Optimizing Ischemia/Reperfusion in the Failing Rat Heart—Improved Myocardial Protection With Acute ACE Inhibition

Bruno K. Podesser, MD; Jan Schirnhofer, MD; Oliver Y. Bernecker, MD; Andreas Kröner, MD; Maximilian Franz, MD; Severin Semsroth, MD; Barbara Fellner, MD; Josef Neumüller, MD; Seth Hallström, PhD; Ernst Wolner, MD

Background—Whereas the number of patients with reduced left ventricular function after myocardial infarction who need revascularization is increasing, the operative outcome is still inadequate. Consequently, drugs that increase myocardial perfusion and decrease oxygen consumption of the remodeled myocardium are of particular interest to cardiac surgeons. Angiotensin-converting enzyme inhibitors (ACE-I) provide this pharmacologic profile. This study tests the hypothesis whether acute ACE inhibition during cardioplegic arrest improves outcome in failing rat hearts.

Methods and Results—Male Wistar rats (260 ± 15 g) underwent coronary ligation. Ten weeks later the rats had developed heart failure (HF). Hearts were harvested and studied on a red cell-perfused working heart: 60 minutes of ischemia, protected by cold blood cardioplegia (CP) every 20 minutes, and 45 minutes of reperfusion. Rats were randomly assigned to 2 groups, 1 group receiving the ACE-I quinaprilat with CP (QuinaMI, n = 11), and 1 group receiving CP only (MI, n = 8). Hemodynamic recovery, high-energy phosphates (HEP), and morphometry were analyzed. Groups showed similar degrees of myocardial infarction (44 ± 5 versus 39 ± 4% of LVmass), LVEDP (5.0 ± 1 versus 4 ± 1 mm Hg) and no differences in baseline values such as external heart work (EHW) and coronary flow (CF). At the end of reperfusion, EHW and CF were significantly higher in QuinaMI than MI (P < 0.05 and 0.01), LVEDP had returned to baseline in QuinaMI (P < 0.01). HEP were significantly higher preserved in QuinaMI than MI (P < 0.05).

Conclusions—Acute ACE inhibition during CP improves postischemic systolic and diastolic function, coronary perfusion as well as HEP-levels in a rat model of HF. These results may have clinical impact on patients with HF undergoing cardiac surgery. (Circulation. 2002;106[suppl I]:I-277-I-283.)

Key Words: heart failure ■ cardiopulmonary bypass ■ ACE inhibitors

According to the American Heart Association, the number of patients with chronic heart failure (CHF) is constantly increasing. In the United States, approximately 5 million people suffer from heart failure, the annual incident rate is 300 000 and mortality per year is 250 000.1 Similar numbers can be assumed for Europe. Generally, the reasons for the growing number of patients with CHF are an increase in the overall expected life span, and the cumulative improvement of conservative and interventional cardiology as well as heart surgery. To cardiac surgeons this means that the number of patients with reduced left ventricular (LV) function as a result of myocardial infarction or valvular heart disease is increasing. In end-stage CHF, cardiac transplantation is the method of choice, if age and comorbidity are no contradiction. However, whenever myocardial revascularization or valve replacement/reconstruction is feasible, patients with CHF will undergo the respective therapy. It is therefore necessary to minimize the damaging potential of intraoperative ischemia/reperfusion (I/R).

Although intraoperative myocardial protection has reached a high standard, cardiopulmonary solutions currently used specifically focus on the protection of the myocardium.2 It is now evident that endothelial dysfunction following I/R leads to nitric oxide (NO) deficiency with consecutive “no or low reflow”3,4 and promotes myocardial stunning.5,6 Consequently, drugs that increase myocardial perfusion and reduce myocardial oxygen consumption are of particular interest. This is especially important for the hypertrophied, viable myocardium of remodeled ischemic hearts.

ACE inhibitors (ACE-I) provide this pharmacologic profile: they (1) block the conversion of angiotensin I to angiotensin II, thereby lowering pre- and afterload, and reducing systolic and diastolic wall stress, and (2) increase bradykinin and consecutively NO, leading to relaxation of...
smooth muscle cells and vasodilatation.\textsuperscript{7,8} Besides the treatment of myocardial protection in the failing heart.

Methods

Infarct Model

Myocardial infarction was induced in male Wistar rats (250 to 300 g) by ligation of the left anterior descending artery with a 6-0 suture next to the left atrium. Animals were anesthetized (0.02 mL/100 g rompun and 0.1 mL/100 g ketamidor i.p.) and heparinized (200 IU intravenously). The beating heart was rapidly excised and placed on the "working heart" apparatus within 10 seconds to measure in vitro hemodynamics. The perfusion system has been described previously by the author.\textsuperscript{13} Briefly, an isolated, erythrocyte-perfused, working heart model (Hugo Sachs Elektronik, Freiburg, Germany) was used. The perfusate consisted of a Krebs-Henseleit buffer based suspension of purified bovine erythrocytes (hematocrit 30%). Oxygenation was performed with low gas (75% O\textsubscript{2}, 5% CO\textsubscript{2}) to provide a constant pO\textsubscript{2} of 100 to 10 mm Hg. Composition of the buffer was as follows (in mmol/L): NaCl 118; KCl 4.7; CaCl\textsubscript{2} 2.5; MgSO\textsubscript{4} 1.2; KH\textsubscript{2}PO\textsubscript{4} 1.2; NaEDTA 0.5; NaHCO\textsubscript{3} 25; glucose 11.1; insulin, 2.5 IU/L; bovine albumin, 2 g/L. Rats were randomly assigned to 2 groups. One group received 0.3 mg of quinaprilat (QuinaMI; 1 \mu g/mL perfusate) starting with the beginning of cardioplegic arrest, and 1 group received cardioplegia without adjunct and served as the control group (MI). In the final analysis only rats with infarcts greater than 30% of left ventricular wall were included, leading to 11 hearts in the QuinaMI group and 8 in the MI group with an average weight of 260±15 g at the time of myocardial infarction.

The perfusion was conducted according to a standardized protocol, which is depicted in Figure 1. The Langendorff mode (LD, before ischemia; rLD, during reperfusion), provided constant pressure coronary perfusion at 70 mm Hg. In the subsequent working heart mode (WH, before ischemia; rWH, during reperfusion), after left atrial loading (mean atrial pressure of 5 mm Hg), the left ventricle ejected against a predefined afterload giving rise to 70 mm Hg mean aortic pressure. Cardioplegic arrest was induced with cold blood CP according to Buckberg (Buckberg Kardioplegie, Köhler Chemie GmbH, Koblenz, Germany; 4:1 ratio of perfusate to Buckberg’s stock solution, 4°C at 50 mm Hg). CP continued with 2 cold reinfusions (4°C) every 20 minutes and ended with a "hot shot"(37°C) immediately before reperfusion (Figure 1).

Drugs

Quinaprilat (Go\textregistered9018 to 1, Gödecke AG, Freiburg, Germany) is a parenterally applicable carboxyl type ACE-I. It contains a carboxyl type zinc ligand, which binds the active site of the conversion enzyme and is free of sulfhydryl moieties. Even though the initial elimination half-life in plasma is short (2 hours), quinaprilat has a prolonged terminal half-life of 25 hours that corresponds to its pharmacological activity. This phenomenon is explained by its high affinity binding to tissue ACE with consecutive slow dissociation.\textsuperscript{14}

Hemodynamic Data Acquisition

Hemodynamic data were obtained from the following defined time-points: LD2, LD5, and LD15 denote the time-point measured in minutes from the beginning of the preischemic Langendorff perfusion, whereas WH 5 indicates the minutes elapsed after conversion to working heart mode. Analogous time-points in the reperfusion period were denoted rLD2, rLD5, rLD15, rWH 2, rWH 5, rWH 10, rWH 20, and rWH 30.

All hemodynamic parameters were registered as mean values, derived from respective pressure and flow tracings. The following parameters were evaluated: The coronary flow (CF, mL/min) was calculated by subtracting aortic flow (AF, mL/min, Flowmeter Narcomatic RT-500, Narco Biosystems) from left atrial flow (LAF, mL/min, Flowmeter Narcomatic RT-500, Narco Biosystems). Because the mean aortic pressure remained constant in all phases of perfusion (70 mm Hg, Statham P23XL, Spectramed Inc., USA), variations in CF primarily reflected alterations in coronary resistance.

Three related parameters were used to evaluate myocardial function: cardiac output (CO, mL/min), identical to the LAF (in a closed system), represented the primary reading. By multiplying cardiac output with systolic LV pressure the external heart work (EHW=Co×sysLVP) was derived as measurement of pressure-volume work performed per minute. To conform with traditionally used units the results were expressed in (g×m/min):

\[ \text{EHW (g×m/min)} = \text{CO (mL/min)} \times \frac{\text{sysLVP (mm Hg)}}{0.0136} \]

LV pressure was measured with a high fidelity microtip catheter (Millar SP-407, Millar) and used to determine LV end-diastolic pressure (LVEDP, mm Hg) as measurement of the preload. To adjust for minor deviations in baseline hemodynamics, readings from the reperfusion period were expressed as recovery (percentage of baseline). The mean recovery encompasses all time points of the working heart period during reperfusion.

To determine the influence of increasing preload on these failing hearts, before ischemia and at the end of the experiment series of pressure-flow curves were made in the working mode. Hearts were paced at 4 Hz and afterload was fixed at 70 mm Hg. Then pre-load (mean LAP) was increased from 0 to 20 mm Hg in 5 mm Hg increments and CO and LVEDP were monitored.

Biochemical and Infarct Size Evaluation

Two different protocols were used to measure biochemical and histologic changes in 1 heart. The first consisted of measurements to assess myocardial energy status. At the end of reperfusion, hearts were switched to LD again. A biopsy of the noninfarcted septum,
close to the apex, was taken from the beating heart with a precooled forceps, immediately frozen in liquid nitrogen, and stored for further processing. The second protocol was to determine histologic grad of CHF. After the biopsy was taken the heart was flushed with Krebs-Henseleit buffer to wash out the red cells, arrested with KCl, and fixed with 7% formalin for further histologic analysis. Total heart weight was assessed, before the atria, the right ventricle and the left ventricle were separated and weighed. For the infarct-size quantification the left ventricle was dissected into 5 slices from the apex parallel to the base of the heart.

Biochemical Evaluation
The biochemical analysis of high-energy phosphates (HEP) encompassed the determination of tissue concentrations of adenosine nucleotides (ie, ATP, ADP, and AMP) and of creatine phosphate (CdP). The frozen biopsies were weighted and 50 to 100 mg of each myocardial specimen was homogenized using a microdisemembranator (Braun, Melsung, Germany). HEP (in µmol/g wet weight) were analyzed by means of ion-pair high-performance liquid chromatography (HPLC). Additionally, the total energy-charge (EC) was calculated according to the formula:

\[ EC = \frac{([ATP] + 1/2[ADP])}{([ATP] + [ADP] + [AMP])} \]

Arterial and coronary venous blood gas analysis performed in each working heart period (at baseline and after 10 minutes in rWH) allowed calculation of myocardial oxygen consumption (MVO₂) according to Fick’s law (MVO₂ in mL/min/100g bw = [Sat(O₂) – C(O₂)] × 1.34 mL/g × CV/heart weight) × 100.

Histologic Evaluation
The formalin-fixed slices were embedded into paraffin and cut into semithin sections (1 μm). These specimens were dehydrated in a grading of series of alcohols and xylene before colored with Van Gieson stain by using iron-hematoxylin and picrin and fuchsin acid. The histologic sections of each heart with a Ziess Axioplan 2 imaging-analysis microcomputer (Zeiss, Jena, Germany) after being pictured with a Zeiss KS 400 program (Zeiss, Oberkochen, Germany), the picture became a pixelscan and the measurements were made. Infarct size was expressed as a percentage of the total LV volume.

Animal Care
This study was approved by the Animal Care Commission of the University of Vienna and by the Ministry of Science, Republic of Austria. Care of animals was in accordance with the "Guide for the Care and use of Laboratory Animals" (NIH publication 85-123, revised 1985).

Statistical Analysis
All data in the text, figures, and tables were expressed as means±SEM. ANOVA was performed on a SPSS 8.0 software package. Statistical significant results were specified post hoc using Fischer’s LSD test. For the comparison of pre- and postischemic values a paired, two-tailed Student t test was used. Statistical significance was achieved at a probability value of <0.05.

Results

Animal Characteristics
Table 1 presents animal characteristics. The ratios of right (RV) and LV weight to body weight are an index for myocardial hypertrophy, liver, and lung wet-to-dry ratios for CHF. As expected there were no significant differences in any of these parameters.

Table 2 presents histological findings. As expected, in both groups a high percentage of the LV mass is infarcted (44±5% versus 39±4%; QuinaMI versus MI, NS). Consequently the septum/radius ratio, indicating compensatory hypertrophy, is similarly increased. A representative example of a failing heart is shown in Figure 2.

Hemodynamic Data
Table 3 summarizes all hemodynamic baseline measurements. There were no significant differences between the 2 groups. Again, the increased baseline LVEDP in these hearts corresponds to CHF. The spontaneous HR showed only minor variability between groups. During reperfusion all hearts promptly resumed sinus rhythm with adequate HR (mean recovery QuinaMI: 102±7%; MI: 100±6%, NS). The postischemic myocardial function was markedly improved in the treatment group, showing substantially elevated AF (mean recovery, QuinaMI: 77±7%; MI: 55±9%, *P<0.05) and CO (mean recovery, QuinaMI: 80±6%; MI: 55±8%, *P<0.05; Figure 3A). These differences were paralleled by superior recovery of EHW (mean recovery, QuinaMI: 77±6%; MI: 53±10%, *P<0.05), thereby confirming the

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<th>TABLE 1. Animal Characteristics</th>
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<td>QuinaMI (n=11)</td>
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<td>MI (n=8)</td>
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<td>P-value</td>
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The total LV volume and infarct volume of each slice was determined by using the Zeiss KS 400 program (Zeiss, Oberkochen, Germany), the picture became a pixelscan and the measurements were made. Infarct size was expressed as a percentage of the total LV volume.
marked improvement in myocardial function. LVEDP, representing diastolic function of the heart, constantly increased in the MI-group, whereas it remained stable in the treatment group during reperfusion and became significantly different at the end of the experiment (mean recovery, QuinaMI: 99±10%; MI: 149±15%, *P<0.05; Fig. 3B).

The measurements of CF showed posts ischemic flow reserve in both groups. However after 15 minutes of reperfusion, CF constantly declined in the control group, whereas it remained stable in the QuinaMI group. By the end of the experiment, this difference became significant (QuinaMI: 83±14%; MI: 43±5%, *P<0.05; Fig. 3C).

The evaluation of preload-dependent CO or LVEDP is depicted in Figure 4A and 4B. For any given left atrial pressure, there was no difference of preischemic CO between groups. After 60 minutes of ischemia and 45 minutes of reperfusion, both groups showed reduced measurements of CO compared with preischemic measurements. However, this reduction was significant only in control hearts (‡‡‡P<0.001 at 20 mm Hg; Figure 4A). If LVEDP was plotted against left atrial pressure, there was no difference of preischemic LVEDP between groups. After 60 minutes of ischemia and 45 minutes of reperfusion, both groups showed an increase in LVEDP. This increase was significant only in control hearts (‡‡P<0.01 at 20 mm Hg; Figure 4B).

### Biochemical Data

There were no significant differences in preischemic MVO2 (in mL/min/100g QuinaMI: 2.96±0.5; MI: 2.87±0.9; NS). During reperfusion, mean MVO2 decreased in both groups.

### TABLE 3. Baseline Hemodynamics

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<th>HR (bpm)</th>
<th>CF (mL/min)</th>
<th>AF (mL/min)</th>
<th>CO (mL/min)</th>
<th>EHW (gm/min)</th>
<th>LVEDP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QuinaMI (n=11)</td>
<td>212±11</td>
<td>3±0.2</td>
<td>30±2</td>
<td>34±1</td>
<td>2668±163</td>
<td>5±1</td>
</tr>
<tr>
<td>MI (n=8)</td>
<td>209±12</td>
<td>3±0.4</td>
<td>36±3</td>
<td>39±5</td>
<td>2792±381</td>
<td>4±1</td>
</tr>
</tbody>
</table>

P-value ns ns ns ns ns ns

HR indicates heart rate; CF, coronary flow; AF, aortic flow; CO, cardiac output; EHW, external heart work; LVEDP, left ventricular end-diastolic pressure; P-value, all not significant (ns).
The lack of platelets, leukocytes, and inflammatory cytokines systemically constitutes the primary limiting factor. Organ preparations, the artificial isolation from intervening systemic variables lends itself for studies of the heart from systemic variables lends itself for studies. Consequently, ADP and AMP tended to be lower in QuinaMI than in MI and reached statistical significance (QuinaMI: 19%*; MI: 7%; *P<0.05).

Mean levels (µmol/g wet weight) of ATP (QuinaMI: 1.63±0.08**; MI: 0.99±0.1; **P<0.01), CreP (QuinaMI: 1.21±0.43; MI: 0.38±0.05; *P<0.05) and the energy charge (QuinaMI: 0.81±0.03; MI: 0.67±0.02; **P<0.01) clearly stated the superior preservation of quinaprilat-treated hearts. Consequently, ADP and AMP tended to be lower in QuinaMI: ADP (QuinaMI: 0.62±0.19; MI: 0.81±0.04; NS) and AMP (QuinaMI: 0.18±0.05; MI: 0.27±0.02; NS).

**Discussion**

Experimental study always raises a question about the validity of clinical conclusions extrapolated from the results. In organ preparations, the artificial isolation from intervening systemic influences constitutes the primary limiting factor. The lack of platelets, leukocytes, and inflammatory cytokines has to be taken into account. However, cardioplegic arrest as a paradigm for global I/R injury with comparable separation of the heart from systemic variables lends itself for studies using the isolated heart. The addition of red blood cells to the more commonly used crystalloid perfusion fluid affords oxygen carrying capacity and CF autoregulation within the physiologic range, as described recently. Additionally, red cells provide crucial biochemical functions, such as buffering of oxygen radicals and metabolism of NO. The chronic infarct model in the rat is a common model of ischemic heart failure. In an earlier report, Pfeffer et al showed that only infarcts greater than 30% LV mass showed reduced peak flow indices and developed congestive heart failure. Therefore only rats with infarcts greater than 30% were included in this study. The “hot shot” is part of the widely used clinical concept of integral myocardial protection in hearts with reduced LV function. Therefore, we used this concept also in the present experiments to parallel the clinical setting.

The major finding of the present study is that acute inhibition of intracardiac ACE/kininase II by quinaprilat, using cardioplegia as vehicle of application, improves hemodynamic function, stabilizes CF, preserves cardiac HEP and reduces myocardial oxygen consumption in failing rat hearts. In a recent study of our laboratory in noninfarcted, adult rabbit hearts quinaprilat was started either during ischemia or with the beginning of reperfusion. Mechanical function was significantly improved in both groups compared with control. However, CF was only significantly elevated when quinaprilat was administered during ischemia with CP. In an additional group, L-arginine was administered with CP. Again there was a marked improvement of mechanical function but no improvement of CF. In addition to the hemodynamic findings, a significant preservation of HEP and mitochondrial integrity was observed. From these experimental findings, the present study design was adapted, mainly focusing on hemodynamic and biochemical changes after application of quinaprilat in failing hearts during ischemia only.

Quinaprilat does not convey direct positive inotropic effects. Therefore, in the present study, the superior mechanical function seems to result from heightened prevention of myocardial I/R damage. In the literature, 2 groups obtained comparable results using isolated buffer-perfused LD model and subjected hearts to warm cardioplegic arrest. Menasché et al tested the effects of pretreatment with either captopril or enalapril. Gurevitch et al administered captopril either during CP or reperfusion. Both groups observed improvement in CF and myocardial recovery. However, it is important to stress that in both experiments warm or tepid CP was used. Therefore, the results cannot be directly compared with our experiments with cold CP. Beyond this, the differences in perfusion media (crystalloid perfusion) and experimental setup (Langendorff model) must be taken into account. Lazar et al used a porcine model with regional ischemia followed by acute surgical revascularization, and showed beneficial effects of systemic enalaprilat administered before the cardioplegic arrest. Similar results were found in neonatal cardiac rat myocytes exposed to hypoxia and reperfusion. The ACE-I cilazaprilat and bradykinin significantly inhibited the release of creatine kinase and preserved myocyte ATP content. This observation was blocked by HOE 140 and L-NMMA, therefore a NO-induced effect was considered to be responsible for the cardioprotective effect.
In our experiments, the improvement of diastolic function is of particular interest. Menasché et al described a similar improvement in rats undergoing I/R, pretreated with captopril. However, no underlying concept was presented. Pinsky and Malinski could show in a beat-to-beat measurement that NO is important to the relaxation of the normal heart. It is known that postinfarct remodeling and CHF increase diastolic dysfunction, indicated by reduced diastolic relaxation. The measurements of LVEDP and the preload dependent changes of LVEDP show a significant improvement of diastolic function in failing hearts treated with quin. The mechanism behind might be the known NO release, leading to improved diastolic and consequently systolic function. A direct biochemical characterization of the underlying mediator was not obtained in the current study; however, this has been well established in the literature. Linz and colleagues elucidated the mediation by bradykinin and NO while using their respective inhibitors. Likewise Kitakaze et al demonstrated an equal blunting of ACE inhibitor-induced effects with either HOE 140 or L-NAME. Zahler et al elegantly described the antioxidant capacity in isolated, Krebs-Henseleit perfused guinea pig hearts after 15 minutes of warm, global ischemia followed by 30 minutes of repertusion: ACE inhibition resulted in decreased LDH release and increased NO release. By measuring NO production and consumption, the authors stated that during early repertusion NO is consumed to detoxify oxygen radicals. In the recent study from our laboratory, we looked at concentration of nitrate/nitrite to describe NO metabolism. However, our analysis showed that baseline concentrations of nitrate/nitrite in the perfusate were too high to assess small differences in NO production of the coronary endothelium through nitrate/nitrite determination in the perfusate. This situation is similar to in vivo conditions. Only dramatic increases in NO production (eg, in septic shock) are reflected by higher concentrations of nitrate/nitrite in plasma. Therefore, we did not measure this marker in the present study.

The myocardial metabolism has to be discussed with respect to the underlying differences in posts ischemic myocardial work. In light of the markedly increased posts ischemic cardiac work in the QuinaMI group, the significant reduction in MVO₂ is of special importance and in accordance with findings from Loke et al in failing human hearts, in which the ACE-I ramiprilat and bradykinin decreased MVO₂. Analysis of high-energy phosphates at the end of our experimental protocol provides posts ischemic steady state levels, as determined by both synthesis and expenditure. Superior preservation of mitochondrial oxidative phosphorylation and prevention of the inadequate expenditure of high-energetic compounds precipitated by I/R damage may account for these results. Additionally, a direct drug effect such as the assumed inhibition of enzymes in the respiratory chain by NO might also be involved. Cargnoni and coworkers demonstrated higher recovery of ATP and CreP after global ischemia and repertusion in isolated rabbit hearts pretreated with quinaprilat.

In control hearts, post ischemic CF constantly declined whereas it remained at 80% of preischemic values in quinaprilat-treated hearts. This difference became significant at the end of the experiment. In accordance with literature, these findings may be explained by improved vascular auto-regulation by means of preserved endothelial function or by a direct vasodilatory effect. Because the drug is applied during ischemia, a protective effect on vasomotor function can be assumed. This hypothesis is supported in 2 experiments using porcine models, 1 in which ACE inhibitors were administered during short-term ischemia and a second in which L-arginine was added to blood cardioplegia. Both experiments demonstrated a postischemic reduction of endothelium-dependent vasodilation, which was reversed by the respective treatment modalities. Improved vascular protection is of particular interest because standard potassium CP is designed primarily for myocardial preservation, and the relatively unprotected vascular structures, especially endothelial cells, appear to be highly susceptible to ischemic damage. It was observed that endothelial injury is an early event during cardioplegic arrest and functional disturbance (diminished release of NO) was observable immediately at the beginning of repertusion; this emphasizes the significance of early drug administration to prevent endothelial stunning. Furthermore, vasomotor dysfunction has been described as an untoward effect of depolarizing cardioplegic solutions. Alternatively, it might be reasoned that ACE inhibition has a direct vasodilatory effect requiring a latency period. The need for early ACE inhibition could be explained by ongoing angiotensin II-mediated vasoconstriction after initiation of ACE inhibition, secondary to a prolonged elimination half-life of angiotensin II in interstitial tissue.

Finally, results of acute oral ACE inhibition 24 hours before aortic valve surgery need to be mentioned: the authors reported reduced postoperative ejection fraction in the ACE-I-treated patients whereas results from electron microscopy and creatine phosphokinase favored ACE-I. Reviewing the results carefully show that ejection fraction is reduced only during early repertusion in ACE-I-treated patients. However, the problem with this measurement is that it was performed “a few days after operation”, which is a very inaccurate timing for the crucial finding of the entire study. Therefore, the conclusion from another study in patients with good left ventricular function undergoing coronary bypass surgery is more likely: omitting ACE-I before surgery does not have sufficient enough of an advantage to be recommended. In conclusion, acute ACE inhibition during cardioplegic arrest significantly improves posts ischemic systolic and diastolic function in a rat model of HF. These results can not be explained by improved coronary perfusion alone, but point toward a prevention of endothelial damage due to the scavenging capacity of NO. This antioxidant capacity of NO along with the known NO-dependent reduction of MVO₂ could explain the significantly higher preservation of HEP in the QuinaMI group. The results of this study may have clinical impact in the increasing number of patients with CHF undergoing cardiac surgery. Acute, adjuvant, intraoperative ACE inhibition is a reasonable concept of myocardial protection for these high-risk patients. Improved metabolic preservation leading to improved hemodynamic performance could optimize operative outcome.
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References

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