



The New England Journal of Medicine

TEMPORAL ASPECTS OF HEPARIN-INDUCED THROMBOCYTOPENIA

Theodore E. Warkentin, John G. Kelton

(*N Engl J Med* 2001;344:1286-92.)

Background. Heparin-induced thrombocytopenia is a relatively common antibody-mediated drug reaction. We studied the temporal relation between previous or current heparin therapy and the onset of heparin-induced thrombocytopenia.

Methods. We examined the time between the start of heparin therapy and the onset of thrombocytopenia in 243 patients with serologically confirmed heparin-induced thrombocytopenia. We also investigated the persistence of circulating heparin-dependent antibodies by performing a platelet serotonin-release assay and an assay for antibodies against platelet factor 4. The outcome in seven patients who had previously had an episode of heparin-induced thrombocytopenia and were later treated again with heparin was also examined.

Results. A fall in the platelet count beginning four or more days after the start of heparin therapy occurred in 170 of the 243 patients (70 percent); in these patients, a history of previous heparin treatment did not influence the timing of the onset of thrombocytopenia. In the remaining 73 patients (30 percent), the onset of thrombocytopenia was rapid (median time of onset, 10.5 hours after the start of heparin administration); all these patients had been treated with heparin within the previous 100 days. During recovery from thrombocytopenia, heparin-dependent antibodies in the serum fell to undetectable levels at a median of 50 to 85 days, depending on the assay performed. In the seven patients who were given heparin again after the disappearance of heparin-dependent antibodies, a new episode of heparin-induced thrombocytopenia did not occur.

Conclusions. Heparin-induced thrombocytopenia can begin rapidly in patients who have received heparin within the previous 100 days. Heparin-dependent antibodies do not invariably reappear with subsequent heparin use. (*N Engl J Med* 2001;344:1286-92.)

Circulation



JOURNAL OF THE AMERICAN HEART ASSOCIATION

Fighting Heart Disease and Stroke

INCREMENTAL PROGNOSTIC VALUE OF ELEVATED BASELINE C-REACTIVE PROTEIN AMONG ESTABLISHED MARKERS OF RISK IN PERCUTANEOUS CORONARY INTERVENTION

Derek P. Chew, Deepak L. Bhatt, Mark A. Robbins, Marc S. Penn, Jakob P. Schneider, Michael S. Lauer, Eric J. Topol, Stephen G. Ellis.

(*Circulation*. 2001;104:992.)

Background— Established methods of risk assessment in percutaneous coronary intervention have focused on clinical and anatomical lesion characteristics. Emerging evidence indicates the substantial contribution of inflammatory processes to short-term and long-term outcomes in coronary artery disease.

Methods and Results— Within a single-center registry of contemporary percutaneous coronary revascularization strategies with postprocedural creatine kinase and clinical events routinely recorded, we assessed the association of baseline C-reactive protein with death or myocardial infarction within the first 30 days. Predictive usefulness of baseline C-reactive protein within the context of established clinical and angiographic predictors of risk was also examined. Among 727 consecutive patients, elevated baseline C-reactive protein before percutaneous coronary intervention was associated with progressive increase in death or myocardial infarction at 30 days (lowest quartile, 3.9%, versus highest quartile, 14.2%; $P=0.002$). Among clinical and procedural characteristics, baseline C-reactive protein remained independently predictive of adverse events, with the highest quartile of C-reactive protein associated with an odds ratio for excess 30-day death or myocardial infarction of 3.68 (95% CI, 1.51 to 8.99; $P=0.004$). A predictive model that included baseline C-reactive protein quartiles, American College of Cardiology/American Heart Association lesion score, acute coronary syndrome presentation, and coronary stenting appears strongly predictive of 30-day death or myocardial infarction within this population (C-statistic, 0.735) and among individual patients (Brier score, 0.006).

Conclusions— Elevated baseline C-reactive protein portends heightened risk of 30-day death or myocardial infarction after coronary intervention. Coupled anatomic, clinical, and inflammatory risk stratification demonstrates strong predictive utility among patients undergoing percutaneous coronary intervention and may be useful for guiding future strategies.

ORAL ANTICOAGULANT THERAPY DURING AND AFTER CORONARY ANGIOPLASTY. THE INTENSITY AND DURATION OF ANTICOAGULATION ARE ESSENTIAL TO REDUCE THROMBOTIC COMPLICATIONS

Jurriën M. ten Berg, MD; Barbara A. Hutten, Msc; Johannes C. Kelder, MD; Freek W. A. Verheugt, MD, PhD; H. W. Thijs Plokker, MD, PhD

(*Circulation* 103: 2042-2047)

Background—In the randomized Balloon Angioplasty and Anticoagulation Study (BAAS), the addition of oral anticoagulants to aspirin significantly reduced early and late events after coronary angioplasty. However, bleeding episodes were increased. The present report studied the intensity and the duration of anticoagulation as predictors of thrombotic and bleeding events.

Methods and Results—A total of 530 patients, 34% of whom received a stent, were treated with aspirin plus coumarins. Half of the patients were randomized to angiographic follow-up. The target international normalized ratio (INR) was 2.1 to 4.8 during angioplasty and 6-month follow-up. Thrombotic events were death, myocardial infarction, target lesion revascularization, and thrombotic stroke. Bleeding complications were hemorrhagic stroke, major extracranial bleeding, and false aneurysm. "Optimal" anticoagulation was defined as an INR in the target range for at least 70% of the follow-up time. There were 17 early thrombotic events (3.2%), 7 early bleeding episodes (1.3%), and 10 false aneurysms (1.9%). The incidence rate for both early thrombotic and bleeding events was lowest in patients in the target range. A total of 61 late thrombotic events occurred (11.6%). Optimal anticoagulation was an independent predictor of late thrombotic events (relative risk, 0.33; 95% CI, 0.19 to 0.57) and was associated with a 0.21 mm (95% CI, 0.17 to 0.42) larger vessel lumen at 6 months. Late bleeding episodes (1.4%) were lowest in patients in the target range.

Conclusions—Coumarins started before coronary angioplasty with a target INR of 2.1 to 4.8 led to the lowest procedural event rate, without an increase in bleeding episodes. During follow-up, optimal anticoagulation was associated with a decrease in the incidence of late events by 67% and a significant improvement in 6-month angiographic outcome.

RANDOMIZED, SINGLE-BLIND, PLACEBO-CONTROLLED PILOT STUDY OF CATHETER-BASED MYOCARDIAL GENE TRANSFER FOR THERAPEUTIC ANGIOGENESIS USING LEFT VENTRICULAR ELECTROMECHANICAL MAPPING IN PATIENTS WITH CHRONIC MYOCARDIAL ISCHEMIA

Peter R. Vale, MD; Douglas W. Losordo, MD; Charles E. Milliken, MS; Maria C. McDonald, BSN; Laura M. Gravelin; Cynthia M. Curry, BS; Darryl D. Esakof, MD; Michael Maysky, MD; James F. Symes, MD; Jeffrey M. Isner, MD

(*Circulation*. 2001;103:2138.)

Background—Catheter-based myocardial gene transfer (GTx) has not been previously tested in human subjects. Accordingly, we performed a pilot study to investigate the feasibility and safety of catheter-based myocardial GTx of naked plasmid DNA encoding vascular endothelial growth factor-2 (phVEGF-2) in patients with chronic myocardial ischemia.

Methods and Results—A steerable, deflectable 8F catheter incorporating a 27-gauge needle was advanced percutaneously to the left ventricular myocardium of 6 patients with chronic myocardial ischemia. Patients were randomized (1:1) to receive phVEGF-2 (total dose, 200 µg), which was administered as 6 injections into ischemic myocardium (total, 6.0 mL), or placebo (mock procedure). Injections were guided by NOGA left ventricular electromechanical mapping. Patients initially randomized to placebo became eligible for phVEGF-2 GTx if they had no clinical improvement 90 days after their initial procedure. Catheter injections (n=36) caused no changes in heart rate or blood pressure. No sustained ventricular arrhythmias, ECG evidence of infarction, or ventricular perforations were observed. phVEGF-2-transfected patients experienced reduced angina (before versus after GTx, 36.2±2.3 versus 3.5±1.2 episodes/week) and reduced nitroglycerin consumption (33.8±2.3 versus 4.1±1.5 tablets/week) for up to 360 days after GTx; reduced ischemia by electromechanical mapping (mean area of ischemia, 10.2±3.5 versus 2.8±1.6 cm², P=0.04); and improved myocardial perfusion by SPECT-sestamibi scanning for up to 90 days after GTx when compared with images obtained after control procedure.

Conclusions—This randomized trial of catheter-based phVEGF-2 myocardial GTx provides preliminary indications regarding the feasibility, safety, and potential efficacy of percutaneous myocardial GTx to human left ventricular myocardium.

**IMPACT OF PERI-STENT REMODELING ON RESTENOSIS
A VOLUMETRIC INTRAVASCULAR ULTRASOUND
STUDY**

Mamoo Nakamura, MD; Paul G. Yock, MD; Heidi N. Bonneau, RN; Katsuhiko Kitamura, MD; Tadanori Aizawa, MD; Hideo Tamai, MD; Peter J. Fitzgerald, MD, PhD; Yasuhiro Honda, MD

(*Circulation*. 2001;103:2130.)

Background—Vessel remodeling is an important mechanism of late lumen loss after nonstent coronary interventions. However, its impact on in-stent restenosis has not been systematically investigated.

Methods and Results—Serial volumetric intravascular ultrasound analyses (poststent and follow-up) were performed in 55 lesions treated with a balloon-expandable stent (ACS MultiLink) using standard stent deployment techniques. The vessel volume (VV), lumen volume (LV), and volume bordered by the stent (SV) were measured using Simpson's method. The volume of plaque and neointima outside the stent (peri-stent volume, PSV) and volume of neointima within the stent (intra-stent volume) were also measured. The change of each parameter during the follow-up period (follow-up minus poststent) was calculated and then divided by SV to normalize these values (designated as percent change [% Δ]). As expected, % Δ PSV directly correlated with % Δ VV ($P<0.0001$, $r=0.935$), with no significant Δ SV. A highly significant inverse correlation was seen between % Δ PSV and the percent change of intra-stent volume ($P<0.0001$, $r=0.517$). Consequently, % Δ LV significantly correlated with peri-stent remodeling, as measured by % Δ VV ($P<0.0001$, $r=0.602$).

Conclusion—Positive remodeling of the vessel exterior to a coronary stent occurs to a variable degree after stent implantation. There is a distinct trade-off between positive remodeling and in-stent hyperplasia: in segments in which the degree of peri-stent remodeling is less, intrastent neointimal proliferation is greater and accompanied by more significant late lumen loss.

**BALLOON DILATION ANGIOPLASTY OF PERIPHERAL
PULMONARY STENOSIS ASSOCIATED WITH WILLIAMS
SYNDROME**

Robert L. Geggel, MD; Kimberlee Gauvreau, ScD; James E. Lock, MD

From the Department of Cardiology, Children's Hospital, and the Department of Pediatrics, Harvard Medical School, Boston, Mass.

(*Circulation*. 2001;103:2165.)

Background—Experience of balloon dilation of peripheral pulmonary stenosis (PPS) in Williams syndrome (WS) is limited.

Methods and Results—Catheterizations in all patients with WS undergoing therapy for PPS from 1984 to 1999 were reviewed. Criteria for successful dilation included an increase $>50\%$ in predilation diameter and a decrease $>20\%$ in ratio of right ventricular (RV) to aortic (Ao) systolic pressure. Median age and weight were 1.5 years and 9.5 kg. There were 134 dilations during 39 procedures in 25 patients. The success rate for initial dilations was 51%. In multivariate analysis, successful dilation was more likely (1) in distal than in central pulmonary arteries ($P=0.02$), (2) if the balloon waist resolved with inflation ($P=0.001$), and (3) with larger balloon/stenosis ratio ($P<0.001$). RV pressure was unchanged after dilation (96 ± 30 versus 97 ± 31 mm Hg), primarily because of failure to enlarge central pulmonary arteries. The Ao pressure increased (102 ± 14 versus 109 ± 19 mm Hg, $P=0.03$), and the RV/Ao pressure ratio decreased (0.97 ± 0.34 versus 0.91 ± 0.30 , $P=0.05$). Aneurysms developed after 24 dilations (18%) and were not related to balloon/stenosis ratio. Balloon rupture in 12 dilations produced an aneurysm in all 7 cases when rupture was in a hypoplastic segment. Three patients died, none from pulmonary artery trauma, and all before 1994.

Conclusions—Mortality occurred early in our experience. Despite successful dilation of distal pulmonary arteries, there was modest initial hemodynamic improvement, mainly because of persistent central pulmonary artery obstruction. A serial approach of distal dilations followed by surgical repair of proximal obstruction may be a rational and successful therapy.

CONTINUED BENEFIT OF CORONARY STENTING
VERSUS BALLOON ANGIOPLASTY: FIVE-YEAR
CLINICAL FOLLOW-UP OF BENESTENT-I TRIAL

Ferdinand Kiemeneij, Patrick W. Serruys, Carlos Macaya, Wolfgang Rutsch, Guy Heyndrickx, Per Albertsson, Jean Fajadet, Victor Legrand, Berre Materne, Jorge Belardi, Ulrich Sigwart, Antonio Colombo, Jean-Jacques Goy, Clemens M.C. Disco and Marie-Angèle Morel on behalf of the Benestent I Study Group

(*J Am Coll Cardiol*, 37:6:1598-1603.)

Objectives: This study sought to establish whether the early favorable results in the Benestent-I randomized trial comparing elective Palmaz-Schatz stent implantation with balloon angioplasty in 516 patients with stable angina pectoris are maintained at 5 years.

Background: The size of the required sample was based on a 40% reduction in clinical events in the stent group. Seven months and one-year follow-up in this trial showed a decreased incidence of restenosis and clinical events in patients randomized to stent implantation.

Methods: Data at five years were collected by outpatient visit, via telephone and via the referring cardiologist. Three patients in the stent group and one in the percutaneous transluminal coronary angioplasty (PTCA) group were lost to follow-up at five years. Major clinical events, anginal status and use of cardiac medication were recorded according to the intention to treat principle.

Results: No significant differences were found in anginal status and use of cardiac medication between the two groups. In the PTCA group, 27.3% of patients underwent target lesion revascularization (TLR) versus 17.2% of patients in the stent group ($p = 0.008$). No significant differences in mortality (5.9% vs. 3.1%), cerebrovascular accident (0.8% vs. 1.2%), myocardial infarction (9.4% vs. 6.3%) or coronary bypass surgery (11.7% vs. 9.8%) were found between the stent and PTCA groups, respectively. At five years, the event-free survival rate (59.8% vs. 65.6%; $P = 0.20$) between the stent and PTCA groups no longer achieved statistical significance.

Conclusions: The original 10% absolute difference in TLR in favor of the stent group has remained unchanged at five years, emphasizing the long-term stability of the stented target site.

PACLITAXEL STENT COATING INHIBITS NEOINTIMAL
HYPERPLASIA AT 4 WEEKS IN A PORCINE MODEL OF
CORONARY RESTENOSIS

Alan W. Heldman, MD; Linda Cheng, PhD; G. Mark Jenkins, MD; Phillip F. Heller, PhD; Dong-Woon Kim, MD; Melvin Ware, Jr, LAT; Cynthia Nater, BS; Ralph H. Hruban, MD; Banafsheh Rezai, MD; Benjamin S. Abella, MD; Katherine E. Bunge, MD; James L. Kinsella, PhD; Steven J. Sollott, MD; Edward G. Lakatta, MD; Jeffrey A. Brinker, MD; William L. Hunter, MD; Jeffrey P. Froehlich, MD

(*Circulation* 2001;103:2289.)

Background—Despite limiting elastic recoil and late vascular remodeling after angioplasty, coronary stents remain vulnerable to restenosis, caused primarily by neointimal hyperplasia. Paclitaxel, a microtubule-stabilizing drug, has been shown to inhibit vascular smooth muscle cell migration and proliferation contributing to neointimal hyperplasia. We tested whether paclitaxel-coated coronary stents are effective at preventing neointimal proliferation in a porcine model of restenosis.

Methods and Results—Palmaz-Schatz stents were dip-coated with paclitaxel (0, 0.2, 15, or 187 $\mu\text{g}/\text{stent}$) by immersion in ethanolic paclitaxel and evaporation of the solvent. Stents were deployed with mild oversizing in the left anterior descending coronary artery (LAD) of 41 minipigs. The treatment effect was assessed 4 weeks after stent implantation. The angiographic late loss index (mean luminal diameter) decreased with increasing paclitaxel dose ($P < 0.0028$ by ANOVA), declining by 84.3% (from 0.352 to 0.055, $P < 0.05$) at the highest level tested (187 $\mu\text{g}/\text{stent}$ versus control). Accompanying this change, the neointimal area decreased (by 39.5%, high-dose versus control; $P < 0.05$) with increasing dose ($P < 0.040$ by ANOVA), whereas the luminal area increased (by 90.4%, high-dose versus control; $P < 0.05$) with escalating dose ($P < 0.0004$ by ANOVA). Inflammatory cells were seen infrequently, and there were no cases of aneurysm or thrombosis.

Conclusions—Paclitaxel-coated coronary stents produced a significant dose-dependent inhibition of neointimal hyperplasia and luminal encroachment in the pig LAD 28 days after implantation; later effects require further study. These results demonstrate the potential therapeutic benefit of paclitaxel-coated coronary stents in the prevention and treatment of human coronary restenosis.



PERCUTANEOUS AND SURGICAL INTERVENTIONS FOR IN-STENT RESTENOSIS: LONG-TERM OUTCOMES AND EFFECT OF DIABETES MELLITUS

Ali Moustapha MD , Abid R. Assali MD , Stefano Sdringola MD , William K. Vaughn PhD , R. David Fish FACC MD , Oscar Rosales FACC MD , George Schroth FACC MD , Zvonimir Krajcer FACC MD , Richard W. Smalling FACC MD, PhD and H. Vernon Anderson FACC MD

(*J Am Coll Cardiol*, 37:7:1877-1882)

Objective: We examined long-term outcomes of patients with in-stent restenosis (ISR) who underwent different percutaneous interventions at the discretion of individual operators: balloon angioplasty (BA), repeat stent or rotational atherectomy (RA). We also examined long-term outcomes of patients with ISR who underwent coronary artery bypass surgery (CABG). **BACKGROUND**In-stent restenosis remains a challenging problem, and its optimal management is still unknown.

Methods:Symptomatic patients (n = 510) with ISR were identified using cardiac catheterization laboratory data. Management for ISR included BA (169 patients), repeat stenting (117 patients), RA (107 patients) or CABG (117 patients). Clinical outcome events of interest included death, myocardial infarction, target vessel revascularization (TVR) and a combined end point of these major adverse cardiovascular events (MACE). Mean follow-up was 19.

RESULTS:Patients with ISR treated with repeat stent had significantly larger average post-procedure minimal lumen diameter compared with BA or RA (3.3)

CONCLUSIONSIn this large cohort of patients with ISR and in the subset of patients without diabetes, long-term outcomes were similar in the BA, repeat stent and RA groups. Tissue debulking with RA yielded better results only in diabetic patients. Bypass surgery for patients with multivessel disease and ISR provided the best outcomes.

STRUT THICKNESS EFFECT ON RESTENOSIS OUTCOME (ISAR-STEREO) TRIAL

Adnan Kastrati, MD; Julinda Mehilli, MD; Josef Dirschinger, MD; Franz Dotzer, MD; Helmut Schühlen, MD; Franz-Josef Neumann, MD; Martin Fleckenstein, MD; Conrad Pfaffert, MD; Melchior Seyfarth, MD; Albert Schömig, MD

(*Circulation*. 2001;103:2816.)

Background—Increased thrombogenicity and smooth muscle cell proliferative response induced by the metal struts compromise the advantages of coronary stenting. The objective of this randomized, multicenter study was to assess whether a reduced strut thickness of coronary stents is associated with improved follow-up angiographic and clinical results.

Methods and Results—A total of 651 patients with coronary lesions situated in native vessels >2.8 mm in diameter were randomly assigned to receive 1 of 2 commercially available stents of comparable design but different thickness: 326 patients to the thin-strut stent (strut thickness of 50 μ m) and 325 patients to the thick-strut stent (strut thickness of 140 μ m). The primary end point was the angiographic restenosis ($\geq 50\%$ diameter stenosis at follow-up angiography). Secondary end points were the incidence of reinterventions due to restenosis-induced ischemia and the combined rate of death and myocardial infarctions at 1 year. The incidence of angiographic restenosis was 15.0% in the thin-strut group and 25.8% in the thick-strut group (relative risk, 0.58; 95% CI, 0.39 to 0.87; $P=0.003$). Clinical restenosis was also significantly reduced, with a reintervention rate of 8.6% among thin-strut patients and 13.8% among thick-strut patients (relative risk, 0.62; 95% CI, 0.39 to 0.99; $P=0.03$). No difference was observed in the combined 1-year rate of death and myocardial infarction.

Conclusions—The use of a thinner-strut device is associated with a significant reduction of angiographic and clinical restenosis after coronary artery stenting. These findings may have relevant implications for the currently most widely used percutaneous coronary intervention.



PERCUTANEOUS CORONARY INTERVENTION VERSUS CORONARY ARTERY BYPASS GRAFT SURGERY FOR PATIENTS WITH MEDICALLY REFRACTORY MYOCARDIAL ISCHEMIA AND RISK FACTORS FOR ADVERSE OUTCOMES WITH BYPASS: A MULTICENTER, RANDOMIZED TRIAL *

Douglass A. Morrison , Gulshan Sethi, Jerome Sacks, William Henderson, Frederick Grover, Steven Sedlis, Rick Esposito, Kodangudi Ramanathan, Darryl Weiman, Jorge Saucedo, Tamim Antakli, Venki Paramesh, Stuart Pett, Sarah Vernon, Vladimir Birjiniuk, Frederick Welt, Mitchell Krucoff, Walter Wolfe, John C. Lucke, Sundeep Mediratta, David Booth, Charles Barbieri , Daniel Lewis and for the Investigators of the Department of Veterans Affairs Cooperative Study 385 the Angina With Extremely Serious Operative Mortality Evaluation(AWESOME)

(*J Am Col. ICardiol* 2001; 38:143-149)

Background: Percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery (CABG) are being applied to high-risk populations, but previous randomized trials comparing revascularization methods have excluded a number of important high-risk groups.

Objectives: This five-year, multicenter, randomized clinical trial was designed to compare long-term survival among patients with medically refractory myocardial ischemia and a high risk of adverse outcomes assigned to either a CABG or a PCI strategy, which could include stents.

Methods: Patients from 16 Veterans Affairs Medical Centers were screened to identify myocardial ischemia refractory to medical management and the presence of one or more risk factors for adverse outcome with CABG, including prior open-heart surgery, age >70 years, left ventricular ejection fraction <0.35, myocardial infarction within seven days or intraaortic balloon pump required. Clinically eligible patients (n = 2,431) underwent coronary angiography; 781 were angiographically acceptable; 454 (58% of eligible) patients consented to random assignment between CABG and PCI.

Results: A total of 232 patients was randomized to CABG and 222 to PCI. The 30-day survival for CABG and PCI were 95% and 97%, respectively. Survival rates for CABG and PCI were 90% versus 94% at six months and 79% versus 80% at 36 months (log-rank test, P = 0.46).

Conclusions: Percutaneous coronary intervention is an alternative to CABG for patients with medically refractory myocardial ischemia and a high risk of adverse outcomes with CABG.

ARE WE MAKING PROGRESS WITH PERCUTANEOUS SAPHENOUS VEIN GRAFT TREATMENT? : A COMPARISON OF 1990 TO 1994 AND 1995 TO 1998 RESULTS *

Mun K. Hong , Roxana Mehran, George Dangas, Gary S. Mintz , Alexandra Lansky , Kenneth M. Kent, Augusto D. Pichard , Lowell F. Satler , Gregg W. Stone and Martin B. Leon

(*J Am Col. ICardiol* 2001; 38:150-154)

Objectives: We sought to determine whether strategies to reduce procedural distal embolization and late repeat revascularization have resulted in more favorable outcomes after saphenous vein graft (SVG) angioplasty.

Background: Angioplasty of SVG lesions has been associated with frequent procedural and late cardiac events. Therefore, evolving strategies have been attempted to improve outcomes after SVG angioplasty.

Methods: We compared our earlier experience (1990 to 1994) of 1,055 patients with 1,412 SVG lesions with a recent group (1995 to 1998) of 964 patients with 1,315 lesions.

Results: Baseline characteristics were similar between the groups. However, there were significantly more unfavorable lesion characteristics (older, longer and significantly more degenerated SVGs) in the recent series. Between the two periods, there was decreased use of atheroablative devices, whereas stent use increased. The procedural success rates (96.6% vs. 96.1%) were similar. However, one-year outcome (event-free survival) was significantly improved in the more recent experience (70.7% vs. 59.1%, p < 0.0001), especially late mortality (6.1% vs. 11.3%, p < 0.0001). Multivariate analysis showed stent use to be the only protective variable for both periods.

Conclusions: This study shows that despite higher risk lesions, strategies to reduce distal embolization have maintained high procedural success. Late cardiac events, including mortality, have also been substantially reduced.



CLINICAL AND ECONOMIC IMPACT OF DIABETES MELLITUS ON PERCUTANEOUS AND SURGICAL TREATMENT OF MULTIVESSEL CORONARY DISEASE PATIENTS
Insights From the Arterial Revascularization Therapy Study (ARTS) Trial

Alexandre Abizaid, MD, PhD; Marco A. Costa, MD, PhD; Marinella Centemero, MD; Andrea S. Abizaid, MD; Victor M.G. Legrand, MD; Robert V. Limet, MD; Gerhard Schuler, MD; Friedrich W. Mohr, MD; Wietze Lindeboom, MSc; Amanda G.M.R. Sousa, MD, PhD; J. Eduardo Sousa, MD, PhD; Ben van Hout, PhD; Paul G. Hugenholtz, MD, PhD; Felix Unger, MD; Patrick W. Serruys, MD, PhD; on behalf of the ARTS Investigators

(*Circulation* 2001;104: 533-538)

Background— Our aims were to compare coronary artery bypass grafting (CABG) and stenting for the treatment of diabetic patients with multivessel coronary disease enrolled in the Arterial Revascularization Therapy Study (ARTS) trial and to determine the costs of these 2 treatment strategies.

Methods and Results— Patients (n=1205) were randomly assigned to stent implantation (n=600; diabetic, 112) or CABG (n=605; diabetic, 96). Costs per patient were calculated as the product of each patient's use of resources and the corresponding unit costs. Baseline characteristics were similar between the groups. At 1 year, diabetic patients treated with stenting had the lowest event-free survival rate (63.4%) because of a higher incidence of repeat revascularization compared with both diabetic patients treated with CABG (84.4%, $P<0.001$) and nondiabetic patients treated with stents (76.2%, $P=0.04$). Conversely, diabetic and nondiabetic patients experienced similar 1-year event-free survival rates when treated with CABG (84.4% and 88.4%). The total 1-year costs for stenting and CABG in diabetic patients were \$12 855 and \$16 585 ($P<0.001$) and in the nondiabetic groups, \$10 164 for stenting and \$13 082 for surgery.

Conclusions— Multivessel diabetic patients treated with stenting had a worse 1-year outcome than patients assigned to CABG or nondiabetics treated with stenting. The strategy of stenting was less costly than CABG, however, regardless of diabetic status.

RANDOMIZED COMPARISON OF TICLOPIDINE AND CLOPIDOGREL AFTER INTRACORONARY STENT IMPLANTATION IN A BROAD PATIENT POPULATION

Megumi Taniuchi, MD, PhD; Howard I. Kurz, MD; John M. Lasala, MD, PhD

(*Circulation*. 2001;104:539)

Background— Although clopidogrel is used to prevent subacute stent thrombosis, its safety and efficacy have not been compared with ticlopidine in a randomized manner in the United States.

Methods and Results— Patients with successful intracoronary stent implantation were randomly assigned to therapy with ticlopidine or clopidogrel. Loading doses were administered immediately after the procedure, and the drugs were prescribed for 2 weeks. One thousand sixteen patients were enrolled: 522 patients were randomly assigned to ticlopidine therapy and 494 to clopidogrel. High-risk characteristics included recent myocardial infarction in 41.4% of the cases, angiographically evident thrombus in 20.9%, and abrupt or threatened closure in 3.64%. An intravenous glycoprotein IIb/IIIa inhibitor was used in 48.2% of the cases, and thrombocytopenia occurred in 1.43% of these patients. Failure to complete 2 weeks of therapy occurred in 3.64% of the patients treated with ticlopidine and in 1.62% of the patients treated with clopidogrel ($P=0.043$). Within 30 days, thrombosis of the stent occurred in 1.92% of the patients in the ticlopidine group and in 2.02% of the clopidogrel group ($P=0.901$). A major adverse cardiac event occurred in 4.60% of patients receiving ticlopidine and in 3.85% of patients receiving clopidogrel ($P=0.551$).

Conclusions— Clopidogrel is better tolerated than ticlopidine during a 2-week regimen after intracoronary stent implantation. Combining either thienopyridine with an intravenous platelet IIb/IIIa inhibitor appears to be safe. When applied to a broad spectrum of patients receiving stent implantation, clopidogrel confers similar protection as ticlopidine against subacute stent thrombosis and major adverse cardiac events.