% had abnormal echocardiogram, and left ventricular hypertrophy was the most common finding (24%). Since left ventricular hypertrophy is a cardio-
vascular risk in both uraemic and non-uraemic populations, the prevention of hypertrophy, its early detection, and reduction of left ventricular mass index at early stages of chronic renal failure appear to be promising for the reduction of cardiovascular events in patients with chronic uraemia [4,27,29,30].

In the last few years a growing number of experimental and clinical reports have analysed the structural left ventricular changes during ACE-inhibition in uraemia. The results are controversial. Rambausek et al. [31] have described left ventricular hypertrophy development and progression in uraemic animals despite blood pressure normalization by ACE inhibitors. These results are in accordance with recent findings of Roithinger et al. [32], who concluded that the ACE inhibitor lisinopril, at a dose which left the blood pressure unchanged throughout the study period, was not able to induce reduction of left ventricular mass.

In contrast, the data in our study indicate that in patients with chronic renal failure and moderate arterial hypertension, long-term treatment with the ACE inhibitors, captopril or enalapril, significantly lowered arterial pressure and reduced left ventricular hypertrophy. A significant difference in respect of blood pressure diminishing and reduction of left ventricular mass index between the two treatments was not evident. In agreement with our results, London et al. [11] showed that despite similar effects on blood pressure in patients with left ventricular hypertrophy and end-stage renal failure, a reduction in left ventricular mass and volume was observed with ACE inhibition but not with calcium-channel blockade.

The present study, left ventricular mass index was found to be reduced by 12 and 14% after 6 months of treatment with captopril and enalapril respectively. The degree of left ventricular mass index reduction in our study was in agreement with some short-term previous studies of ACE inhibitor treatment in patients with essential hypertension and end-stage renal failure [11,24,33].

The time course of regression of left ventricular hypertrophy during antihypertensive therapy has been evaluated in several studies. In some clinical reports a reduction in posterior wall thickness and left ventricular mass index occurs as early as 4 weeks after the beginning of treatment, with further reduction during the subsequent 1–4 months and no significant change thereafter for up to 1 year [13,34]. In contrast, several studies have clearly demonstrated that the magnitude of the reduction in left ventricular mass index is related to the duration of treatment [35,36]. In our study, left ventricular mass index continued to decrease with continuous treatment with ACE inhibitors, and after 12 months was 20 and 19% less than pretreatment values for captopril and enalapril groups respectively. The data herein indicate that the period of 3–6 months used in most previous studies is insufficient to document the time course of left ventricular mass reduction.

It is unclear whether the regression of left ventricular hypertrophy is due to a lowering of blood pressure or to a direct effect of the drugs on the myocardium, or both. In the present study, the decrement in left ventricular hypertrophy was not correlated with the reduction in the systolic and diastolic blood pressure. In agreement with our findings, other clinical and experimental studies have shown that the left ventricular mass correlated poorly with blood pressure level during both the development and the reversal of hypertensive left ventricular hypertrophy [13,37]. However, several studies reported the crucial role of a decrease in blood pressure diminishing in the reduction of left ventricular mass in end-stage renal disease, as well as in essential hypertension [17,29,35]. The disparity in the reported findings may be attributable to the different antihypertensive drugs used in these studies, and to interstudy differences in methods of blood pressure measurements (casual blood pressure versus 24-h ambulatory blood pressure monitoring).

**Changes in diastolic function during treatment**

The present study showed that regression of left ventricular hypertrophy during antihypertensive treatment of chronic renal failure patients with ACE inhibitors captopril and enalapril is associated with significant improvement in the diastolic function of the left ventricle. In contrast with our findings, Roithinger et al. [32] were unable to show improvement in diastolic filling in patients with chronic renal failure receiving an ACE inhibitor.

It is speculated that reduction in left ventricular mass with antihypertensive treatment increases the fibrosis/myocardial muscle fibre ratio, leaving the ventricle less compliant and perhaps with worsened diastolic function [12,13]. The data in this study, as well as that of others, do not support this concept, since regression of hypertrophy was accompanied by improvement in left ventricular filling dynamics in all reports [35].

**Changes in systolic function during treatment**

There has been some concern, based on a previous experimental study, that regression of left ventricular hypertrophy with antihypertensive treatment might lead to a deterioration of left ventricular systolic performance [38]. However, this concern has not been borne out by clinical studies that have shown either no change, or an improvement, in left ventricular systolic function after regression of left ventricular hypertrophy in essential hypertension, even when treatment was withdrawn and blood pressure had increased again [35,36]. We have also demonstrated no deterioration in left ventricular systolic function after reduction of left ventricular mass with antihypertensive treatment of patients with end-stage renal disease [18]. In the present study, left ventricular shortening fraction was unaltered in both groups after 6 months and significantly increased after 12 months of treatment. Our findings of left ventricular shortening fraction dynamics after regression of left ventricular hypertrophy confirm those of previous reports [18,35].
In conclusion, our randomized prospective longitudinal study shows that antihypertensive monotherapy with ACE inhibitors captopril and enalapril in patients with chronic renal failure results in regression of left ventricular mass index associated with significant improvement in the diastolic function of the left ventricle. Both ACE inhibitors are equipotent in bringing about regression of left ventricular hypertrophy and improving disturbances of diastolic left ventricular function. The present study demonstrates that regression of left ventricular hypertrophy in chronic renal failure patients is accompanied by improvement of left ventricular diastolic function. Also the study showed that a substantial reduction of left ventricular mass index can be achieved safely, without a demonstrable deterioration in left ventricular systolic performance. Further larger-scale randomized studies of different antihypertensive agents, using 24-h blood pressure control, are necessary in patients with chronic uraemia, including end-stage renal disease as well as earlier stages of chronic renal failure. In addition, long-term trials targeted at determining whether pharmacological regression of left ventricular hypertrophy results in a decrease in cardiovascular morbidity and mortality rates are necessary.

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