Meeting Highlights
James J. Ferguson III, MD

With this issue of Circulation, a new feature has been added. A summary is provided of major developments in cardiovascular medicine that have been presented at national and international meetings. This section highlights significant developments as they happen, and it keeps readers informed of the fast-paced advances in cardiovascular care. The following studies were presented at the 42nd Annual Scientific Sessions of the American College of Cardiology in Anaheim, Calif, March 14 to 18, 1993.

Interventional Cardiology: Clinical Trials
EPIC: Use of the Platelet Antibody 7E3 for High-Risk Percutaneous Transluminal Coronary Angioplasty

Dr Neal Kleiman of Baylor College of Medicine in Houston, Tex, presented the results of the multicenter EPIC trial, a randomized, controlled trial of 7E3 (a platelet Gp IIb/IIIa receptor antibody) in patients undergoing high-risk angioplasty or atherectomy. “High-risk” was defined as unstable angina (23% of the patients in the study), acute myocardial infarction (3% of patients), or high-risk lesion morphology (74% of patients). A total of 2099 patients at 56 clinical sites were randomized to one of three treatment arms in addition to standard aspirin pretreatment and intraprocedure and postprocedure administration of heparin: bolus of 7E3 plus a 12-hour 7E3 infusion, bolus of 7E3 plus placebo infusion, or placebo bolus plus placebo infusion. Efficacy was defined as freedom from death, nonfatal myocardial infarction, and urgent intervention. Safety end points included major bleeding and transfusion. With regard to efficacy, 12.8% of patients in the placebo bolus/placebo infusion group experienced an event compared with 11.5% in the 7E3 bolus/placebo infusion group and 8.3% in the 7E3 bolus/7E3 infusion group (representing a 35% reduction in events). Urgent intervention and nonfatal myocardial infarction composed most of the differences among the three groups. Ischemic events requiring urgent repeat intervention in placebo bolus/placebo infusion began to occur within hours after the procedure and continued for several days, whereas the onset of events in the group given 7E3 bolus/placebo infusion were delayed slightly, and the onset of events in the group given 7E3 bolus/7E3 infusion were delayed even further, suggesting that the 12-hour infusion of 7E3 had a sustained effect. Major bleeding complications (decrease in hemoglobin of more than 5 g/dL) occurred in 14% of patients receiving 7E3 bolus/7E3 infusion, 11% of patients receiving 7E3 bolus/placebo infusion, and 7% of patients receiving placebo bolus/placebo infusion. Interestingly, when body weight was factored into the analysis, the heavier patients appeared to benefit the most from 7E3 treatment, whereas lighter patients benefited the least, and the increased risk of bleeding was almost completely confined to the lightest patients. This may have been a consequence of the fixed doses used for heparin and 7E3 infusions. Dr Kleiman concluded from these data that 7E3 antibody reduced ischemic events following high-risk percutaneous transluminal coronary angioplasty (PTCA) and that the benefit extended for some time after Gp IIb/IIIa receptor function returned to normal, that a bolus dose of 7E3 was insufficient protection against ischemic complications, and that the benefits of 7E3 therapy in these patients are achieved at the risk of increased bleeding.

GABI: German Study of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Graft Surgery for Multivessel Disease

Dr Thomas Ischinger of the Klinikum Bogenhausen in Munich, Germany, presented preliminary data from the German Angioplasty Bypass Surgery Investigation (GABI), which is a randomized, multicenter trial of percutaneous transluminal coronary angioplasty (PTCA) versus coronary artery bypass graft surgery (CABG) in eight clinical centers in Germany. Patients were eligible for the study if revascularization was indicated for at least two major coronary vessels and if PTCA and CABG were considered technically feasible. The goal of treatment was complete revascularization. The primary end point of the study was angina pectoris at 1 year; secondary end points included cardiac events (death, myocardial infarction) and repeat interventions (in-hospital and at 1-year follow-up). Patients with total occlusions, stenosis of more than 2 cm, recent (within 1 month) myocardial infarction, prior interventions, and age of more than 75 years were excluded.

The total population screened for randomization comprised 8591 patients with multivessel disease. Of the nonrandomized patients (8233), 15% underwent PTCA as the treatment of choice, 53% underwent CABG, and 32% received medical therapy. Thus, the 379 patients included in the study were a highly selective group in a very narrow “middle ground” between alternative therapies. The surgical and PTCA groups did not differ with respect to age, history of prior myocardial infarction, presence of New York Heart Association functional class IV angina or diabetes, or sex. There were an average of 2.5 vessels treated per patient in each group. Internal mammary grafts were used in 35% of surgical cases; there was a 3% incidence of emergency CABG after PTCA. Patients randomized to bypass surgery

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waited 77 days between randomization and surgery compared with a wait of 38 days for PTCA patients. This was explained by the somewhat limited number of heart surgery facilities in Germany. The average length of hospital stay was 21 days for CABG and 7 days for PTCA, which was partially explained as a result of the German health care system. Preprocedural deaths were more frequent in the CABG group (reflecting the longer wait). Perioperative mortality was slightly, but not significantly, higher for surgery (2.5% versus 1.2%). The incidences of perioperative infarction (5.3% versus 1.5%) and pneumonia (10% versus 2.5%) were higher after CABG.

In approximately 10% of PTCA patients, in-hospital reintervention (usually CABG) was necessary compared with 2% of CABG patients (an additional 2% required re-exploration).

There was a striking difference between groups in the need for reintervention at 6 months: 40% of the PTCA group had required an additional intervention (half of whom had crossed over to bypass surgery) compared with less than 10% of the CABG patients who had required reintervention.

There was no difference between groups in the number of patients (60%) who had not returned to full work at 6 months.

Dr Ischinger emphasized the fact that these are preliminary results; full 1-year follow-up data are not yet available. He concluded that according to the present analysis, surgery is associated with higher initial morbidity and length of hospitalization; function improvement is comparable between PTCA and CABG, although return-to-work rates are disappointingly low; early reintervention is much more frequent after PTCA; a similar clinical outcome is achieved with angioplasty at the expense of more physician contact and more interventions; and the cost of PTCA is lower initially but increases with interventions. Both procedures must be viewed as treatment strategies rather than one-time definitive final therapy. Thus, PTCA and CABG remain very different treatment strategies; the former is a less invasive procedure with a higher rate of initial and subsequent clinical failure, and the latter is a more invasive and initially more costly procedure with a lower rate of early repeat interventions. How this will translate into long-term (more than 5 years) outcome remains unclear. Disease progression and patient risk factors are likely to be powerful determinants of long-term outcome and may, to some extent, in the long run overshadow initial therapeutic choices.

**PAMI: Primary Angioplasty in Myocardial Infarction**

Dr Cindy Grines of William Beaumont Hospital in Royal Oak, Mich, presented 6-month follow-up data from the Primary Angioplasty in Myocardial Infarction (PAMI) trial. This study was designed to compare the long-term outcome of patients with acute myocardial infarction randomized to primary PTCA (n=195) versus conventional intravenous thrombolytic therapy (n=200). The acute and short-term results suggested that thrombolytic therapy was associated with a higher rate of stroke, recurrent ischemia, and death or reintervention and a longer time to resolution of chest pain. New 6-month follow-up data demonstrate no significant difference between groups in subsequent clinical ischemic symptomatic status or necessity for bypass surgery after hospital discharge. The overall cumulative incidence of PTCA or CABG in the thrombolytic group was 63%. The differences between groups in death or reinfarction, recurrent ischemia, and stroke were maintained at 6 months. In addition, reinfarction alone was significantly higher in the thrombolytic group (11.0% versus 5.1%).

Dr Grines concluded that in comparison to conventional thrombolytic therapy, primary PTCA for acute myocardial infarction is associated with similar hospital costs; a reduced rate of stroke, recurrent ischemia, and reinfarction; and a trend toward improved mortality. The potential benefits of primary PTCA, which are apparent during hospitalization, appear to be maintained up to 1 year.

**TIMI 4 Angiographic Substudy: Consequences of TIMI 2 Versus TIMI 3 Flow After Myocardial Infarction**

Dr Michael Gibson of Brigham and Women’s Hospital presented angiographic data from the Thrombolysis in Myocardial Infarction (TIMI) 4 study, a randomized study of anisolated plasminogen streptokinase activator complex (APSAC) versus front-loaded tissue-type plasminogen activator (t-PA) versus APSAC plus t-PA in the treatment of acute myocardial infarction. The study has not been unblinded, so no information on treatment assignment is available; however, substudy analysis of a large data set is possible. The present substudy analysis focused specifically on whether infarct arteries with posttreatment angiographic TIMI grade 2 flow are more likely to occlude than arteries with TIMI grade 3 flow. Paired angiograms were analyzed in 220 patients with TIMI grade 2 or 3 flow 90 minutes after the initiation of treatment who had repeat angiography at 18 to 36 hours. All patients received adjunctive aspirin and full-dose heparin. TIMI grade 2 flow was subdivided further into grade 2 "fast" and grade 2 "slow," depending on the number of cineangiogram frames that it took to opacify the vessel.

The frequency of reocclusion at 18 to 36 hours was significantly higher in patients with 90-minute TIMI grade 2 flow (12%) than in patients with 90-minute TIMI grade 3 flow (3%). A final end point of TIMI grade 3 flow of 18 to 36 hours was achieved in 86% of patients with 90-minute grade 3 flow, in 53% of patients with 90-minute grade 2 "fast" flow, and in only 32% of patients with 90-minute grade 2 "slow" flow.

Dr. Gibson concluded that despite vessel patency, patients with 90-minute TIMI grade 2 flow are more likely to reocclude at 18 to 36 hours than are patients with TIMI grade 3 flow. These data are consistent with the less favorable outcome of patients with TIMI grade 2 flow as previously reported by the TIMI 4 group, who documented that TIMI grade 2 "slow" flow is associated with higher integrated creatine kinase values over the first 24 hours than is TIMI grade 3 flow.

**Canadian Coronary Atherectomy Trial**

Dr Allan Adelman at Mount Sinai Hospital in Toronto presented the data from the multicenter Canadian Coronary Atherectomy Trial. This was a randomized trial of PTCA versus directional atherectomy in 274 patients who were referred for nonsurgical revascularization of de novo proximal left anterior descending
coronary artery lesions. Nine Canadian centers participated in the trial; all operators had at least 2 years of PTCA experience and at least 20 prior directional coronary atherectomy (DCA) procedures. Computer-assisted quantitative coronary angiography was performed on all preprocedural, postprocedural, and 6-month follow-up angiograms. The primary end point of the study was 6-month angiographic restenosis (using a definition of more-than-50% diameter stenosis at follow-up).

Patients randomized to DCA were slightly older and had a higher frequency of lesion angulation of more than 45°; patients randomized to PTCA had more unstable angina. Procedural success (postprocedure diameter stenosis of 50% or less after a completed procedure) was achieved in 94% of DCA patients and 88% of PTCA patients \( (P=0.06) \). There was no difference in the incidence of major in-hospital complications (death, myocardial infarction, CABG) between groups. The incidence of angiographic restenosis was 46% for DCA and 42% for PTCA \( (P=0.63) \). There was a larger acute gain noted for DCA \( (1.44±0.44 \text{ versus } 1.16±0.47 \text{ mm for PTCA}) \); this was balanced by a larger late loss of DCA \( (0.79±0.62 \text{ versus } 0.47±0.64 \text{ mm for PTCA}) \). There was no difference between groups in lumen diameter at follow-up. There also were no differences between the two groups in clinical outcome at 6 months. Dr Adelman concluded from these data that there is no difference in late angiographic outcome or clinical outcome of DCA versus PTCA for de novo proximal LAD lesions.

GUIDE Trial: Use of Intravascular Ultrasound as an Adjunct to Coronary Interventions

Dr William Mullen of the University of California San Francisco presented phase I results of the GUIDE trial, a multicenter study designed to assess the clinical usefulness of intravascular ultrasound images in guiding coronary interventions. Phase I of the study examined the effects of intravascular ultrasound on operator assessment of the lesion and therapeutic decisions at key decision points in 136 patients scheduled to undergo PTCA or DCA. Examples of therapeutic decisions included repeating an inflation, changing balloon or atherectomy device size, switching devices, use of a perfusion balloon, and treating additional lesions.

In 68% of cases, intravascular ultrasound led to a change in the assessment of the lesion by the operator. More than one type of change in assessment was possible for any one given lesion. These changes included a change in estimation of lesion severity (58%, most frequently underestimated by angiography), a change in the impression of plaque distribution (eccentric versus concentric [33%]), and detection of tears and/or dissections that were not visible on angiography (23%).

In 44% of cases (41% of PTCA and 51% of DCA), decisions were made to change therapy based on the ultrasound images. Again, more than one type of therapeutic change was possible for any one given lesion. The changes for PTCA included further inflations with the same balloon (22%), use of a larger balloon (54%), use of a perfusion catheter to treat tears and dissections (16%), termination of the procedure (10%), and other (24%), including switching to an atherectomy device, treating an area remote from the target lesion, and choosing a smaller balloon size. The changes for DCA included additional passes with the same cutter (17%), cutting in a different location in the vessel wall (30%), changing device size, usually upsizing (22%), use of an adjunctive balloon (35%), or achievement of a satisfactory end point.

Dr Mullen concluded from these data that intravascular ultrasound images frequently alter both the assessment of the lesion by the operator and the therapeutic approach used.

CAVEAT: PTCA Versus Directional Atherectomy

Dr Eric Topol of the Cleveland Clinic in Cleveland, Ohio, presented an update of the Coronary Angioplasty Versus Excisional Atherectomy Trial (CAVEAT). This was a randomized study comparing standard PTCA \( (n=500) \) with DCA \( (n=52) \) for de novo atherosclerotic lesions (more than 60%) in native coronary arteries. Other prerequisites for inclusion in the study included lesions 12 mm or less in length, reference vessels at least 3 mm, and nontotal occlusions. From the standpoint of procedural outcome, the use of DCA was associated with higher incidences of myocardial infarction (6.3% versus 3.4%) and abrupt closure (6.8% versus 3.0%). A composite clinical end point of death, myocardial infarction, or abrupt closure was present in 11% of the DCA patients but only 5% of the PTCA patients. Core laboratory (but not on-site) analysis of procedural success showed an advantage (88.1% versus 80.5%) for DCA.

At 6-month follow-up, the DCA group had a higher incidence of subsequent myocardial infarction (7.6% versus 4.4%), but no significant difference in death, CABG, or need for repeat interventions. DCA was associated with an approximately $1300 higher procedural cost. There was a trend toward a lower incidence of restenosis in the DCA group \( (49.6\% \text{ versus } 56.7\%; \text{ } P=0.06) \); continuous analysis of minimal lumen diameter \( (P=0.07) \) and percent stenosis \( (P=0.03) \) results slightly favored DCA. Subgroup analysis suggests that there may be potential benefit of DCA for the proximal left anterior descending coronary artery, with higher success rates, higher acute gains, and less restenosis. However, this was not associated with advantages in clinical outcomes for the proximal left anterior descending coronary artery subgroup.

Dr Topol concluded that the higher procedural angiographic success of DCA is achieved at the expense of more procedural complications and higher procedural costs, with no differences in long-term outcome between DCA and PTCA.

RITA: PTCA Versus CABG in the United Kingdom

Dr Edgar Sowton of Guy's Hospital in London, UK, presented preliminary data from the Randomized Intervention Treatment of Angina (RITA) trial. This study includes 1011 patients from 16 centers in the United Kingdom who were randomized to PTCA \( (n=510) \) or CABG \( (n=501) \). Patients are stratified as to one, two, and three treated vessels; patients with previous PTCA or CABG are excluded, but those with totally occluded vessels can be included. The primary end point of the study is the combined incidence of death and nonfatal myocardial infarction at 5 years. The current results represent a mean follow-up of 2.5 years.
There were no significant differences between the CABG and PTCA groups in terms of previous myocardial infarction (43%), recent unstable angina (55%), age (mean, 57 years), or sex (19% women). Of the total group of patients, 45% had one treated vessel, 43% had two treated vessels, and 12% had three treated vessels.

At the present point of follow-up, there have been 18 deaths in the CABG group and 16 deaths in the PTCA group. Approximately half of these deaths have been noncardiac. Nonfatal myocardial infarctions have occurred in 26 CABG patients and 34 PTCA patients. There is no significant difference between groups in the primary end point (death or nonfatal myocardial infarction) at the present follow-up.

In the PTCA group, 38% of patients have reached end points of PTCA, CABG, myocardial infarction, or death in contrast to 11% of CABG patients (P<.001). Repeat angiography has been performed in 31% of PTCA patients and 7% of CABG patients. Angina, particularly unstable angina, and use of antianginal therapy were more common in the PTCA group. There were fewer physically active patients 1 month after CABG (38%) than 1 month after PTCA (52%), but there is no evidence of any difference at later time points. Arrhythmias were more common after CABG than after PTCA.

On the basis of the present data, Dr Sowton concluded that after 2.5 years of follow-up, there is no difference in the incidence of nonfatal myocardial infarction or death between CABG or PTCA. CABG provides better medium-term relief of angina but results in a higher incidence of early heart failure and arrhythmias. There appears to be a much higher incidence of repeat procedures in the PTCA group.

Peripheral and Coronary Ultrasound Angioplasty

Dr Robert Siegel of Cedars Sinai Medical Center and University of California Los Angeles School of Medicine presented data on ultrasound angioplasty using catheter-delivered low-frequency (20 kHz) high-intensity ultrasound (Baxter-Edwards LIS Division, Irvine, Calif). Patients were studied at Royal Hallamshire and Northern General Hospitals in Sheffield, England, and the San Francisco Heart Institute in Daly City, California. They have treated 61 peripheral arterial lesions in 57 patients with symptomatic peripheral vascular disease. There were 48 superficial femoral, 10 popliteal, and 3 tibial artery lesions; 47 were total occlusions. There was radiographic calcium evident in 22 vessels, and the mean lesion length was 7 cm (range, 1 to 28 cm). Ultrasound was successful in recanalizing 43 of the 47 occlusions. Overall, the mean percent diameter stenosis decreased from 94±11% to 55±23% after ultrasound angioplasty. Adjunctive balloon angioplasty (used in 78% of lesions) resulted in a mean final residual stenosis of 10±7%.

Improvements in catheter technology also have allowed the application of this technique to coronary vessels. In a preliminary safety and efficacy study, Siegel and colleagues, in conjunction with Dr David Cumberland of Sheffield, UK, have used ultrasound coronary angioplasty with a prototype 5F Monorail coronary catheter in 13 patients. Percent diameter stenosis decreased from 78±14% to 49±20% after ultrasound angioplasty and to 24±12% after adjunctive balloon angioplasty, using a mean of 3.3 ATM to achieve maximal balloon size. There were no complications of ultrasound angioplasty in any of the patients.

Dr Siegel concluded that ultrasound angioplasty is safe and appears to be useful for debulking selective atherosclerotic lesions, although adjunctive balloon angioplasty generally is required. No data on restenosis are available, but this technique appears promising and may find application in other areas, such as the treatment of intra-arterial thrombus.

PARK: Ketanserin for the Prevention of Restenosis After PTCA

Dr Patrick Serruys of the Thoraxcenter in Rotterdam presented the findings of the Post-Angioplasty Restenosis Ketanserin (PARK) trial. This placebo-controlled, double-blind study randomized PTCA patients with de novo atherosclerotic lesions in native coronary arteries to either ketanserin (a selective serotonin receptor antagonist) or placebo. Ketanserin was administered at least 1 hour before balloon insertion and continued as an oral maintenance dose of 40 mg BID for 6 months after the procedure. Computer-assisted quantitative angiographic measurements of minimal lumen diameter were made on pre-PTCA, post-PTCA, and 6-month follow-up angiograms. A total of 704 patients were randomized; 44 did not undergo treatment, leaving 656 patients for the intention-to-treat analysis. Follow-up angiograms were available in 592 patients; 67 did not fulfill compliance criteria, leaving 525 patients included in the per-protocol analysis.

The primary clinical end point of the study was a combined clinical end point of death, myocardial infarction, repeat PTCA, and CABG, within 6 months after the initial PTCA, including interventions initiated on the basis of the follow-up angiogram. There were no significant differences between the ketanserin and placebo groups in terms of death (less than 1% in both), myocardial infarction (4% versus 3%, respectively), CABG (6% versus 8%), repeat PTCA (21% versus 23%), or the overall combined clinical end point (28% in the ketanserin group and 32% in the placebo group).

The primary angiographic end point of the study was the per-patient change in minimal lumen diameter at follow-up relative to baseline. There were no significant differences between the two groups in terms of either the change in minimal lumen diameter from before PTCA to follow-up or percent diameter stenosis at follow-up. Analysis of the cumulative frequency minimal lumen diameter curves before PTCA, after PTCA, and at 6-month follow-up showed no significant difference. The restenosis rate per lesion (using a more-than-50% diameter stenosis criterion) was 32% for both the ketanserin group and the placebo group.

Dr Serruys concluded that ketanserin in the doses used in this study does not reduce the loss of minimal lumen diameter after PTCA and does not significantly improve clinical outcome.

New Therapies for Patients With Coronary Artery Disease

TIMI 5: Hirudin Versus Heparin in Acute Myocardial Infarction

On behalf of the TIMI 5 Investigators, Dr Christopher Cannon of Brigham and Women’s Hospital in
Boston, Mass, presented data on the TIMI 5 pilot trial, a controlled-dose escalation trial of hirudin (a direct thrombin inhibitor) versus heparin for the treatment of acute myocardial infarction. The trial consisted of myocardial infarction patients who all received 100 mg of front-loaded t-PA and aspirin and were randomized to a 5-day infusion of either heparin (5000-unit bolus; 1000 units/h titrated to the activated partial thromboplastin time [APTT]) or hirudin (four doses ranging from 0.15-mg/kg bolus with a 0.05 [mg/kg]/h infusion to 0.6-mg/kg bolus with a 0.2 [mg/kg]/h infusion). Angiography was performed at 90 minutes and repeated at 18 to 36 hours. The primary end point of the study was failure to achieve early or sustain TIMI grade 3 flow without death or reinfarction before the 18- to 36-hour angiogram.

Because similar findings were observed for each of the four hirudin doses, for the purpose of comparison with heparin all hirudin-treated patients were combined. Of the 246 patients enrolled in the study (162 hirudin and 84 heparin), 57% of the hirudin-treated patients were “not low risk” compared with 42% of the heparin-treated patients. Angiography at 90 minutes showed patency (TIMI grade 2 or 3 flow) in 82% of the hirudin-treated group and 79% of the heparin-treated group. Angiography at 90 minutes showed patency (TIMI grade 2 or 3 flow) in 82% of the hirudin-treated group and 79% of the heparin-treated group. Repeat angiography after 18 to 36 hours of treatment showed patency in 98% of the hirudin-treated group and 89% of the heparin-treated group (P=.01). Reocclusion at 18 to 36 hours occurred in 2% of the hirudin-treated group and 7% of the heparin-treated group (P=.07). Of 14 patients with an occluded infarct artery at 90 minutes who did not undergo rescue PTCA, 8 of 9 hirudin-treated patients had patent arteries at 18 to 36 hours compared with 2 of 5 heparin-treated patients (P=.05). With regard to the primary end point, 38% of hirudin-treated patients failed to achieve and sustain TIMI grade 3 flow compared with 51% of heparin-treated patients (P=.07). Death or reinfarction before discharge occurred in 6% of hirudin-treated patients compared with 16% of heparin-treated patients (P<.01). The differences in death and reinfarction persisted through 6 weeks. The total incidence of major hemorrhage was 17% for hirudin and 23% for heparin. There was also much less APTT variability in the patients treated with hirudin.

Dr Cannon and colleagues concluded that hirudin appeared to have a number of advantages over heparin in the setting of thrombolysis for acute myocardial infarction. These advantages included improved achievement of early and sustained TIMI grade 3 flow, higher patency of the infarct-related artery (with less reocclusion), and decreased rates of death and recurrent myocardial infarction up to 6 weeks after treatment. These advantages were achieved without increased risk of bleeding complications. Further testing is under way to definitively compare hirudin with heparin.

**β-Blockers and Silent Myocardial Ischemia**

**ASIST: Atenolol Silent Ischemia Trial**

Dr Carl Pepine of the University of Florida in Gainesville, Fla, presented the preliminary results of the Atenolol Silent Ischemia Trial (ASIST). This randomized, placebo-controlled trial was designed to assess the effect of treating silent ischemia on subsequent clinical outcome. Qualifying asymptomatic or minimally symptomatic patients were required to have a positive exercise test, documented coronary artery disease, and documented silent ischemia by ambulatory monitoring. A total of 306 patients were randomized to placebo (n=154) or 100 mg atenolol (n=152). The primary end point of the study was event-free survival at 1 year; events included death, resuscitated ventricular tachycardia or fibrillation, nonfatal myocardial infarction, hospitalization for unstable angina, aggravation of angina, and revascularization. The study was terminated prematurely by the Data Safety Monitoring Committee after the treatment arm showed a reduction in events that exceeded predetermined boundaries. The major finding of the study was a decrease in end point events of approximately 50% in the atenolol-treated group. Atenolol use was associated with less ambulatory monitored ischemia at 4 weeks; there was a significant reduction in both the total number of ischemic episodes and the total duration of ischemia. Furthermore, freedom from ischemia at 4 weeks was strongly associated with event-free survival at 1 year.

Dr Pepine concluded that treatment of silent ischemia with atenolol is associated with improved clinical outcome at 1 year. This is one of the first trials to document that reducing silent ischemia has a favorable effect on outcome.
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