

### **TAXUS III Trial In-Stent Restenosis Treated With Stent-Based Delivery of Paclitaxel Incorporated in a Slow-Release Polymer Formulation**

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**Background**— The first clinical study of paclitaxel-eluting stent for de novo lesions showed promising results. We performed the TAXUS III trial to evaluate the feasibility and safety of paclitaxel-eluting stent for the treatment of in-stent restenosis (ISR).

**Methods and Results**— The TAXUS III trial was a single-arm, 2-center study that enrolled 28 patients with ISR meeting the criteria of lesion length  $\leq 30$  mm, 50% to 99% diameter stenosis, and vessel diameter 3.0 to 3.5 mm. They were treated with one or more TAXUS NIRx paclitaxel-eluting stents. Twenty-five patients completed the angiographic follow-up at 6 months, and 17 of these underwent intravascular ultrasound (IVUS) examination. No subacute stent thrombosis occurred up to 12 months, but there was one late chronic total occlusion, and additional 3 patients showed angiographic restenosis. The mean late loss was 0.54 mm, with neointimal hyperplasia volume of 20.3 mm<sup>3</sup>. The major adverse cardiac event rate was 29% (8 patients; 1 non-Q-wave myocardial infarction, 1 coronary artery bypass grafting, and 6 target lesion revascularization [TLR]). Of the patients with TLR, 1 had restenosis in a bare stent implanted for edge dissection and 2 had restenosis in a gap between 2 paclitaxel-eluting stents. Two patients without angiographic restenosis underwent TLR as a result of the IVUS assessment at follow-up (1 incomplete apposition and 1 insufficient expansion of the stent).

**Conclusions**— Paclitaxel-eluting stent implantation is considered safe and potentially efficacious in the treatment of ISR. IVUS guidance to ensure good stent deployment with complete coverage of target lesion may reduce reintervention.

### **Intravascular Ultrasound Guidance Improves Angiographic and Clinical Outcome of Stent Implantation for Long Coronary Artery Stenoses: Final Results of a Randomized Comparison With Angiographic Guidance (TULIP Study)**

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Circulation 2003; 107: 62 – 67

**Background**— Long coronary lesions treated with stents have a poor outcome. This study compared the 6-month outcome of stent implantation for long lesions in patients randomized to intravascular ultrasound (IVUS; n=73) or angiographic guidance (n=71).

**Methods and Results**— Stenoses  $>20$  mm in length and a reference diameter that permitted a stent diameter  $\geq 3$  mm were eligible. Primary end points were 6-month minimal lumen diameter (MLD) and the combined end point of death, myocardial infarction, and target-lesion revascularization (TLR). Baseline clinical and angiographic data were comparable in both groups. At 6 months, MLD in the IVUS group ( $1.82 \pm 0.53$  mm) was larger than in the angiography group ( $1.51 \pm 0.71$  mm;  $P=0.042$ ). TLR and combined end-point rates at 6 months were 4% (n=3) and 6% (n=4) in the IVUS group and 14% (n=10) and 20% (n=14) in the angiography group, respectively ( $P=0.037$  for TLR and  $P=0.01$  for combined events). Restenosis ( $>50\%$  diameter stenosis) was found in 23% of the IVUS group and 45% of the angiography group ( $P=0.008$ ). At 12 months, TLR and the combined end point occurred in 10% (n=7) and 12% (n=9) of the IVUS group and 23% (n=17) and 27% (n=19) of the angiography group ( $P=0.018$  and  $P=0.026$ ), respectively.

**Conclusions**— Angiographic and clinical outcome up to 12 months after long stent placement guided by IVUS is superior to guidance by angiography.

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### Two-Year Angiographic and Intravascular Ultrasound Follow-Up After Implantation of Sirolimus-Eluting Stents in Human Coronary Arteries

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**Background**— The safety and efficacy of sirolimus-eluting stenting have been demonstrated, but the outcome of patients treated with this novel technology beyond the first year remains unknown. We sought to evaluate the angiographic, intravascular ultrasound (IVUS), and clinical outcomes of patients treated with sirolimus-eluting stents 2 years after implantation.

**Methods and Results**— This study included 30 patients treated with sirolimus-eluting Bx Velocity stenting (slow release [SR], n=15, and fast release [FR], n=15) in São Paulo, Brazil. Twenty-eight patients underwent 2-year angiographic and IVUS follow-up. No deaths occurred during the study period. In-stent late loss was slightly greater in the FR group ( $0.28 \pm 0.4$  mm) than in the SR group ( $-0.09 \pm 0.23$  mm,  $P=0.007$ ). No patient had in-stent restenosis. At 2-year follow-up, only 1 patient (FR group) had a 52% diameter stenosis within the lesion segment, which required repeat revascularization. The target-vessel revascularization rate for the entire cohort was 10% (3/30) at 2 years. All other patients had  $\leq 35\%$  diameter stenosis. Angiographic lumen loss at the stent edges was also minimal (in-lesion late loss was  $0.33 \pm 0.42$  mm [FR] and  $0.13 \pm 0.29$  mm [SR]). In-stent neointimal hyperplasia volume, as detected by IVUS, remained minimal after 2 years (FR =  $9.90 \pm 9$  mm<sup>3</sup> and SR =  $10.35 \pm 9.3$  mm<sup>3</sup>).

**Conclusions**— This study demonstrates the safety and efficacy of sirolimus-eluting Bx Velocity stents 2 years after implantation in humans. In-stent lumen dimensions remained essentially unchanged at 2-year follow-up in the 2 groups, although angiographic lumen loss was slightly higher in the FR group. Restenosis "catch-up" was not found in our patient population.

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### Paclitaxel Coating Reduces In-Stent Intimal Hyperplasia in Human Coronary Arteries: A Serial Volumetric Intravascular Ultrasound Analysis From the ASian Paclitaxel-Eluting Stent Clinical Trial (ASPECT)

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**Background**— The aim of this study was to use serial volumetric intravascular ultrasound (IVUS) to evaluate the effect of a paclitaxel coating on in-stent intimal hyperplasia (IH).

**Methods and Results**— Patients were randomized to placebo (bare metal stents) or 1 of 2 doses of paclitaxel (low dose:  $1.28$   $\mu\text{g}/\text{mm}^2$ ; high dose:  $3.10$   $\mu\text{g}/\text{mm}^2$ ). Complete post-stent implantation and follow-up IVUS were available in 81 patients, including 25 control patients and in 28 receiving a low-dose and 28 receiving a high dose. Volumetric analysis of the stented segment and of both reference segments was performed. Baseline stent measurements and both reference measurements were similar among the groups. With increasing doses, there was a stepwise reduction in IH accumulation within the stented segment ( $31 \pm 22$  mm<sup>3</sup> in control,  $18 \pm 15$  mm<sup>3</sup> in low dose, and  $13 \pm 14$  mm<sup>3</sup> in high dose,  $P < 0.001$ ). Post hoc analysis showed less IH accumulation when low- and high-dose patients were compared with control ( $P=0.009$  and  $P < 0.001$ , respectively), but not when low-dose patients were compared with high-dose patients ( $P=0.2$ ). Focal late malapposition was seen in 1 high-dose patient. With increasing doses, there was no significant change in the reference segments.

**Conclusions**— Paclitaxel-coated stents are effective in reducing in-stent neointimal tissue proliferation in humans. They are not associated with edge restenosis or significant late malapposition.

### **Heparin-Coated Stent Placement for the Treatment of Stenoses in Small Coronary Arteries of Symptomatic Patients**

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*Circulation* 2003; 107: 1265 – 1270

**Background**— The role of stents, especially of heparin-coated stents for the treatment of stenoses in small coronary arteries, is still unclear. Therefore, we performed this prospective, randomized trial to evaluate the angiographic and clinical outcome after treatment of stenoses in small coronary arteries (2.0 to 2.6 mm) of symptomatic patients.

**Methods and Results**— We randomly assigned 588 patients to angioplasty (n=195), bare stenting (n=196), or heparin-coated stenting (n=197). The primary end point was minimal lumen diameter (MLD) at 6 months. With comparable baseline parameters, the two stent arms showed a larger postinterventional MLD, larger acute gain, and smaller residual percent diameter stenosis, although a residual stenosis of 12±16% was achieved in the angioplasty arm, including a 27% crossover rate to stenting. Eighty percent of patients had follow-up angiography, which documented a borderline significantly larger MLD and smaller percent diameter stenosis for the two stent groups (1.34±0.48 mm and 42±20% after angioplasty, 1.47±0.48 mm and 36±20% after bare stenting, and 1.45±0.54 mm and 38±23% after heparin-coated stenting;  $P=0.049$  and  $P=0.038$ , respectively), but restenosis rates were not different (32%, 25%, and 30%). Thrombotic events occurred in 1.0% after angioplasty and 0.5% after bare or heparin-coated stenting. Survival without myocardial infarction or target vessel revascularization at 250 days was 84.6% (angioplasty), 88.3% (bare stenting), and 88.3% (heparin-coated stenting; log-rank  $P=0.39$ ).

**Conclusion**— Compared with angioplasty with provisional stenting, bare and heparin-coated stenting confer superior angiographic results and a nonsignificant 24% reduction in clinical events, with no difference between bare and heparin-coated stenting in the treatment of stenoses in small coronary arteries.

### **Adjunctive Platelet Glycoprotein IIb/IIIa Receptor Inhibition With Tirofiban Before Primary Angioplasty Improves Angiographic Outcomes: Results of the Tirofiban Given in the Emergency Room before Primary Angioplasty (TIGER-PA) Pilot Trial**

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*Circulation* 2003; 107: 1497 - 1501

**Background**— Previous work has suggested that platelet glycoprotein IIb/IIIa receptor blockade may confer benefit in the treatment of acute myocardial infarction. The TIGER-PA pilot trial was a single-center randomized study to evaluate the safety, feasibility, and utility of early tirofiban administration before planned primary angioplasty in patients presenting with acute myocardial infarction.

**Methods and Results**— A total of 100 patients presenting with acute myocardial infarction were randomized to either early administration of tirofiban in the emergency room or later administration in the catheterization laboratory. The primary outcome measures were initial TIMI grade flow, corrected TIMI frame counts, and TIMI grade myocardial perfusion ("blush"). Thirty-day major adverse cardiac events were also assessed. Angiographic outcomes demonstrate a significant improvement in initial TIMI grade flow, corrected TIMI frame counts, and TIMI grade myocardial perfusion when patients are given tirofiban in the emergency room before primary angioplasty. The rate of 30-day major adverse cardiac events suggests that early administration may be beneficial.

**Conclusions**— This pilot study suggests that early administration of tirofiban improves angiographic outcomes and is safe and feasible in patients undergoing primary angioplasty for acute myocardial infarction.

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### **Detection of Coronary Artery Stenoses With Thin-Slice Multi-Detector Row Spiral Computed Tomography and Multiplanar Reconstruction**

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Circulation 2003; 107: 664 – 666

**Background**— We analyzed the accuracy of multi-detector row spiral computed tomography (MDCT) using a 16-slice CT scanner with improved spatial and temporal resolution, as well as routine premedication with  $\beta$ -blockers for detection of coronary stenoses.

**Methods and Results**— Seventy-seven patients with suspected coronary disease were studied by MDCT (12x0.75-mm cross-sections, 420 ms rotation, 100 mL contrast agent IV at 5 mL/s). Patients with a heart rate above 60/min received 50 mg atenolol before the scan. In axial MDCT images and multiplanar reconstructions, all coronary arteries and side branches with a diameter of 1.5 mm or more were assessed for the presence of stenoses exceeding 50% diameter reduction. In comparison to invasive coronary angiography, MDCT correctly classified 35 of 41 patients (85%) as having at least 1 coronary stenosis and correctly detected 57 of 78 coronary lesions (73%). After excluding 38 of 308 coronary arteries (left main, left anterior descending, left circumflex, and right coronary artery in 77 patients) classified as unevaluable by MDCT (12%), 57 of 62 lesions were detected, and absence of stenosis was correctly identified in 194 of 208 arteries (sensitivity: 92%; specificity: 93%; accuracy: 93%; positive and negative predictive values: 79% and 97%).

**Conclusions**— MDCT coronary angiography with improved spatial resolution and premedication with oral  $\beta$ -blockade permits detection of coronary artery stenoses with high accuracy and a low rate of unevaluable arteries.

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### **Intracardiac Echocardiography Is Superior to Conventional Monitoring for Guiding Device Closure of Interatrial Communications**

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Circulation 2003; 107: 795 - 797

**Background**— This study sought to test whether intracardiac echocardiography (ICE) is superior to conventional monitoring in guiding device closure of interatrial communications (atrial septal defect [ASD] and patent foramen ovale [PFO]).

**Methods and Results**— Forty-four patients undergoing device closure of ASD (n=6) or PFO (n=38) were randomized to have the procedure guided by either ICE (group 1; n=22) or by transesophageal echocardiography (TEE) (group 2; n=22). All interventions were completed successfully. In 1 patient from group 2, atrial fibrillation occurred 1 day after device implantation; the patient was successfully cardioverted on the next day. There were no other complications. Fluoroscopy time (FT) ( $6.0 \pm 1.7$  minutes versus  $9.5 \pm 1.6$  minutes;  $P < 0.0001$ ) as well as procedure time (PT) ( $33.4 \pm 4.7$  minutes versus  $37.8 \pm 5.6$  minutes;  $P < 0.01$ ) were shorter in group 1 than in group 2. Group 2 patients required general anesthesia without (n=19) or with endotracheal intubation (n=3). In contrast, ICE allowed continuous monitoring of the whole procedure, including balloon sizing before device closure, without sedation.

**Conclusions**— ICE is a safe tool to guide device closure of PFO and ASD. Supine patients tolerate ICE better than TEE. ICE reduces FT and PT. ICE seems to be advantageous, especially when long continuous or repeated echocardiographic viewing is required.

### **Early and Late Effects of Clopidogrel in Patients With Acute Coronary Syndromes**

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Circulation 2003; 107: 966 – 972

**Background**— The risk of ischemic events is high, both early and late after acute coronary syndromes (ACS). We examine the benefits and risks associated with the use of adding clopidogrel to aspirin within the first 30 days and later (31 days to 12 months) in 12 562 patients with ACS.

**Methods and Results**— A total of 12 562 ACS patients were randomized to receive clopidogrel (300 mg initially followed by 75 mg/d) or placebo for 3 to 12 months. The proportion of patients experiencing cardiovascular death, myocardial infarction, or strokes (primary outcome) at 30 days was 5.4% in the placebo group and 4.3% in the active group (relative risk 0.79, 95% CI 0.67 to 0.92). Beyond 30 days, the corresponding rates were 6.3% versus 5.2% (relative risk 0.82, 95% CI 0.70 to 0.95). There was no significant excess in life-threatening bleeds in each period (0.97% versus 1.28%, relative risk 1.32, 95% CI 0.95 to 1.84 for 0 to 30 days; 0.83% versus 0.91%, relative risk 1.09, 95% CI 0.75 to 1.59 for 31 days to 12 months). Further subdivision of the early data indicates benefits within 24 hours with consistently lower rates of the primary outcome in combination with refractory or severe ischemia.

**Conclusions**— Clopidogrel reduces the risk of ischemic vascular events, with the benefits emerging within 24 hours of initiation of treatment and continuing throughout the 12 months (mean 9 months) of the study.

### **Pilot Trial of Oral Rapamycin for Recalcitrant Restenosis**

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Circulation 2003; 107: 1722 – 1724

**Background**— Sirolimus-coated stents are a promising new therapy for restenosis. We treated a select group of patients at especially high risk for restenosis with oral sirolimus.

**Methods and Results**— Patients were treated with an oral sirolimus-loading dose of 6 mg after coronary angioplasty, followed by 2 mg/d for 4 weeks. Serum electrolytes, lipid profile, renal panel, and complete blood cell count were measured at 1, 3, and 5 weeks after drug initiation. Oral sirolimus was prescribed to 22 patients who had a total of 28 lesions and were at high risk for restenosis. Of the 22 study patients, 11 (50%) discontinued oral sirolimus early because of side effects or laboratory abnormalities. Hypertriglyceridemia and leukopenia were the most frequent adverse events, occurring in 3 patients each. All adverse drug effects were reversible after discontinuation. Follow-up was obtained in 100% of patients at a mean of  $9.9 \pm 1.8$  months, ranging from 6.5 to 11.8 months. Target lesion revascularization (TLR) occurred in 15 of 28 lesions (53.6%) and 13 of 22 patients (59.1%). There was no difference in TLR for patients receiving a complete course of sirolimus ( $n=8$ ; 72.7%) compared with patients who terminated treatment prematurely ( $n=5$ ; 45.5%;  $P=NS$ ). Clinically driven repeat cardiac catheterization was obtained in 15 (68.2%) patients; restenosis (>50% diameter stenosis at follow-up) was present in 13 (86.7%).

**Conclusion**— Oral sirolimus does not appear to provide benefit to patients with recalcitrant restenosis. Adverse drug effects are frequent, underscoring the importance of local drug delivery to achieve high tissue concentrations without systemic adverse drug effects.

### **Noninvasive Determination of Coronary Blood Flow Velocity With Cardiovascular Magnetic Resonance in Patients After Stent Deployment**

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Circulation 2003; 107: 1738 – 1743

**Background**— In patients with coronary artery stents, no direct noninvasive coronary artery imaging is possible with magnetic resonance (MR). A well-established method for the assessment of the functional significance of a coronary lesion is the measurement of coronary flow reserve by invasive intracoronary Doppler. The purpose of the study was to determine coronary flow velocity reserve (CFVR) with MR after stent deployment.

**Methods and Results**— Thirty-eight patients after successful PTCA and stent deployment were included. CFVR was measured perpendicular to the artery distal to the stent using phase-contrast velocity quantification at rest and during adenosine-stimulated hyperemia with a 1.5T MR tomograph (ACS NT, Philips). Measurements were repeated after 3 months and compared with invasive coronary angiography. In 18 patients, additional invasive Doppler flow measurements were obtained. CFVR could be determined in 29 of 38 (76%) of the patients. After 3 months, significant differences were obtained between coronary arteries with and without restenosis. Using a threshold of 1.2, a sensitivity of 83% with a specificity of 94% was achieved for  $\geq 75\%$  stenoses. CFVR with CMR was similar to Doppler results ( $r=0.87$ ), with a mean relative difference of 7.5%.

**Conclusions**— In patients with preserved coronary microcirculating vasoreactivity that are suitable for MR coronary angiography and flow assessments, CMR measures of coronary blood flow velocities reserve may be used to detect in-stent restenosis.

### **Relation of Inflammation and Benefit of Statins After Percutaneous Coronary Interventions**

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Circulation 2003; 107: 1750 – 1756

**Background**— Beyond lipid lowering, statins are known to possess antiinflammatory and antithrombotic properties. Recent studies suggested an association between statins and early reduction in death or myocardial infarction (MI) after percutaneous coronary interventions (PCIs). We sought to examine the interrelationship between inflammation, statin use, and PCI outcomes.

**Methods and Results**— In the year 2000, 1552 consecutive United States residents underwent elective or urgent PCI at the Cleveland Clinic and were prospectively followed for 1 year. Preprocedural serum high-sensitivity C-reactive protein (hsCRP) levels were routinely measured. Patients who had statins initiated before the procedure (39.6%) had a lower median hsCRP level (0.40 versus 0.50 mg/dL,  $P=0.012$ ) independent of the baseline cholesterol levels and had less frequent periprocedural MI (defined by CKMB  $\geq 3$  upper limit of normal, 5.7% versus 8.1%,  $P=0.038$ ). At 1 year, statin pretreatment was predictive of survival predominantly among patients within the highest hsCRP quartile (mortality rate with statin pretreatment versus no pretreatment when  $hsCRP \geq 1.11$  mg/dL, 5.7% versus 14.8%,  $P=0.009$ ). Using multivariate analysis, preprocedural hsCRP level remained an independent predictor for 1-year death or MI only in patients without statin therapy (hazard ratio, 1.32/quartile;  $P=0.001$ ). After adjusting for the propensity of receiving statins, statin pretreatment was an independent predictor for 1-year survival within the highest hsCRP quartile (hazard ratio, 0.44;  $P=0.039$ ).

**Conclusions**— Statin therapy before PCI is associated with a marked reduction in mortality among patients with high hsCRP levels. A hsCRP-guided strategy may improve targeting of statin therapy and clinical outcome among patients undergoing PCI.

### Reduction of Major Adverse Cardiac Events With Intracoronary Compared With Intravenous Bolus Application of Abciximab in Patients With Acute Myocardial Infarction or Unstable Angina Undergoing Coronary Angioplasty

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Circulation 2003; 107: 1840 – 1843

**Background**— In patients with acute myocardial infarction or unstable angina undergoing coronary angioplasty, abciximab reduces major adverse cardiac events (MACE). Clinical trials have studied intravenous administration only. Intracoronary bolus application of abciximab causes very high local drug concentrations and may be more effective. We studied whether intracoronary bolus administration of abciximab is associated with a reduced MACE rate compared with the standard intravenous bolus application.

**Methods and Results**— We stratified 403 consecutive patients with acute myocardial infarction or unstable angina undergoing coronary angioplasty according to the type of application of abciximab. A 20-mg bolus of abciximab was given intravenously in 109 patients and intracoronarily in 294 patients. There were no differences between the groups with regard to diabetes mellitus, cardiogenic shock, successful intervention, or preprocedural and postprocedural TIMI flow. At 30 days, the incidence of MACE (death, myocardial infarction, urgent revascularization) was significantly lower in the patients with intracoronary compared with intravenous administration of abciximab (10.2% versus 20.2%;  $P < 0.008$ ), which was independent from stenting in multivariate analysis. The effect was most pronounced in patients with preprocedural TIMI 0/1 flow (MACE: intracoronary 11.8% versus intravenous 27.5%,  $P < 0.002$ ;  $n = 273$ ).

**Conclusions**— In patients with acute myocardial infarction or unstable angina undergoing emergency coronary angioplasty, intracoronary bolus application of abciximab is associated with a reduction of MACE compared with the standard intravenous bolus application of abciximab. Prospective, randomized trials are warranted to further assess intracoronary application of abciximab.

### Intracoronary and Intravenous Adenosine 5'-Triphosphate, Adenosine, Papaverine, and Contrast Medium to Assess Fractional Flow Reserve in Humans

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Circulation 2003; 107: 1877 – 1883

**Background**— Inducing both maximal and steady-state coronary hyperemia is of clinical importance to take full advantage of fractional flow reserve measurements. The present study compares different dosages and routes of administration of adenosine 5'-triphosphate (ATP), adenosine, contrast medium, and papaverine regarding their potential to achieve both maximal and steady-state hyperemia.

**Methods and Results**— In 21 patients with an isolated coronary stenosis, coronary vasodilation was induced successively by papaverine (20 mg intracoronary), adenosine (20 and 40  $\mu\text{g}$  intracoronary), ATP (20 and 40  $\mu\text{g}$  intracoronary), iohexol (6 mL intracoronary), adenosine or ATP through an antecubital vein (140 and 180  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ), or adenosine or ATP through a femoral vein (140 and 180  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ). Because vessel dimensions did not change, the ratio of distal coronary pressure ( $P_d$ ) to aortic pressure ( $P_a$ ) was used as an index of myocardial resistance.  $P_d/P_a$  was  $0.77 \pm 0.21$  at rest and decreased to  $0.61 \pm 0.21$  after papaverine.  $P_d/P_a$  decreased to a similar level with all other vasodilators, except with contrast medium ( $0.68 \pm 0.21$ ;  $P < 0.01$  versus papaverine). Steady-state hyperemia could only be obtained by intracoronary papaverine and by intravenous ATP or adenosine. In another 23 patients, an intravenous infusion of ATP was varied from 0 to 280  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ . At doses  $> 140 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ , there was neither a further decrease in  $P_d/P_a$  ratio nor a further increase in coronary flow velocities.

**Conclusion**— Provided sufficient dosages are used, ATP, adenosine, and papaverine (but not contrast medium) induce maximal hyperemia and are therefore suitable to assess fractional flow reserve. Only intracoronary papaverine and intravenous ATP or adenosine induce steady-state hyperemia enabling a pressure pullback maneuver that is useful in assessing diffuse coronary atherosclerosis.

### Angiographic Assessment of Reperfusion in Acute Myocardial Infarction by Myocardial Blush Grade

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Circulation 2003; 107: 2115 - 2119

**Background**— Angiographic successful reperfusion in acute myocardial infarction has been defined as TIMI 3 flow. However, TIMI 3 flow does not always result in effective myocardial reperfusion. Myocardial blush grade (MBG) is an angiographic measure of myocardial perfusion. We hypothesized that optimal angiographic reperfusion is defined by TIMI 3 flow and MBG 2 or 3.

**Methods and Results**— In 924 consecutive patients with TIMI 3 flow after angioplasty for acute myocardial infarction, we prospectively studied the value of MBG. End points were death, MACE, enzymatic infarct size, and residual left ventricular ejection fraction. Follow-up was 16±11 months. Of the 924 patients, 101 (11%) patients had MBG 0 or 1. Mortality was significantly higher in patients with MBG 0 or 1 compared with patients with MBG 2 or 3 (relative risk, 4.7; 95% CI, 2.3 to 9.5;  $P<0.001$ ). The combined incidence of MACE was higher in patients with MBG 0 or 1 compared with patients with MBG 2 or 3 (relative risk, 1.8; 95% CI, 1.1 to 2.8;  $P=0.009$ ). Enzymatic infarct size was larger (1437±2388 versus 809±1672,  $P=0.001$ ) and left ventricular ejection fraction was lower (37.7±10.6 versus 43.8±11.1,  $P<0.001$ ) in patients with MBG 0 or 1 compared with patients with MBG 2 or 3.

**Conclusions**— MBG is a strong angiographic predictor of mortality in patients with TIMI 3 flow after primary angioplasty. Enzymatic infarct size is larger and residual left ventricular ejection fraction is lower in patients with MBG 0 or 1 compared with MBG 2 or 3. Angiographic definition of successful reperfusion should include both TIMI 3 flow as well as MBG 2 or 3.

### Stenting of Culprit Lesions in Unstable Angina Leads to a Marked Reduction in Plaque Burden: A Major Role of Plaque Embolization?: A Serial Intravascular Ultrasound Study

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Circulation 2003; 107: 2320 – 2325

**Background**— Intravascular ultrasound (IVUS) studies have shown that a mechanism of plaque compression/embolization contributes toward the poststenting increase in lumen area. The aim of this IVUS study was to compare the mechanisms of lumen enlargement after coronary stenting in 54 consecutive patients with unstable angina (UA) (group 1) and 56 with stable angina (group 2) to verify whether plaque embolization plays a major role in the former.

**Methods and Results**— Both groups underwent the IVUS assessment (speed, 0.5 mm/sec) before the intervention and after stent implantation. The lumen area, the external elastic membrane area, and the plaque+media area (PA) were measured at 0.5-mm intervals. PA reduction in the lesion site was significantly greater in group 1 ( $-2.50±1.97$  versus  $-0.53±1.43$  mm<sup>2</sup>,  $P<0.001$ ). After stenting, 47% of the lumen area increase in group 1 was obtained by means of PA reduction, and 53% was attributable to external elastic membrane area increase; the corresponding figures in group 2 were 13% and 87% ( $P<0.05$ ). Decrease in PA after stenting was the only significant predictor of the MB fraction of creatinine kinase (CK-MB) release in a multiple regression model ( $P=0.047$ ).

**Conclusions**— Serial volumetric IVUS assessment revealed in UA lesions a marked poststenting reduction in plaque volume, which is significantly greater than in stable angina and is associated with postprocedural CK-MB release. The decrease in PA during the procedure predicts CK-MB release in a multiple regression model. These findings suggest that stent deployment is often associated with plaque embolization in patients with UA.