Improvement of Myocardial Blood Flow to Ischemic Regions by Angiotensin-Converting Enzyme Inhibition With Quinaprilat IV

A Study Using [15O] Water Dobutamine Stress Positron Emission Tomography

Christian A. Schneider, MD, Eberhard Voth, MD,* Detlef Moka, MD,* Frank M. Baer, MD, Jacques Melin, MD, FACC,† Anne Bol, PhD,‡ Rainer Wagner, PhD,‡ Harald Schicha, MD,* Erland Erdmann, MD, FACC, Udo Sechtem, MD, FACC

Cologne, Germany, and Louvain, Belgium

OBJECTIVES

This study was designed to analyze the effects of acute angiotensin-converting enzyme (ACE) inhibition on myocardial blood flow (MBF) in control and ischemic regions.

BACKGROUND

Although animal studies indicate an improvement of MBF to ischemic regions after ACE inhibition, this effect has not been conclusively demonstrated in patients with coronary artery disease.

METHODS

Myocardial blood flow was analyzed in ischemic and nonischemic regions of 10 symptomatic patients with coronary artery disease using repetitive [15O] water positron emission tomography at rest and during maximal dobutamine stress before and after ACE inhibition with quinaprilat 10 mg IV. To exclude the possibility that repetitive ischemia may cause an increase in MBF, eight patients underwent the same protocol without quinaprilat (placebo patients).

RESULTS

Rate pressure product in control and quinaprilat patients was comparable. In placebo patients, repetitive dobutamine stress did not change MBF to ischemic regions (1.41 ± 0.17 during the first stress vs. 1.39 ± 0.19 ml/min/g during the second stress, p = 0.93). In contrast, MBF in ischemic regions increased significantly after acute ACE inhibition with quinaprilat during repetitive dobutamine stress (1.10 ± 0.13 vs. 1.69 ± 0.17 ml/min/g, p < 0.015). Dobutamine coronary reserve in ischemic regions remained unchanged in placebo patients (1.07 ± 0.11 vs. 1.10 ± 0.16, p = 0.92), but increased significantly after quinaprilat (0.97 ± 0.10 vs. 1.44 ± 0.14, p < 0.002). Total coronary resistance decreased after ACE inhibition (123 ± 19 vs. 71 ± 10 mm Hg/ml/min, p < 0.02).

CONCLUSIONS

Angiotensin-converting enzyme inhibition by quinaprilat significantly improves MBF to ischemic regions in patients with coronary artery disease. (J Am Coll Cardiol 1999;34:1005–11) © 1999 by the American College of Cardiology

Angiotensin-converting enzyme (ACE) inhibition significantly improves myocardial blood flow (MBF) at rest (1), during hypoperfusion (2), after myocardial infarction (3) and during reperfusion (4) in experimental animals.

However, attempts to reproduce these findings in humans gave mixed results (5–7), possibly because coronary sinus flow was determined that represents a global estimate of MBF and cannot separate blood flow from ischemic and nonischemic regions. With the introduction of positron emission tomography (PET) with [13N] ammonia or [15O] water, the separate analysis of regional MBF in normal and ischemic regions of patients with coronary artery disease has become feasible (8,9).

The purpose of this study was to examine noninvasively regional changes in MBF during acute ischemia in patients before and after ACE inhibition. Based on experimental data (1–4), we hypothesized that ACE inhibition might acutely increase MBF to regions made ischemic by pharmacologic stress.

METHODS

Subjects. Twenty normotensive patients (4 female, mean age 59 years) with either a positive exercise stress electrocardiogram (ECG) (ST-segment depression >0.2 mV, n =
14) or a positive thallium scan (n = 6), a proximal high-grade stenosis of the left anterior descending or the left circumflex artery (>70% diameter reduction) and normal left ventricular function referred for coronary angioplasty between November 1994 and August 1997 were prospectively studied. All patients had long-acting nitrates and aspirin; three patients also had beta-blocking drugs as antianginal medication.

Patients with diabetes mellitus, unstable angina pectoris, pretreatment with an ACE inhibitor, hypotension (rest systolic blood pressure <100 mm Hg) or hypertension (rest blood pressure >160/90 mm Hg) were not included in the study. Furthermore, patients with stenosis of the right coronary artery were not included in the study, as MBF was analyzed in a midventricular transaxial slice (10), which does not display the inferior wall. The study was approved by the Hospital Human Rights Committee (Institutional Review Board), and written informed consent was obtained from every patient.

Two patients did not undergo the second rest/stress protocol on the day of the PET examination and were excluded from further study according to the protocol. The first patient showed persisting negative T-waves after the first dobutamine stress, which resolved spontaneously 20 min later. The second patient developed persistent hypotension (systolic blood pressure of 90 mm Hg 10 min after the end of the first dobutamine stress). The remaining 18 patients formed the study population (Table 1).

**Study protocol. DOBUTAMINE STRESS TEST.** After cessation of the antianginal medication for 48 h all patients underwent dobutamine stress ECG the day before the PET examination to identify the maximal, individually tolerated dobutamine dose.

Incremental doses of dobutamine (Dobutrex, Lilly Deutschland GmbH) were infused into a peripheral vein using a digital infusion pump (Secura FT, Braun AG). Every 5 min the dose was increased by 10 mg/kg body weight/min up to a total dose of 40 mg/kg/min or until the termination criteria were fulfilled. Heart rate and ECG were monitored continuously, and blood pressure was recorded every 2 min. Termination criteria for dobutamine stress were ST segment depression >0.2 mV, blood pressure increase >220/120 mm Hg, blood pressure drop during dobutamine stress, newly developed arrhythmias (premature ventricular beats), severe angina pectoris, reaching 90% of the age-predicted maximal heart rate or obtaining the maximal dobutamine dose (40 mg/kg/min). The identical, individually determined dobutamine stress protocol was used for stress testing of the same patient during the PET examination on the following day. This was necessary for having [15O] water prepared and delivered at maximum dobutamine stress.

**Positron emission tomography. DATA ACQUISITION.** Positron emission tomography imaging was performed using a whole-body scanner (Siemens CTI ECAT EXACT 921 [Hoffman Estates, Illinois] having an axial field of view of 16.2 cm. The transaxial resolution was 6 mm full width at half maximum (11). The study protocol (Fig. 1) started

![Figure 1. Schematic diagram of the study protocol.](image-url)
A common problem of scintigraphic techniques is the definition of the perfusion territory served by a segment of the coronary artery distal to the stenosis. To avoid the erroneous inclusion of normal regions in the ischemic group by predefining regions on an anatomic basis, a functional approach was implemented to identify ischemic regions in the perfusion territory of interest. First, six regions of interest, which were assigned to the left anterior descending and circumflex artery, were drawn in the anterior and in the lateral wall of a midventricular, transaxial FDG image. Second, a region of interest was defined as ischemic during dobutamine stress if the increase in MBF in the target region (e.g., anterior wall for the left anterior descending artery) was less than expected for the changes of the rate pressure product (RPP), which is a strong determinant of myocardial oxygen consumption and MBF (15). Hence, only regions of the perfusion territory of the stenosed coronary artery with a RPP corrected increase in MBF of less than one were defined as ischemic regions (n = 14 in the control group, n = 18 in the quinaprilat group). The remaining regions were defined as nonischemic regions.

To account for differences of the RPP (and hence MBF) in response to dobutamine stress and to compare the individual values under different conditions, all values of MBF were corrected for differences in RPP. This was done separately for rest and stress conditions by multiplying the

<table>
<thead>
<tr>
<th>Table 3. Hemodynamic Parameters During Dobutamine Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Placebo</strong></td>
</tr>
<tr>
<td><strong>Before Placebo</strong></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
</tr>
<tr>
<td>Rate pressure product [(mm Hg/min)×10²]</td>
</tr>
</tbody>
</table>

Mean (SEM; 95% confidence interval).

with a rest [¹⁵O] water scan: 15 to 20 mCi of [¹⁵O] water was injected over 30 s and 24 cross-sectional images were obtained for 300 s (6 for 5 s, 18 for 15 s). After completion of the first [¹⁵O] water PET scan, dobutamine stress was started and performed in the same way as determined on the previous day. The second [¹⁵O] water scan was started and performed in the same way as determined on the first scan (30 min) and an emission scan of six images for 6 for 5 s, 18 for 15 s). After completion of the second stress protocol, a second [¹⁵O] water scan was started during the maximal dose of dobutamine 2 min before the end of the stress test. If systolic blood pressure after completion of the second [¹⁵O] water scan was higher than 100 mm Hg, 10 mg of quinaprilat or 5 ml of physiologic saline solution was administered IV over 5 min. The patient remained in the scanner for another 30 min without changing position and the rest/stress protocol was repeated as described above.

After completion of the second stress protocol, a [¹⁸F]fluoro-deoxyglucose (FDG) scan was carried out: 10 mCi of FDG was injected and followed by a transmission scan (30 min) and an emission scan of six images for 5 min each. Thirty minutes before the start of the PET protocol all patients had received 50 g of oral glucose to enhance myocardial glucose uptake. Thus, the total time of the patient in the scanner was about 2 h. By means of a laser device the correct position of the patient in the scanner was checked at regular intervals.

**IMAGE ANALYSIS.** All sets of PET images were number-coded and randomly analyzed by a single observer unaware of treatment allocation. Images were corrected for attenuation, random events, deadtime losses and scattered radiation (12). The deadtime losses were less than 15% for all studies.

The data of the three midventricular transaxial slices showing the largest left ventricular cavity were summed. The summed slice was chosen for placement of the regions of interest. Six regions of interest (1 cm³) were drawn on the last image of the FDG scan encompassing the lateral and anterior wall. One region of interest (1.5 cm³) was placed in the region of the left atrium to obtain the input function. These seven regions were copied on all dynamic [¹⁵O] water scans of that patient. The MBF was calculated using a single compartment model including correction for partial volume effects. This procedure has been validated previously (10,12–14).

Mean (SEM; 95% confidence interval). *p < 0.01 vs. before quinaprilat. †p < 0.05 vs. before quinaprilat.

**Table 2. Hemodynamic Parameters During Rest**

<table>
<thead>
<tr>
<th></th>
<th>Placebo Before Placebo</th>
<th>Placebo After Placebo</th>
<th>Quinaprilat Before Quinaprilat</th>
<th>Quinaprilat After Quinaprilat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>65 (3; 58 to 72)</td>
<td>64 (3; 56 to 73)</td>
<td>70 (4; 61 to 78)</td>
<td>70 (4; 61 to 80)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>129 (7; 112 to 145)</td>
<td>126 (6; 112 to 140)</td>
<td>132 (4; 123 to 140)</td>
<td>119 (4; 110 to 128)*</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>79 (4; 69 to 88)</td>
<td>80 (3; 72 to 88)</td>
<td>82 (2; 78 to 86)</td>
<td>78 (2; 73 to 83)</td>
</tr>
<tr>
<td>Rate pressure product [(mm Hg/min)×10²]</td>
<td>84 (6; 68 to 99)</td>
<td>80 (5; 68 to 91)</td>
<td>92 (6; 69 to 99)</td>
<td>83 (49; 72 to 94)†</td>
</tr>
</tbody>
</table>

Mean (SEM; 95% confidence interval).
mean RPP in the patients as the group, divided by the RPP in the individual patient (14).

The ratio of MBF during dobutamine stress over rest MBF was defined as “dobutamine coronary reserve.”

Total coronary resistance (TCR) at rest was calculated by dividing the mean arterial pressure by the flow at rest, and TCR during maximal dobutamine stress was calculated by dividing the mean arterial pressure by the flow during maximal dobutamine stress (14).

The intraobserver variability of MBF analyzed in a random sample of six patients was 5.6%; the correlation between the first and the second reading was significant (r = 0.95, p < 0.001). The within-subject standard deviation as a parameter of measurement error was 0.3 ml/min·g for control patients. The correlation between the MBF values of the first rest/stress protocol and the second rest/stress protocol for control patients was significant (r = 0.78, p < 0.0001).

**STATISTICAL ANALYSIS.** All data are expressed as mean ± SEM (standard error of the mean [SEM]; 95% confidence interval of the mean). For paired or unpaired data, either the Wilcoxon signed rank-sum test or the Mann-Whitney U test was used to test for significant differences in means. For multiple comparisons the Holm procedure was used (16). A p value of less than 0.05 was considered significant.

**RESULTS**

Clinical and hemodynamic observations during dobutamine PET. Baseline characteristics of the patients can be found in Table 1. No major side effects of dobutamine or quinaprilat were noted: Four patients complained of flushing and five patients complained of severe heart pounding during dobutamine infusion, which did not cause termination of the study. The incidence of angina pectoris and significant ST-segment depression was low: Three patients in the control group and four patients in the quinaprilat group had anginal complaints during the first dobutamine stress. During the second stress protocol, two patients in the control and in the quinaprilat group had angina (NS). Dobutamine stress-induced ST-segment depression (>0.2 mV) was found in one patient of the control group and in one patient of the quinaprilat group. Newly developed ventricular arrhythmias were found in two of the control patients and one of the quinaprilat patients.

During dobutamine stress, heart rate and systolic blood pressure increased significantly and RPP almost doubled in the control and quinaprilat group (Tables 2 and 3; p < 0.001 for all comparisons of systolic blood pressure, heart rate and RPP between rest and the respective stress values). Before the initiation of the second stress protocol, blood pressure and heart rate had returned to baseline rest levels in the control group.

Quinaprilat IV significantly decreased systolic blood pressure and RPP during rest, whereas diastolic blood pressure and heart rate were unchanged (Table 2). During the second dobutamine stress, blood pressure, heart rate and RPP were similar to the stress values before ACE inhibition (Table 3). In addition, RPP during rest and stress were comparable in placebo and quinaprilat patients (Tables 2 and 3).

**MBF. EFFECT OF REPETITIVE DOBUTAMINE STRESS ON MBF IN THE CONTROL GROUP.** The MBF in nonischemic regions increased during dobutamine stress, from 1.13 to 3.19 ml/min·g (p < 0.0001; Table 4) and was significantly correlated to the RPP (r = 0.81, p < 0.001; Fig. 2). The MBF in ischemic regions remained almost unchanged (1.34 vs. 1.41 ml/min·g, NS; Table 5). Dobutamine coronary reserve was 3.12 in nonischemic regions and 1.07 in ischemic regions (p = 0.003 vs. before quinaprilat IV/rest).

### Table 4. Myocardial Blood Flow: Nonischemic Regions

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>After Placebo</th>
<th>Quinaprilat IV</th>
<th>After Quinaprilat IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>Placebo</td>
<td>Quinaprilat IV</td>
<td>Quinaprilat IV</td>
</tr>
<tr>
<td></td>
<td>Rest</td>
<td>Stress</td>
<td>IV</td>
<td>IV</td>
</tr>
<tr>
<td>Rest</td>
<td>1.13 (0.08; 0.96 to 1.29)</td>
<td>1.27 (0.10; 1.07 to 1.48)</td>
<td>0.93 (0.06; 0.80 to 1.05)</td>
<td>1.23 (0.07; 1.08 to 1.38)</td>
</tr>
<tr>
<td>Stress</td>
<td>3.19 (0.33; 2.51 to 3.86)†</td>
<td>2.65 (0.29; 2.06 to 3.25)‡</td>
<td>2.04 (0.19; 1.67 to 2.42)‡</td>
<td>2.84 (0.35; 2.12 to 3.56)§</td>
</tr>
</tbody>
</table>

Mean (SEM; 95% confidence interval). *p < 0.0001 vs. before placebo/rest. †p < 0.0001 vs. after placebo/rest. ‡p < 0.0001 vs. before quinaprilat IV/rest. §p < 0.0001 vs. after quinaprilat IV/rest.

Figure 2. Correlation between myocardial blood flow and RPP of control regions of all 18 patients during rest and stress.
(Table 4; p < 0.0001), whereas in the ischemic regions MBF decreased slightly (1.29 vs. 1.10 ml/min/g, NS; Table 5). After the administration of quinaprilat, rest MBF of control regions increased from 0.93 to 1.23 ml/min/g (p < 0.003; Table 4). After quinaprilat, dobutamine stress increased MBF in nonischemic regions from 1.23 to 2.84 ml/min (p < 0.001; Table 4).

In contrast to the results in the placebo group, dobutamine stress increased MBF in ischemic regions after quinaprilat significantly, from 1.27 to 1.69 ml/min/g (p < 0.015; Table 5; Fig. 3). The differences of stress MBF between the first and the second stress protocol was −0.02 ml/min/g (0.24; −0.5 to 0.5) in the control group and +0.59 ml/min/g (0.19; 0.17 to 1.0) in the quinaprilat group (p < 0.04).

Accordingly, dobutamine coronary reserve of nonischemic regions was 2.40 for the first stress protocol and 2.38 for the second stress protocol (NS; Table 6). For ischemic regions, dobutamine coronary reserve was 0.97 for the first stress protocol and 1.44 for the second stress protocol (p < 0.002; Table 6). The differences of dobutamine coronary reserve between first and second rest/stress protocol were −0.01 (0.21; −0.47 to 0.48) in the control group and 0.48 (0.14; 0.20 to 0.77) in the quinaprilat group (p < 0.05).

**DISCUSSION**

The main finding of this study was that ACE inhibition by quinaprilat IV significantly increased MBF (Table 5; Fig. 3) and decreased TCR of ischemic regions in normotensive patients with coronary artery disease (Fig. 5).

Only a few studies have examined the effects of ACE inhibition on MBF in patients with coronary artery disease using coronary sinus thermodilution technique. Kiokowski et al. (6) used bicycle exercise before and after ACE inhibition by cilazapril and could not detect any change in coronary blood flow in a small study population. Ikram et al. (5) showed a tendency toward improved coronary blood flow after captopril using atrial pacing as exercise technique before and after ACE inhibition with captopril.

In contrast to these studies, we used [15O] water PET to analyze regional changes of MBF in ischemic and nonischemic regions. Previous studies using [13N] ammonia or [15O] water PET and dobutamine stress showed a good correlation between the increase in RPP (a measure of oxygen demand) and MBF (8,9). In addition, it was shown that ischemic myocardial regions of patients with coronary artery disease were characterized by a blunted or even absent increase in MBF during dobutamine stress (9). These data are in excellent agreement with our own data: MBF and RPP were significantly correlated in control regions (Fig. 2) and ischemic regions were characterized by an almost absent

---

**Table 5. Myocardial Blood Flow: Ischemic Regions**

<table>
<thead>
<tr>
<th>(ml/min/g)</th>
<th>Placebo Before Placebo</th>
<th>Placebo After Placebo</th>
<th>Quinapril IV Before Quinapril IV</th>
<th>Quinapril IV After Quinapril IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>1.34 (0.11; 1.11 to 1.58)</td>
<td>1.40 (0.13; 1.11 to 1.67)</td>
<td>1.29 (0.16; 0.96 to 1.62)</td>
<td>1.27 (0.14; 0.98 to 1.56)</td>
</tr>
<tr>
<td>Stress</td>
<td>1.41 (0.17; 1.04 to 1.78)</td>
<td>1.39 (0.19; 0.97 to 1.82)</td>
<td>1.10 (0.13; 0.83 to 1.37)</td>
<td>1.69 (0.17; 1.33 to 2.05)†</td>
</tr>
</tbody>
</table>

Mean (SEM; 95% confidence interval). *p < 0.015 vs. after quinaprilat IV/rest. †p < 0.015 vs. before quinaprilat IV/stress.

---

**Table 6. Dobutamine Coronary Reserve**

<table>
<thead>
<tr>
<th></th>
<th>Placebo Before Placebo</th>
<th>Placebo After Placebo</th>
<th>Quinapril IV Before Quinapril IV</th>
<th>Quinapril IV After Quinapril IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonischemic regions</td>
<td>3.12 (0.32; 2.47 to 3.77)</td>
<td>2.42 (0.36; 1.70 to 3.15)</td>
<td>2.40 (0.20; 1.99 to 2.81)</td>
<td>2.38 (0.25; 1.87 to 2.89)§</td>
</tr>
<tr>
<td>Ischemic regions</td>
<td>1.07 (0.11; 0.8 to 1.32)†</td>
<td>1.10 (0.16; 0.76 to 1.45)*</td>
<td>0.97 (0.10; 0.78 to 1.17)‖</td>
<td>1.44 (0.14; 1.14 to 1.75)‡</td>
</tr>
</tbody>
</table>

Mean (SEM; 95% confidence interval). *p < 0.0001 vs. nonischemic regions/after placebo. †p < 0.003 vs. nonischemic regions/before placebo. §p < 0.002 vs. ischemic regions/before quinaprilat. †p < 0.02 vs. ischemic regions/after quinaprilat. ‖p < 0.001 vs. nonischemic regions/before quinaprilat.
increase in MBF, which probably reflects the high degree of stenosis in our patient population (Table 5).

**Ischemia-related coronary vasomotion.** Under physiologic conditions an increase in myocardial oxygen demand during exercise is closely matched by a linear increase in MBF (15). However, in the presence of a critical coronary artery stenosis the oxygen demand cannot be sufficiently met by an increase in MBF, and thus myocardial ischemia develops. Ischemia in turn can result in an increase in the local vasoconstrictor tone at the level of the stenosis as well as in the depending coronary arteries (17,18). The underlying mechanisms for the increase in coronary artery resistance during exercise-induced ischemia include an increase in circulating catecholamines, an insufficient production of endothelial relaxing factor, platelet aggregation and release of vasoconstricting agents or a passive collapse of the vessel (18). In addition, it has been recently shown that tissue ACE is increased in human coronary atherosclerotic plaques (19), which might contribute to a local increase in angiotensin II, resulting in an increase in coronary resistance during ischemia. In light of these pathophysiologic sequels during ischemia, the improvement of MBF in ischemic regions by ACE inhibition effected by IV quinaprilat may be the result of different mechanisms: ACE inhibition may counteract local vasoconstriction of the coronary artery by decreasing systemic and local angiotensin concentrations (20–24). In addition, MBF may be improved by attenuation of sympathetic nerve activation and a concomitant decrease in the activation of alpha adrenergic receptors (7,17,25–27) because it was shown that an intracoronary angiotensin II infusion leads to an increase in coronary vascular resistance during sympathetic stimulation (28). Finally, an increase in the local concentration of bradykinin and nitric oxide (NO) by ACE inhibition may result in coronary vasodilation and improvement of MBF (1,2,29–31).

Although our data indicate that the main effect of ACE inhibition is found in the ischemic regions (Table 5), we found also a slight increase in MBF during rest and dobutamine stress in nonischemic regions (Table 4). Thus, a direct vasodilating effect of the ACE inhibitor quinapril on coronary vessels may explain the increase of MBF to nonischemic and may contribute to some extent to the increase in MBF to ischemic myocardium. The concept of a direct vasodilating effect of quinaprilat is supported by two recently published studies analyzing blood flow in arterial forearm vessels of healthy volunteers (30,31). Quinaprilat acutely increased blood flow by 46% and 31%, respectively, and decreased resistance by 28% (31), changes that are probably mediated by bradykinin/NO-dependent mechanisms. However, no such effects on MBF have been shown previously in patients with coronary artery disease during dobutamine stress. It is likely that a combination of all the above-mentioned mechanisms will also be operative in human ischemic myocardium.

**Study limitations.** A limitation of our study is the lack of a double-blind design. However, we analyzed MBF in a control group and analyzed the data in a blinded fashion to avoid any systematic misinterpretation of the data. A second...
limitation is that we examined a highly selected study population with normal left ventricular function and normal blood pressure. The applicability of our results to a broader patient population is not known.

Conclusions. Our data indicate that quinaprilat IV improves MFB to ischemic regions in patients with stable coronary artery disease. These data may influence the choice of ACE inhibitors for treatment of hypertension or heart failure in an individual patient with concomitant coronary heart disease. However, before such an approach can be recommended the effect of oral quinaprilat on MFB and clinical outcome needs to be established in larger studies.

Reprint requests and correspondence: Dr. Christian Schneider, Klinik III für Innere Medizin, Joseph-Stelzmann-Strasse 9, D-50924 Cologne, Germany. E-mail: christian.schneider@medizin.uni-koeln.de.

REFERENCES