Use of Aortic Counterpulsation to Improve Sustained Coronary Artery Patency During Acute Myocardial Infarction

Results of a Randomized Trial

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Aortic counterpulsation has been observed to reduce the rate of reocclusion of the infarct-related artery after patency has been restored during acute myocardial infarction in observational studies. To evaluate the benefit-to-risk ratio of aortic counterpulsation during the early phase of myocardial infarction, a multicenter randomized clinical trial was performed.

Methods and Results Patients who had patency restored during acute cardiac catheterization within the first 24 hours of onset of myocardial infarction were randomly assigned to aortic counterpulsation for 48 hours versus standard care. Intravenous heparin was used similarly in both groups and was continued for a median (25th, 75th percentile) of 5 (2.7) days. A total of 182 patients were enrolled; 96 were assigned to aortic counterpulsation and 86 to standard care. Repeat cardiac catheterization was performed at a median of 5 (4.6) days after randomization in 89% of patients assigned to aortic counterpulsation and in 90% of control patients. Patients randomized to aortic counterpulsation had similar rates of severe bleeding complications (2% versus 1%), number of units of blood transfused (mean, 1.3±2.6 versus 0.9±1.8 units), and vascular repair or thrombectomy (5% versus 2%) compared with patients treated in a conventional manner. Patients randomized to aortic counterpulsation had significantly less reocclusion of the infarct-related artery during follow-up compared with control patients (8% versus 21%, P<.03). In addition, there was a significantly lower event rate in patients assigned to aortic counterpulsation in terms of a composite clinical end point (death, stroke, reinfarction, need for emergency revascularization with angioplasty or bypass surgery, or recurrent ischemia): 13% versus 24%, P<.04.

Conclusions This randomized trial showed that careful use of prophylactic aortic counterpulsation can prevent reocclusion of the infarct-related artery and improve overall clinical outcome in patients undergoing acute cardiac catheterization during myocardial infarction. (Circulation. 1994;90:792-799.)

Key Words • aorta • myocardial infarction • aortic counterpulsation • angioplasty
Methods

Patients in whom patency of the infarct-related artery was established during emergency cardiac catheterization during the first 24 hours after acute myocardial infarction at 11 hospitals between October 1989 and October 1992 were considered for entry into the study. The protocol was approved by the Institutional Review Board in each hospital, and all patients gave informed consent before enrollment. The clinical sites, investigators, and study coordinators are listed in the "Appendix." The study was conducted and managed by the Duke University Coordinating Center independently of the sponsor of the trial. The relationship between the Coordinating Center, primary investigators, and sponsor was in accordance with guidelines previously published.12

Inclusion and Exclusion Criteria

Consecutive patients of any age were considered eligible for the study if they had emergency cardiac catheterization within 24 hours after the onset of an acute myocardial infarction. Those who had emergency cardiac catheterization between 6 and 24 hours after onset of symptoms were required to have evidence of ongoing symptomatic ischemia as evidenced by persistent chest pain or persistent ST elevation (>2 mm) on the ECG. Patency had to be successfully restored (from TIMI grade flow 0 to 1 or 2 or 3)13 in the infarct-related artery by primary or rescue angioplasty or intracoronary thrombolytic administration. Patients with significant obstruction (>75% stenosis) in all three major epicardial arteries and successful reperfusion (TIMI grade flow 2 or 3) in the infarct-related artery were also eligible.

Patients were excluded if they had cardiogenic shock, hypotension (systolic blood pressure <90 mm Hg) unresponsive to intravenous fluids or pressor therapy, or pulmonary edema requiring aortic counterpulsation. Patients with severe peripheral vascular disease (defined as diminished femoral pulses and absent pedal pulses) or tortuous or aneurysmal descending or abdominal aorta were not eligible for inclusion. Patients with significant obstruction (>75% stenosis) in one or two major epicardial arteries and successful reperfusion (TIMI grade flow 2 or 3) in the infarct-related artery by intravenous thrombolytic therapy were excluded. Contraindication to intravenous heparin was another criterion for exclusion.

Cardiac Catheterization and Coronary Angioplasty

Cardiac catheterization was performed by the femoral route in all patients. Arteriography of the infarct-related artery was performed with several injections in various orthogonal and hemispatial views. The flow pattern of the infarct-related vessel was graded according to TIMI trial classification.13 Injections were also made of the noninfarct vessels. Contrast ventriculography was performed in the right anterior oblique projection.

Primary or rescue coronary angioplasty was performed in a conventional manner using fixed or over-the-wire balloon systems. Primary angioplasty without prior systemic thrombolytic therapy was used in 106 patients to restore patency. Rescue angioplasty was performed in 51 patients. In the remaining 25 patients, patency was restored by a variety of methods, including intracoronary thrombolytic therapy or repeated dye injections. Intracoronary thrombolytic therapy was administered at the discretion of the angioplasty operator during the procedure. Overall intracoronary urokinase (up to 500 000 units) was administered in 66 patients, and intracoronary tissue-type plasminogen activator (TPA) was given to 16 patients (up to 30 mg).

Study Protocol and Procedures

Patients were randomized to aortic counterpulsation or standard therapy at the end of the emergency cardiac catheterization and/or angioplasty procedure. All patients received standard heparin therapy, including 5000 units of intravenous heparin administered during the catheterization procedure and 10 000 units during angioplasty. Thereafter, all patients received heparin (1000 to 2000 U/h for a minimum of 48 hours), and coagulation monitoring was used to maintain the therapeutic range, defined during cardiac catheterization as an activated clotting time >300 seconds or during follow-up as an activated partial thromboplastin time >50 seconds.

Aortic Counterpulsation Technique

Patients assigned to intra-aortic balloon pumping (IABP) usually had the pump inserted percutaneously via the same femoral artery in which the cardiac catheterization was performed10; in 14 patients (15%), the angioplasty operator used the contralateral femoral artery for balloon pump insertion based on anatomic considerations. Aortic counterpulsation was continued for 48 hours at a rate of 1:1, and the patient was gradually weaned from the pump over the last 12 hours before removal. Aortic counterpulsation was stopped earlier in case of complications such as limb ischemia or hemorrhage at the access site.

Patients assigned to standard care could cross over to aortic counterpulsation in the event of persistent hypotension, pulmonary edema, cardiogenic shock, reocclusion, reinfarction, or emergency coronary artery bypass surgery.

Medical Therapy

Standard coronary care management was provided. All patients received daily aspirin. Intravenous nitroglycerin, ß-blockers, angiotensin-converting enzyme inhibitors, and lidocaine were used at the discretion of the attending physician.

Repeat Catheterization and Revascularization

Emergency repeat cardiac catheterization was performed for the following reasons: recurrent ischemia defined as angiographic chest pain of at least 20 minutes' duration with new ECG changes or hypotension; pulmonary edema; or cardiac failure leading to hypotension. Patients with reocclusion of the infarct-related artery had patency restored by angioplasty or, if angioplasty failed, they were transferred immediately for bypass surgery. Patients with recurrent ischemia also underwent coronary artery bypass graft surgery at the discretion of the attending cardiologist. Repeat angioplasty of the infarct-related artery was performed only if there was significant (>50%) residual stenosis. In patients without recurrent ischemia, repeat cardiac catheterization was performed according to protocol 5 to 10 days after randomization. Patients with severe multivessel disease or coronary anatomy unsuitable for angioplasty underwent bypass surgery before discharge.

Core Angiographic Laboratory

All cineangiograms underwent blinded review by one observer at the Core Angiographic Laboratory who assessed perfusion status, quantitative stenosis, and ventricular function and visually graded coronary luminal diameter narrowing by an ordinal scale (0, <25%, 25%, 50%, 75%, 95%, 100%) as previously described.14 Images for left ventriculograms were displayed, and silhouettes of end-diastolic and end-systolic frames were drawn with a light-pen system. Cardiac silhouettes were digitized and stored, and images were processed with a digital radiographic computer system. Global ventricular function was determined by the area-length method and expressed as the ejection fraction. There were 137 ventriculograms done during the enrollment cardiac catheterization and 130 ventriculograms during follow-up. Technically inadequate studies due to lack of opacification or multiple premature ventricular beats were excluded from the analysis during the acute cardiac catheterization in 9 patients and during follow-up angiography in 13 patients.
Quantitative Coronary Angiography

All cineangiograms were submitted for analysis by an automated edge-detection digital angiographic system using the Duke University Quantitative/Qualitative Evaluation System (DUQUES).13 Percent diameter stenosis before the procedure, at the end of the procedure, and during follow-up were calculated. It was possible to obtain good-quality digital images in 97% (176/182) of studies before the procedure, 71% (129/182) after the procedure, and 82% (133/162) during follow-up (including emergency studies). The reasons for lack of quantitative coronary angiography in 88 instances were poor vessel separation (14%), guide wire left in place (26%), and poor images (60%).

Definitions of Baseline Characteristics

The following definitions were used. Hypertension was defined as a systolic blood pressure of ≥200 mm Hg and/or a diastolic blood pressure >110 mm Hg. Diabetes was considered present in patients who were told that they were suffering from either type I, insulin-dependent diabetes mellitus, or type II, non-insulin-dependent diabetes mellitus. History of smoking was defined as current or past cigarette smokers. Prior myocardial infarction was defined as a history of hospitalization for treatment of myocardial infarction. Congestive heart failure was defined as a condition characterized by weakness, breathlessness, abdominal discomfort, or edema of the lower extremities resulting from inadequate cardiac output or elevated cardiac filling pressures. It may be characterized by sinus tachycardia, S4 gallop, dyspnea, pulmonary edema, or by a Killip class of 3 or 4. Peripheral vascular disease was defined as any history of claudication, angiographically documented arterial disease, or peripheral vascular (arterial) surgery. Stroke was defined as a loss of neurological function caused by an ischemic event that results in a persistent deficit.

Statistical Analysis

Randomization took place at the end of the initial emergency cardiac catheterization before the patient was transferred to the coronary care unit. The randomization was stratified by clinical site, and permuted block randomization was used within each site to maintain chronological balance in the number of patients allocated to each treatment arm.

The trial was designed to provide adequate statistical power to detect a reduction in the reocclusion rate of the infarct-related artery from 20% to 5%. It was estimated that 180 patients (90 in each arm) were needed to achieve 80% power (based on α = 0.05).

Continuous variables are summarized using the median and 25th and 75th percentiles. The Wilcoxon rank-sum test was used to examine differences between treatment groups. Discrete variables are presented as percentages and analyzed with either the likelihood ratio χ² statistic or Fisher’s exact test if event rates were warranted. All primary treatment comparisons were performed according to the “intention-to-treat” principle.

The primary end point was angiographically detected reocclusion of the infarct-related artery during the hospitalization. Reocclusion was defined as a TIMI grade 0 to 1 flow in a previously patent infarct-related artery. Only the patients (n = 162) who had had repeat angiography were included in the analysis. The reasons for lack of angiographic follow-up in 20 patients was death in 2, coronary artery bypass graft surgery before follow-up angiography in 5, patient refusal in 7, and medical contraindication in 6. Analysis of the primary end point was performed unadjusted and by methods that adjusted for the small differences in infarct-related artery location between the treatment groups. The findings were similar with either method, and unadjusted comparisons are reported.

The secondary clinical end points of adverse cardiac events were death, reinfarction (defined as recurrent chest pain of >20 minutes’ duration with associated ECG changes and reelevation of creatinine kinase MB above the normal range), pulmonary edema (defined as new onset of pulmonary edema diagnosed by presence of rales or by chest radiograph), congestive heart failure (defined as Killip class ≥2), and recurrent ischemia (defined as chest pain <20 minutes in duration responsive to nitroglycerin and associated with ST changes on the ECG). The composite clinical end points of death, stroke, reinfarction, need for emergency revascularization with angioplasty or bypass surgery, or recurrent ischemia was examined with binary logistic regression techniques to assess treatment differences.

Other prespecified secondary comparisons of treatment strategy examined the in-hospital restenosis rate (defined as the occurrence of >50% visual diameter stenosis at follow-up cardiac catheterization in patients with a visual residual stenosis <50% at the end of the initial procedure). General linear modeling techniques were used to analyze differences in residual percent diameter stenosis at follow-up angiography adjusted for end of procedure percent stenosis, global left ventricular function at follow-up cardiac catheterization adjusted for preprocedure left ventricular function, and the change in global left ventricular function between the procedure and follow-up cardiac catheterization. All analyses were performed with the SAS statistical software.

A Data and Safety Monitoring Committee met twice during the study. The first meeting was held after 60 patients had been enrolled; only safety measures (death and vascular and hemorrhagic complications) were examined at this meeting. The committee also met after 120 patients had been enrolled to examine both efficacy and safety measures. No changes were recommended in the protocol. Statistical significance was taken at P < 0.046 on the basis of adjustments made for the two interim analyses. Only two-sided P values are reported.

Results

A total of 182 patients were enrolled in the study. Ninety-six patients were assigned to aortic counterpulsation (IABP) and 86 were assigned to standard care (control). The baseline clinical and angiographic characteristics in the two groups were in general similar (Table 1), except that the infarct-related artery was more frequently the left anterior descending coronary artery in patients randomized to aortic counterpulsation (49% versus 35%). Conversely, more patients in the control arm (54% versus 34%) had the right coronary artery as the infarct-related artery.

The median (25th, 75th percentile) duration of symptoms before emergency cardiac catheterization was similar in both groups [IABP, 7 (4,11) hours; control, 7 (4,14) hours], as was the use of intravenous thrombolytic therapy before emergency cardiac catheterization (IABP, 35%; control, 42%).

The angiographic and procedural information during the emergency cardiac catheterization is shown in Table 2. Angioplasty was used to restore patency in 90% of patients later randomized to aortic counterpulsation and in 83% of patients later assigned to standard care. Intracoronary thrombolytic therapy was used in 42% of patients randomized to aortic counterpulsation and in 46% of patients assigned to the control arm.

The IABP was inserted in all patients randomized to aortic counterpulsation. A 10.5-F sheath was used with the balloon pump catheter in 97%. The median duration of counterpulsation was 48 (43,51) hours. In 10% (9/96), the IABP was terminated within 24 hours. The reasons for early termination were hemorrhagic compli-
1. IABP graft

Diabetes
History of smoking
Prior myocardial infarction
Prior coronary artery bypass

The Hypertension

Dynamics

logistic

complications

had

an

because

two

of
diseased

stent

in the

infarct-related artery

greater

the

residual

stent

in the

infarct-related artery

Therefore,

the

infarct-related artery

in each

patient

that careful

use of aortic counterpulsation can be one method to increase the sustained patency rate and to improve clinical outcome in patients undergoing emergency percutaneous interventions in acute myocardial infarction.

The ability of aortic counterpulsation to reduce reoclusion of the infarct-related artery is consistent with previous observational studies in acute myocardial infarction.

concluded that careful use of aortic counterpulsation can be one method to increase the sustained patency rate in patients undergoing emergency percutaneous interventions in acute myocardial infarction. Additional limitations of this study include the relatively small sample size, which limits the generalizability of the findings. However, the study provides important insights into the potential benefits of prophylactic aortic counterpulsation in patients with acute myocardial infarction, and the findings are consistent with previous observational studies in this area.

Intravenous heparin was used for a similar duration after emergency cardiac catheterization in both randomized groups [IABP, 5 (2,6) days; control, 5 (3,7) days]. Follow-up cardiac catheterization was performed at a median of 5 (4,6) days after randomization in 89% (85/96) of patients randomized to aortic counterpulsation and in 90% (77/86) of patients in the control group. The follow-up cardiac catheterization was performed as an emergency procedure in 10% of patients assigned to aortic counterpulsation and in 15% of patients in the control group.

The findings at the follow-up cardiac catheterization are shown in Table 3. Patients randomized to aortic counterpulsation had a significantly higher sustained patency rate (TIMI grade flow 2 to 3) of the infarct-related artery (P < .03). The residual percent diameter stenosis in the infarct-related artery was similar in both groups at follow-up (P = .19). The in-hospital restenosis rate was similar in patients randomized to aortic counterpulsation (21%) and to standard therapy (33%, P = .12). Left ventricular ejection fraction at follow-up and the change in ejection fraction in patients with paired ventriculograms were also similar (P = .46 and P = .46, respectively).

The hemorrhagic and vascular complications in both groups are shown in Table 4. The rate of major hemorrhagic complications was similar in both groups, with similar rates of transfusions and number of units transfused. However, according to a generalized bleeding formula (Landefeld index) based on change in hematocrit and the number of units transfused, there was a trend (P = .053) toward more hemorrhage in patients assigned to aortic counterpulsation. Vascular access hemorrhage accounted for 77% of all hemorrhagic complications (IABP, 88%; control, 62%). No patient in the study had an aortic dissection or retroperitoneal hemorrhage or required amputation of part of a limb. There were few vascular complications overall, with statistically insignificant differences between both groups.

The clinical outcomes in the study are shown in Table 5. There was a significant reduction in the composite adverse clinical events (death, stroke, reinfarction, need for emergency revascularization with angioplasty or bypass surgery, or recurrent ischemia) in patients randomized to aortic counterpulsation (13%) compared with patients in the control group (24%, P < .04). Patients randomized to prophylactic aortic counterpulsation had significantly reduced rates of reocclusion (P < .03), recurrent ischemia (P = .001), and need for emergency angioplasty (P < .02) during follow-up. The duration of hospitalization was similar in both groups [IABP, 9 (7,11) days; control, 9 (7,12) days].

Discussion

This randomized trial is the first to document that prophylactic aortic counterpulsation can increase sustained coronary artery patency when used for 48 hours after patency has been established during emergency cardiac catheterization for acute myocardial infarction. Aortic counterpulsation also significantly reduced ischemic events after cardiac catheterization, including the need for repeat emergency angioplasty. Additionally, the benefits of aortic counterpulsation in this setting were not offset by higher rates of vascular or hemorrhagic complications. These findings suggest that careful use of aortic counterpulsation can be one method to increase the sustained patency rate and to improve clinical outcome in patients undergoing emergency percutaneous interventions in acute myocardial infarction.

The ability of aortic counterpulsation to reduce reoclusion of the infarct-related artery is consistent with previous observational studies in acute myocardial infarction.

No. of diseased vessels†

1
2
3

Infarct-related artery

Left anterior descending
Left circumflex

Right coronary artery

Saphenous vein graft

IABP indicates intra-aortic balloon pumping.

*Median (25th, 75th percentiles).

†As determined by the Angiographic Core Laboratory.
TABLE 2. Acute Cardiac Catheterization

<table>
<thead>
<tr>
<th></th>
<th>Control (N=86)</th>
<th>IABP (N=96)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Angiographic data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial visual percent stenosis*</td>
<td>100 (100,100)</td>
<td>100 (100,100)</td>
</tr>
<tr>
<td>Initial diameter percent stenosis (by QCA)*</td>
<td>100 (100,100)</td>
<td>100 (100,100)</td>
</tr>
<tr>
<td>Initial TIMI grade flow, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>65 (76)</td>
<td>63 (66)</td>
</tr>
<tr>
<td>1</td>
<td>16 (18)</td>
<td>24 (26)</td>
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<tr>
<td>2</td>
<td>3 (4)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>3</td>
<td>2 (2)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Final visual percent stenosis*</td>
<td>25 (25,50)</td>
<td>25 (25,50)</td>
</tr>
<tr>
<td>Final diameter percent stenosis (by QCA)*</td>
<td>43 (33,55)</td>
<td>42 (32,54)</td>
</tr>
<tr>
<td>Final TIMI grade, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>2</td>
<td>12 (14)</td>
<td>14 (15)</td>
</tr>
<tr>
<td>3</td>
<td>73 (85)</td>
<td>80 (84)</td>
</tr>
<tr>
<td><strong>Left ventricular function</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction, %*</td>
<td>46 (39,54)</td>
<td>49 (40,56)</td>
</tr>
</tbody>
</table>

IABP indicates intra-aortic balloon pumping; QCA, quantitative coronary angiography. All readings performed by the Angiographic Core Laboratory.
*Median (25th, 75th percentiles).

TABLE 3. Follow-up Cardiac Catheterization

<table>
<thead>
<tr>
<th></th>
<th>Control (N=77)</th>
<th>IABP (N=85)</th>
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<tr>
<td><strong>Angiographic Data</strong></td>
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<td></td>
</tr>
<tr>
<td>Visual percent stenosis*</td>
<td>50 (25,75)</td>
<td>50 (25,75)</td>
</tr>
<tr>
<td>Diameter percent stenosis (by QCA)*</td>
<td>45 (32,68)</td>
<td>42 (31,63)</td>
</tr>
<tr>
<td>TIMI grade flow, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>13 (17)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>1</td>
<td>3 (4)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>2</td>
<td>7 (9)</td>
<td>5 (6)</td>
</tr>
<tr>
<td>3</td>
<td>54 (70)</td>
<td>71 (85)</td>
</tr>
<tr>
<td><strong>Left ventricular function</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction, %*</td>
<td>48 (39,55)</td>
<td>49 (42,56)</td>
</tr>
<tr>
<td>Δ ejection fraction, %*</td>
<td>0 (−6,6)</td>
<td>1 (−5,6)</td>
</tr>
</tbody>
</table>

IABP indicates intra-aortic balloon pumping; QCA, quantitative coronary angiography. All readings performed by the Angiographic Core Laboratory.
*Median (25th, 75th percentiles).

TABLE 4. Hemorrhagic and Vascular Complications

<table>
<thead>
<tr>
<th></th>
<th>Control (N=86)</th>
<th>IABP (N=96)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None/mild</td>
<td>72 (84)</td>
<td>72 (75)</td>
</tr>
<tr>
<td>Moderate</td>
<td>13 (15)</td>
<td>22 (23)</td>
</tr>
<tr>
<td>Severe</td>
<td>1 (1)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Life threatening</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Nadir hematocrit*</td>
<td>32 (26,34)</td>
<td>30 (25,35)</td>
</tr>
<tr>
<td>Transfusions, no. (%)</td>
<td>20 (23)</td>
<td>28 (29)</td>
</tr>
<tr>
<td>No. of units†</td>
<td>0.9±1.8</td>
<td>1.3±2.6</td>
</tr>
<tr>
<td>&gt;2 Units</td>
<td>12 (14)</td>
<td>16 (17)</td>
</tr>
<tr>
<td>&gt;2 Units (non-CABG)</td>
<td>6 (8)</td>
<td>10 (11)</td>
</tr>
<tr>
<td>Landefeld index</td>
<td>3.3 (2.4,5.7)</td>
<td>4.0 (3.0,6.4)</td>
</tr>
<tr>
<td>Vascular complications, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep venous thrombosis</td>
<td>2 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vascular repair of thrombectomy</td>
<td>2 (2)</td>
<td>5 (5)</td>
</tr>
</tbody>
</table>

IABP indicates intra-aortic balloon pumping; CABG, coronary artery bypass graft surgery. Landefeld index: [(baseline−nadir hematocrit)/3] + No. of units transfused.
*Median (25th, 75th percentiles).
†Mean±1 SD.

fraction. The TAMI study group observed that patients receiving IABP after intravenous thrombolytic therapy had a lower rate of reocclusion during follow-up.10 These findings were further supported by the evaluation of the preventive impact of aortic counterpulsation on reocclusion rates in a model predictive of reocclusion of the infarct-related artery.16 Ishihara and colleagues5 also found a significant reduction in the rate of reocclusion in patients with anterior myocardial infarction treated with primary angioplasty (without antecedent thrombolytic therapy) and aortic counterpulsation in a nonrandomized study. Collectively, these observations suggest that aortic counterpulsation enhances coronary artery patency in acute myocardial infarction, which is confirmed in the present randomized trial.

Aortic counterpulsation has many physiological effects that may explain the improved patency rate.17,18
Kern and colleagues have shown that aortic counterpulsation significantly augments proximal coronary blood flow velocity as measured by an intracoronary Doppler catheter in patients with acute myocardial infarction, whereas animal models have suggested that the benefit results from the augmented diastolic blood pressure wave. Estimates of coronary flow velocity in patients have been found to be doubled shortly after a stenosis was treated by balloon angioplasty. These findings suggest that aortic counterpulsation is most beneficial when combined with angioplasty in acute myocardial infarction, which is supported by observations from the present study that the rate of reocclusion was low in patients who had angioplasty and IABP during emergency cardiac catheterization to restore patency in the infarct-related artery.

The rate of vascular and hemorrhagic complications observed in this study was similar to that seen with aortic counterpulsation performed with standard angioplasty. There are several possible reasons for the lower rate of such complications, including the exclusion of patients with significant peripheral vascular disease and the insertion of the intra-aortic balloon catheter through an existing vascular access site. Sheathless insertion, which might have reduced the rate of limb ischemia, was used in only a small proportion of patients in the present study because the technique and catheters did not become available and approved until the end of the study.

Previous animal studies using aortic counterpulsation have suggested that important physiological effects such as ventricular unloading and reduced cardiac work load during ischemia may improve the healing of the infarct zone, resulting in improved left ventricular function. Two small randomized trials evaluating aortic counterpulsation in patients with acute myocardial infarction found no improvement in global left ventricular function during follow-up. Similarly, aortic counterpulsation had no impact on measures of left ventricular systolic function in the present study. However, the majority of patients enrolled in the study had infarct-artery patency established more than 6 hours after symptom onset, and delayed patency has been noted to be associated with minimal changes in global left ventricular systolic function.

The present study has several limitations. First, it should be emphasized that this study was performed to evaluate prophylactic aortic counterpulsation in patients with acute myocardial infarction undergoing emergency cardiac catheterization. The data do not imply that similar findings would be achieved in patients with acute myocardial infarction not undergoing cardiac catheterization. Second, the hospitals participating in the study ranged from community hospitals to large academic centers, suggesting that the treatment strategy could be used in most hospitals. However, all the participating hospitals have a large experience with emergency cardiac procedures, including aortic counterpulsation. Third, data on activated clotting time or activated partial thromboplastin time were not collected in this study. All the sites followed the same postangioplasty management with 48 hours of continuous heparin administration. As a result, it is unlikely that there were substantial differences in the level of anticoagulation in the different arms during the early study period. Fourth, it was necessary to exclude high-risk patients such as those with cardiogenic shock or sustained hypotension, because it was felt not to be ethical to withhold aortic counterpulsation in such patients. For this reason, the mortality rate and the occurrence of congestive heart failure were low. Observational data and the present study suggest that aortic counterpulsation is particularly important in situations in which infarct-artery patency is critical for survival, such as in patients with cardiogenic shock.

In conclusion, this study suggests that the selective use of aortic counterpulsation after reperfusion is established during emergency cardiac catheterization can significantly improve in-hospital infarct-artery patency and reduce recurrent ischemic events, thereby reducing the need for repeat interventions. Prophylactic aortic counterpulsation, in experienced hands, may safely be combined with emergency percutaneous interventions to improve patient outcome in acute myocardial infarction.

### Appendix

**Duke Clinical Trials Coordinating Center, Durham, NC**

Robert M. Califf, MD; E. Magnus Ohman, MD; Paul M. Owens, RN; Cheryl Cortright, BSN; Sharon Karnash, BS; Lisa G. Berdan, PAC, MHS; Hyla S. Cohen, MS; Joy Miller, RN; and Robert Wilderman, BA. Statistical Group: Kerry L. Lee, PhD; Jeffrey Leimberger, PhD; Lynn Harrelson-Woodlief, MS; and Gerri Roberts, MS. Electrocardiographic Core Laboratory: E. Magnus Ohman, MD; James E. Tcheng, MD; and Paul M. Owens, RN. Angiographic Core Laboratory: Thomas Bushore, MD; James E. Tcheng, MD; Donald Fortin, MD; Jack Cuima, PhD; Leonard Santoro, BSC; Robert Burgess; and Paul M. Owens, RN. Data Safety Monitoring Board: Robert M. Califf, MD; Kerry L. Lee, PhD; Daniel B. Mark, MD; and James E. Tcheng, MD.

#### Clinical Sites

Duke University Medical Center, Durham, NC: E. Magnus Ohman, MD (Principal Investigator); Peter J. Quigley, MD

### Table 5: Clinical Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control, No. (%) (N=96)</th>
<th>IABP, No. (%) (N=96)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>2 (2)</td>
<td>2 (2)</td>
<td></td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>Reinfarction</td>
<td>7 (8)</td>
<td>3 (3)</td>
<td></td>
</tr>
<tr>
<td>Emergency/urgent CABG</td>
<td>3 (3)</td>
<td>3 (3)</td>
<td></td>
</tr>
<tr>
<td>New pulmonary edema</td>
<td>10 (12)</td>
<td>14 (15)</td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>10 (12)</td>
<td>17 (18)</td>
<td></td>
</tr>
<tr>
<td>Recurrent ischemia</td>
<td>18 (21)</td>
<td>4 (4)</td>
<td>.001</td>
</tr>
<tr>
<td>Emergency PTCA</td>
<td>9 (11)</td>
<td>2 (2)</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>Reocclusion of the infarct-related artery (TIMI grade 0 to 1)*</td>
<td>16 (21)</td>
<td>7 (8)</td>
<td>&lt;.03</td>
</tr>
</tbody>
</table>

* IABP indicates intra-aortic balloon pumping; TIA, transient ischemic attack; CABG, coronary artery bypass graft surgery; and PTCA, percutaneous transluminal coronary angioplasty.

*Angiographic Core Laboratory reading.
(Former Principal Investigator); Robert Bauman, MD; Victor S. Behar, MD; Charles Davidson, MD; Yihong Kong, MD; Mitchell Krucoff, MD; Kenneth Morris, MD; Robert H. Peter, MD; Harry R. Phillips III, MD; Michael H. Sketch Jr, MD; James E. Tcheng, MD; and Richard S. Stack, MD. Coordinators: Eric Berrios, RN; Kim Klinker, RN; Kirby Quintero, RN; Margaret Liu, BSN; Cynthia H. Flanagan, RN; and Cathy Martz, RN.

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St John's Hospital, Springfield, Ill: George Taylor, MD (Principal Investigator), James T. Dove, MD; H. Weston Moses, MD; Gregory J. Mishkel, MD; and Charles Lucore, MD. Coordinator: Tami Wescott, RN.

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Use of aortic counterpulsation to improve sustained coronary artery patency during acute myocardial infarction. Results of a randomized trial. The Randomized IABP Study Group.
E M Ohman, B S George, C J White, M J Kern, P A Gurbel, R J Freedman, C Lundergan, J R Hartmann, J D Talley and M J Frey

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