EXPERIMENTAL STUDIES

Effect of Captopril and Enalapril on Left Ventricular Geometry, Function and Collagen During Healing After Anterior and Inferior Myocardial Infarction in a Dog Model

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Objectives. This study compared the effects of captopril and enalapril on left ventricular geometry, function and mass and on scar collagen and topography during healing after anterior and inferior myocardial infarction in a canine model.

Background. The beneficial effect of prolonged angiotensin-converting enzyme inhibitor therapy on remodeling during healing after myocardial infarction might be greater in anterior than inferior infarcts and more effective with captopril than enalapril therapy.

Methods. The effects of 6 weeks of therapy with captopril (50 mg twice a day), enalapril (2.5 mg twice a day) or placebo on in vivo variables of left ventricular remodeling, function and mass (by echocardiography), hemodynamic function, postmortem topography (by planimetry) and collagen (hydroxyproline levels) were studied in 36 instrumented dogs randomized to receive therapy 48 h after left anterior descending or left circumflex coronary artery occlusion.

Results. Compared with placebo therapy, both captopril and enalapril decreased infarct expansion and thinning, progressive ventricular dilation, ventricular mass and asynergy and infarct collagen levels in anterior and inferior infarcts. Despite similar small scar sizes, the effects on remodeling and dysfunction were greater in anterior than inferior infarcts. In addition, captopril produced greater attenuation of infarct expansion and ventricular enlargement, greater improvement in volume ejection fraction and less decrease in infarct collagen levels than enalapril.

Conclusions. On balance, captopril and enalapril attenuated left ventricular remodeling and preserved function in small anterior and inferior infarcts despite differences in the effects of the drugs on individual remodeling variables. Further studies will be needed to determine whether inhibition of infarct collagen might be harmful, or differences between captopril and enalapril therapy important, in large transmural infarctions.

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Inhibition of angiotensin-converting enzyme after myocardial infarction has the potential for limiting certain remodeling variables and preserving function (1–7). Although angiotensin-converting enzyme inhibitor therapy is recommended after anterior infarction in patients at high risk for left ventricular dilation and dysfunction (8), there has been no systematic comparison of its effects on anterior versus inferior infarction. Whether angiotensin-converting enzyme inhibitors containing thiol (e.g., captopril) are more effective than those without thiol (e.g., enalapril) is controversial (9–12). Because these agents inhibit hypertrophy and fibrosis during postinfarction healing (13–17) in noninfarcted myocardium, they might also increase collagen degradation and inhibit collagen deposition in infarct zones, interfere with scar formation or cause regression of the fibrous scar tissue. It is also not known whether this effect might promote remodeling and impair functional improvement.

Therefore, we compared the effects of therapy with the angiotensin-converting enzyme inhibitors captopril and enalapril during healing after anterior and inferior myocardial infarction on remodeling variables, systolic function, ventricular mass and infarct collagen content in a well defined canine model (15).

Methods

Experimental preparation. The experiments were approved by the institutional animal welfare committee and conformed to the “Position of the American Heart Association on Research Animal Use” adopted by the Association in November 1984. Fifty healthy mongrel dogs (16 to 29 kg) were chronically instrumented through a left lateral thoracotomy under general anesthesia (sodium pentobarbital, 30 mg/kg body weight intravenously), as described previously (3,4). Polyethylene catheters were inserted in the external jugular vein, internal carotid artery and left atrium, filled with heparinized saline solution and their ends brought out behind the neck. The mid-left anterior descending coronary artery (n =
25) or mid-left circumflex coronary artery (n = 25) was ligated with a silk thread. Pairs of metal beads were sutured on anterior, lateral and posterior surfaces of the epicardium at the mid-left ventricular level for consistent echocardiographic imaging. Visible epicardial collateral vessels were ligated to produce more transmural infarction (mean [+SD] 83 ± 4% of wall thickness), as done previously (18). After closure of the pericardium and chest, penicillin (1 million U) and streptomycin (1 g) were given intramuscularly.

**Protocol.** Two days after ligation, 48 healthy survivors were randomized to receive placebo (n = 16), captopril (50 mg) (n = 16) or enalapril (2.5 mg) (n = 16). Each group had eight dogs with a ligated left anterior descending coronary artery and eight with a ligated left circumflex coronary artery. Therapy was given orally, twice daily (every 12 h) for 6 weeks. The dogs were given free access to fluids, and no attempt was made to restrict fluid intake. Hemodynamic variables were also measured at 1 week. Recordings during therapy were made 3 to 4 h after the first daily doses. Echocardiograms were acquired at 2 days after ligation, during therapy at 3 and 6 weeks after ligation; and again 1 to 2 days after therapy was stopped. Hemodynamic variables were also measured at 1 week.

**In vivo measurements during healing.** As described previously (3,4), simultaneous two-dimensional echocardiograms (Toshiba SSH-65A [3.5-MHz transducer]), electrocardiograms (Gould recorder) and hemodynamic variables (Statham P23Db for left atrial and arterial pressures) were recorded in the conscious state with the dogs standing in a sling for support: before therapy at 2 days after ligation, during therapy at 3 and 6 weeks after ligation; and again 1 to 2 days after therapy was stopped. Hemodynamic variables were also measured at 1 week. Recordings during therapy were made 3 to 4 h after the first daily doses. Echocardiograms were acquired at parasternal long- and short-axis views at the mitral, chordal, midpapillary, low papillary and apical levels and apical four- and two-chamber views.

**Analysis of echocardiograms.** As described previously (3,4), coded echocardiograms were analyzed on video playback (0.5-in. tapes) by two independent observers who were unaware of the randomization procedures for in vivo topographic variables; differences were resolved by consensus. Briefly, endocardial and epicardial outlines of the left ventricular images at end-diastole and end-systole were traced with a light pen (Diasonics CardioRevue Center) and copied onto plastic overlays. Anatomic landmarks, such as papillary muscles and right and left ventricular junctions, were indicated on the tracings. Asynery, defined as akinesia (no systolic inward motion and thickening) or dyskinesia (systolic outward motion and thinning), or both, was marked on each endocardial diastolic outline. The circumferential extent of asynery on each short-axis view was then digitized (Hewlett-Packard 9878A and 9835A) and used to compute total endocardial surface area of asynery by a three-dimensional reconstruction algorithm. Outlines from five short-axis and two long-axis views were also used to compute volumes by means of a modified Simpson’s rule algorithm. Global ejection fraction was calculated as end-diastolic volume minus end-systolic volume divided by end-diastolic volume. Interobserver error was <5% in marking asynery, segment length, wall thickness and areas of outlines, in agreement with previous studies (3,4,18).

**Topographic measurements** were made on end-diastolic outlines of short-axis images at the papillary level, and the expansion index (ratio of the lengths of asynergic, or infarct-containing, segments to nonasynergic, or non-infarct-containing, segments) and thinning ratio (ratio of average thicknesses of the asynergic to nonasynergic zones) were computed. Left ventricular aneurysm was defined as the presence of a bulge in diastole and further bulging in systole. Left ventricular mass was calculated by multiplying the volume of myocardium (difference in volumes of epicardial and endocardial shells at end-diastole) by an assumed specific gravity of 1.05 g/ml (19).

**Postmortem measurement of scar size, geometry and collagen content.** As described previously (3,4), the risk region was measured on postmortem coronary arteriograms recorded on whole-heart and transverse section (1- to 1.5-cm thick) radiographs. Outlines of left ventricular rings, risk regions and infarct scars were made on plastic overlays and subjected to computerized planimetry (Hewlett-Packard 9835A computer and 9878A digitizer interfaced with a VAX 750 computer) to assess infarct size and topography and to calculate the “thinning” ratio (ratio of average thickness of infarcted wall to average thickness of normal wall) and “expansion” index (ratio of endocardial lengths of infarct-containing to non-infarct-containing segments demarcated by papillary muscles). Average short-axis topographic maps were made for each group (3,4), Histopathologic analysis of extent of infarct scar and collagen content (20) was performed on a 5-mm slice from the middle of the infarct zone, and triplicate 5-μm thick sections were stained with hematoxylin-eosin, Mallory’s stain or Mason’s trichrome, respectively. Myocardial hydroxyproline (mg/g dry tissue weight), a marker for collagen, was measured in 100- to 200-mg samples from the center and border regions of the infarct scar (after excision of normal tissue on gross examination) and the center of the noninfarct region (20).

**Statistics.** Data were analyzed in blinded manner by 1) analysis of variance for the significance of difference within and between groups; 2) chi-square test for the significance of difference in event frequency between groups; and 3) repeated measures analysis of variance for comparison of serial data within groups. Results are presented as mean value ± SD, unless otherwise stated. Statistical significance was set at p < 0.05 (two-tailed).

**Results**

**Study groups.** Of the 48 dogs that were randomized at 2 days, 12 died over the 6 weeks (placebo n = 4, captopril n = 4, enalapril n = 4). The 36 dogs that were killed at 6 weeks (12 in each group) form the basis of this report. The distribution of dogs with anterior versus inferior infarction in each of the three groups was 6 anterior and 6 inferior in the placebo group; 8 anterior and 4 inferior in the captopril group; and 6 each in the enalapril group.
Infarct scar size. At 6 weeks, infarct scar size with captopril (5 ± 3 g) and enalapril (4 ± 2 g) was not significantly less than that with placebo (6 ± 3 g), and heart size was 5 ± 3 g (7 ± 4% of the left ventricle, or 35 ± 16% of the risk region). Ventricular and risk region mass was similar (77 ± 15 and 15 ± 7 g, respectively). Infarct scar, ventricular and risk region size for anterior and inferior infarction subgroups was also similar (p = NS).

Regional collagen content. Non–infarct region collagen content was slightly lower (p < 0.05) for enalapril than for placebo, but the difference between captopril and placebo did not achieve statistical significance. In contrast, collagen content in the infarct center and border regions was markedly lower with captopril and enalapril than with placebo, and the decrease was greater with enalapril (Fig. 1). There was no difference in infarct or noninfarct collagen content between anterior and inferior infarction subgroups.

Hemodynamic changes. The 2-day baseline hemodynamic changes were similar for all treatment groups and subgroups for all 36 dogs (heart rate 137 ± 21 beats/min; mean arterial pressure 111 ± 15 mm Hg; left atrial pressure 15 ± 1 mm Hg). On day 2, captopril and enalapril produced a marked decrease in left atrial pressure (20% to 40%), a mild decrease in mean arterial pressure (5% to 10%) but no change in heart rate compared with that during placebo. Although these variables decreased in all groups between 2 days and 6 weeks, left atrial and arterial pressures remained lower with angiotensin-converting enzyme inhibition than with placebo, and the decrease in mean arterial pressure with captopril was statistically significant (Table 1). Although the overall decrease in mean arterial pressure was slightly greater with captopril than enalapril (−14 vs. −7%), and the overall decrease in mean left atrial pressure was slightly less with captopril than with enalapril (−34 vs. −49%), these differences were not statistically significant (p < 0.2 and p < 0.1, respectively). After drug withdrawal at 6 weeks, arterial and left atrial pressures increased in the captopril and enalapril groups, such that the changes in arterial (−4% vs. −1% vs. −1%) and atrial (−31% vs. −26% vs. −28%) pressures from baseline were similar in the captopril, enalapril and placebo groups, respectively. There was no difference in hemodynamic changes between the anterior and inferior infarction subgroups.

Left ventricular geometry. The effects on geometry are depicted in Figures 2 to 4. Compared with placebo, captopril and enalapril decreased regional infarct expansion (Fig. 2), infarct thinning (Fig. 3) and left ventricular diastolic volumes (Fig. 4). The placebo subgroup with anterior infarction showed greater elongation of the infarct-containing segment and greater increase in expansion index (Fig. 2), noninfarct wall thickness (Fig. 3), end-diastolic and end-systolic volumes and diastolic endocardial surface area (Fig. 4) than the placebo subgroup with inferior infarction. In addition, the antiremodeling effects on infarct expansion and ventricular enlargement tended to be greater with captopril than enalapril, especially between 3 and 6 weeks (Fig. 2 to 4).

Left ventricular function. Compared with placebo, captopril and enalapril decreased regional left ventricular asynergy, but the effect was more marked in the anterior infarction subgroup (Fig. 5). The decrease in total left ventricular asynergy was less pronounced (Fig. 5). The improvement in global volume ejection fraction was greater with captopril than with enalapril in both anterior and inferior infarction subgroups.

Table 1. Percent Changes in Hemodynamic Variables From Two-Day Baseline Value*  

<table>
<thead>
<tr>
<th>Group</th>
<th>1 wk</th>
<th>3 wk</th>
<th>6 wk</th>
<th>1 wk</th>
<th>3 wk</th>
<th>6 wk</th>
<th>1 wk</th>
<th>3 wk</th>
<th>6 wk</th>
</tr>
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<tbody>
<tr>
<td>Placebo (n = 12)</td>
<td>-16 ± 16</td>
<td>-20 ± 14</td>
<td>-26 ± 15</td>
<td>2 ± 12</td>
<td>1 ± 9</td>
<td>-1 ± 7</td>
<td>-5 ± 14</td>
<td>-23 ± 25</td>
<td>-30 ± 22</td>
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<tr>
<td>Captopril (n = 12)</td>
<td>-22 ± 16</td>
<td>-21 ± 17</td>
<td>-30 ± 16</td>
<td>-9 ± 13</td>
<td>-15 ± 14</td>
<td>-22 ± 31</td>
<td>-22 ± 12</td>
<td>-33 ± 33</td>
<td>-46 ± 18</td>
</tr>
<tr>
<td>Enalapril (n = 12)</td>
<td>-14 ± 16</td>
<td>-16 ± 18</td>
<td>-32 ± 14</td>
<td>-8 ± 13</td>
<td>-7 ± 21</td>
<td>-5 ± 30</td>
<td>-41 ± 35</td>
<td>-52 ± 16</td>
<td>-53 ± 24</td>
</tr>
</tbody>
</table>

*Decreases (minus sign) are significant versus the within-group 2-day value (p ≤ 0.05). †p < 0.05, ‡p < 0.001, §p < 0.005, captopril or enalapril groups versus placebo group. Data presented are mean value ± SD.
June 1995:1718-25 CAPTOPRIL VERSUS ENALAPRIL AFTER INFARCTION

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was lower in the inferior than anterior placebo subgroup (3 of 8 vs. 6 of 6, p < 0.01) and the combined captopril than placebo groups (3 of 12 vs. 9 of 12, p < 0.025). The frequency of left ventricular aneurysm at 6 weeks occurred between 2 days and 6 weeks with infarcts at both anterior and inferior locations in the placebo group. Although there was no difference in extent of infarct thinning at the two infarct locations, the extent infarct expansion and ventricular enlargement was greater in anterior than inferior infarction. 2) Captopril and enalapril therapy improved left ventricular geometry and function between 2 days and 6 weeks after both anterior and inferior infarction. However, the magnitude of the effects on expansion and ventricular enlargement were greater in anterior than inferior infarction. In addition, the effects on expansion, volumes and global function tended to be greater with captopril than enalapril. 3) Captopril and enalapril decreased left ventricular mass in anterior and inferior infarction, but only the decrease with enalapril in anterior infarction was statistically significant. 4) Captopril and enalapril decreased infarct collagen content, but the effect was more marked with enalapril. Enalapril also produced a mild decrease in noninfarct collagen content.

Mechanisms. Both captopril and enalapril decreased left atrial (index of preload) and mean arterial pressures (index of afterload), left ventricular volumes and left ventricular and infarct collagen content in anterior and inferior infarction. Four main mechanisms explain the effects common to the two angiotensin-converting enzyme inhibitors: 1) Angiotensin-converting enzyme inhibitors mediate vasodilation by inhibition of angiotensin II formation and bradykinin breakdown and increased bradykinin, nitric oxide (21), prostaglandin E2 and prostacyclin (22). Vasodilation, in turn, leads to left ventricular unloading, less regional bulging, smaller chamber size and lower diastolic wall stress (by virtue of the Laplace law), less wall stretch, less gene expression of contractile and noncontractile proteins and less hypertrophy (23,24). 2) These agents inhibit tissue angiotensin-converting enzyme and intramyocardial conversion of angiotensin I to angiotensin II, thereby decreasing local angiotensin II; activities of myocyte, fibroblast and transforming-growth factors (25-27); myocyte hypertrophy; and collagen deposition. Release of nitric oxide secondary to increased bradykinin might also inhibit myocyte.

Left ventricular mass. Compared with placebo, both captopril (-2% vs. +2%, p = 0.5) and enalapril (-10% vs. +2%, p = 0.2) lowered left ventricular mass, but only enalapril achieved statistical significance in the anterior infarction subgroup (-11% ± 17% vs. +12% ± 14%, p < 0.05).

Postmortem topography. Topographic maps in the short-axis view at 6 weeks confirmed less cavity area, infarct wall thinning, noninfarct wall thickness and infarct zone bulging with inferior than anterior infarction and with captopril or enalapril than with placebo (Table 2). The cavity area was larger with enalapril than captopril for both anterior and inferior infarction (Table 2), supporting the in vivo finding in Figure 4.

Discussion

There were four major findings in this study: 1) further infarct expansion, infarct thinning and ventricular enlargement occurred between 2 days and 6 weeks with infarcts at both anterior and inferior locations in the placebo group. Although there was no difference in extent of infarct thinning at the two infarct locations, the extent infarct expansion and ventricular enlargement was greater in anterior than inferior infarction. 2) Captopril and enalapril therapy improved left ventricular geometry and function between 2 days and 6 weeks after both anterior and inferior infarction. However, the magnitude of the effects on expansion and ventricular enlargement were greater in anterior than inferior infarction. In addition, the effects on expansion, volumes and global function tended to be greater with captopril than enalapril. 3) Captopril and enalapril decreased left ventricular mass in anterior and inferior infarction, but only the decrease with enalapril in anterior infarction was statistically significant. 4) Captopril and enalapril decreased infarct collagen content, but the effect was more marked with enalapril. Enalapril also produced a mild decrease in noninfarct collagen content.

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Figure 2. Effect of therapy on in vivo changes in infarct expansion. Results are mean value ± SEM; points are offset around time lines for clarity. D = day; pdw = post drug withdrawal; W = week. *p ≤ 0.05, anterior versus inferior infarction subgroups. †p ≤ 0.05, enalapril (V) or captopril (A) versus placebo (O). $p ≤ 0.05, captopril versus enalapril.

Figure 3. Effect of therapy on in vivo changes in infarct thinning. Results are mean value ± SEM; points are offset around time lines for clarity. *p ≤ 0.05, anterior versus inferior infarction subgroups. †p ≤ 0.05, enalapril or captopril versus placebo. $p ≤ 0.05, captopril versus enalapril. Abbreviations and symbols as in Figure 2.
Figure 4. Effect of therapy on in vivo changes in left ventricular enlargement. Results are mean value ± SEM; points are offset around time lines for clarity. *p < 0.05, anterior versus inferior infarction subgroups. tp < 0.05, enalapril or captopril versus placebo. *)(p < 0.05, captopril versus enalapril. Abbreviations and symbols as in Figure 2.

Several differences between the effects of the two angiotensin-converting enzyme inhibitors in this study might relate to differences in their chemistry and pharmacology (32).

1) Captopril, unlike enalapril, has a sulfhydryl group that additionally causes direct vasodilation (10) and increases vasodilatory prostaglandins. These effects might explain the slightly greater decrease in blood pressure with captopril. Although the oxygen-free radical scavenging activity of the sulfhydryl group is protective after reperfusion (11), its role in this permanent occlusion model is not clear.

2) Although captopril is itself the active drug, enalapril has to undergo hepatic deesterification to the active form, enalaprilat. Also, whereas captopril undergoes metabolism to disulfides and primarily urinary excretion, enalaprilat is excreted in urine (61%) and feces (33%) without further metabolism. Enalapril therefore has a slower onset (2 vs. 0.5 h), later peak (6 vs. 1 h) and longer duration (24 vs. 6 h) of action than captopril, and the elimination half-life is longer (>30 vs. 1.7 h). Although the finding of a greater decrease in ventricular mass with enalapril despite a lesser decrease in blood pressure suggests an exaggerated response with this drug, it is also possible that ventricular unloading was sustained for a longer period between doses with enalapril. Because both drugs produced unloading at the doses used and have flat dose-response curves, it is unlikely that doses used played a major role in the differences.

3) Enalapril possesses greater angiotensin-converting enzyme inhibitory potency and more binding sites (seven vs. five) than captopril (32). It might produce greater inhibition of angiotensin II, fibroblast growth factor and transforming growth factor-beta, than captopril. This might explain why enalapril (but not captopril) produced a decrease in noninfarct collagen and why enalapril decreased infarct scar collagen more than captopril. The finding that both agents produced marked lowering of collagen in the infarct scar region but little hypertrophy (28). 3) Angiotensin-converting enzyme inhibitors improve nutrient flow through bradykinin and nitric oxide-mediated dilation of coronary arteries and collateral vessels as well as reduced endocardial compression secondary to decreased diastolic wall stress (3,4). 4) Because high myocardial wall stress and low nutrient flow cause matrix disruption (29,30), lowering diastolic wall stress and increasing flow with angiotensin-converting enzyme inhibition would tend to preserve the supporting matrix, improve the mechanical coupling between collagen fibrils at infarct scar borders and live myocytes (31), limit remodeling and preserve function.
with angiotensin-converting enzyme inhibitors is thought to be weakening the scar and be potentially harmful by allowing greater remodeling under the effect of mechanical forces (33) and by causing defective mechanical coupling at the infarct borders. Whether increased collagenase activity might have played a role is not known. However, no marked deleterious effect was found with the small infarcts in this study.

To our knowledge, a decrease in infarct collagen with long-term angiotensin-converting enzyme inhibition has not been reported previously. Although regression of fibrous tissue and decreased deposition or increased degradation of collagen with angiotensin-converting enzyme inhibitors is thought to be beneficial in pressure overload hypertrophy (34), a similar effect on noninfarct collagen in “volume overload hypertrophy” after infarction (13–17,25) was thought to be harmful (15). In the rat infarction model, which is associated with extensive necrosis of the left ventricular free wall, marked chamber dilation, hypertrophy and fibrosis of the septum, early (14) but not late (16), captopril therapy inhibited deoxyribonucleic acid synthesis, fibroblast proliferation and collagen deposition in noninfarct regions. In the same model, a similar effect was demonstrated with perindopril (13), and nearly complete inhibition of noninfarct collagen was produced by the angiotensin II type I receptor blocker losartan (17). In contrast, the dog infarction model in this study was associated with only mild hypertrophy and very little increase in noninfarct collagen.

**Implications.** The goal of antiremodeling therapy during infarct healing is to preserve left ventricular geometry, prevent dilation and preserve function. A short, thick and strong scar might be desirable. The overall results of the present study suggest that the final outcome with angiotensin-converting enzyme inhibitor therapy represents a balance of positive and negative effects on factors involved in healing and remodeling after infarction (33). The results also suggest that antihypertrophic and collagen-lowering effects might be more potent with enalapril than captopril. Although reduced infarct collagen did not seem to have a marked negative impact on the small nontransmural infarcts in this study, one might expect a different outcome with large transmural infarcts, as was found in the rat model (15). Because patients in clinical trials of angiotensin-converting enzyme inhibitors after infarction received other early therapies, and because the trials included thrombolysis in ~30% to 70% of patients, the infarcts were

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**Table 2. Mean (±SD) Postmortem Measurements at Low Papillary Level on Short-Axis Topographic Maps**

<table>
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<tr>
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<th>Placebo</th>
<th>Captopril</th>
<th>Enalapril</th>
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<tbody>
<tr>
<td><strong>Anterior infarction subgroup</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of dogs</td>
<td>6</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Angular extent of infarct (°)</td>
<td>121 ± 5</td>
<td>81 ± 9*</td>
<td>90 ± 5*</td>
</tr>
<tr>
<td>Infarct wall thickness (mm)</td>
<td>5 ± 1</td>
<td>9 ± 1*</td>
<td>9 ± 1*</td>
</tr>
<tr>
<td>Noninfarct wall thickness (mm)</td>
<td>15 ± 1</td>
<td>11 ± 1*</td>
<td>10 ± 1*</td>
</tr>
<tr>
<td>LV cavity area (cm²)</td>
<td>5.2 ± 0.8</td>
<td>2.6 ± 0.6*</td>
<td>3.5 ± 0.5*†</td>
</tr>
<tr>
<td>Area of endocardial bulge (cm²)</td>
<td>1.3 ± 0.9</td>
<td>0.2 ± 0.1*</td>
<td>0.5 ± 0.1*</td>
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<table>
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<tr>
<td>No. of dogs</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Angular extent of infarct (°)</td>
<td>105 ± 2</td>
<td>76 ± 5*</td>
<td>80 ± 3*</td>
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<td>Infarct wall thickness (mm)</td>
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<td>10 ± 1*</td>
</tr>
<tr>
<td>LV cavity area (cm²)</td>
<td>4.6 ± 0.5</td>
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<td>3.2 ± 0.4†</td>
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<td>Area of endocardial bulge (cm²)</td>
<td>1.0 ± 0.8</td>
<td>0.2 ± 0.0*</td>
<td>0.3 ± 0.0*</td>
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</tbody>
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*p < 0.05, captopril or enalapril versus placebo. †p < 0.05, enalapril versus captopril. LV = left ventricular.
most likely also small and subendocardial. The finding of a survival benefit in most of these studies (33) supports the concept that final outcome represents a balance of effects. However, the current data do not favor one angiotensin-converting enzyme inhibitor over another. Although captopril was associated with decreased mortality in the Survival and Ventricular Enlargement (SAVE) (6) and International Study of Infarct Survival (ISIS-4) (35) trials and with attenuation of ventricular enlargement in a SAVE substudy (7) and other remodeling studies (5,36–38), survival benefit was also found with ramipril in the Acute Infarction Ramipril Efficacy (AIRE) trial (39) and with lisinopril in the Grupo Italiano per lo Studio della Sopravvivenza nell’Infarto Miocardico (GISSI) trial (40). Although no survival benefit was found with enalapril in the Studies of Left Ventricular Dysfunction (SOLVD) (41) and Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS II) (42) trials, the recent “Practical” study (43) that compared captopril and enalapril after infarction showed that both agents attenuated left ventricular dilation and improved ejection fraction, but only enalapril improved survival.

Conclusions. In the present study, therapy with captopril or enalapril during healing of relatively small nontransmural anterior and inferior myocardial infarctions limited remodeling, improved systolic function and preserved left ventricular geometry at 6 weeks despite a marked decrease in infarct collagen content. The beneficial effects on remodeling and function were greater in anterior than inferior infarction. Although the greater enalapril-induced lowering of infarct collagen might explain the lesser improvement in global systolic function than that induced by captopril, it did not seem to have a marked negative impact on in vivo remodeling variables. Whether the infarct-collagen lowering effect of angiotensin-converting enzyme inhibition might be potentially harmful during early healing of large transmural infarctions needs further study.

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References


