The following studies were presented at the 47th Annual Scientific Sessions of the American College of Cardiology in Atlanta, Ga, March 29–April 1, 1998.

Acute Coronary Syndromes

TIMI 14 (Final Results)

**Presenter:** Elliott Antman, MD, Brigham and Women’s Hospital and Harvard Medical School, Boston, Mass.

**The study:** A prospective, multicenter, randomized, controlled trial of combined therapy with thrombolytic agents and the platelet glycoprotein IIb/IIIa antagonist abciximab in patients with AMI. A total of 681 patients were randomized to standard front-loaded tPA (100 mg), streptokinase (500 000, 750 000, 1 250 000, or 1 500 000 U) plus abciximab, low-dose tPA (20, 35, 50, or 65 mg) plus abciximab, or abciximab alone. In the streptokinase groups, lytic therapy was administered as a 30- to 50-minute infusion. In the tPA groups, lytic therapy was administered as either a bolus, a bolus plus a 30-minute infusion, or a bolus plus a 60-minute infusion. The primary endpoint of the study was the incidence of TIMI grade 3 flow at 90-minute angiography.

**The results:** The incidence of TIMI 3 flow at 90 minutes was 58% in the tPA-alone arm (n=146), 32% in the abciximab-alone arm (n=31), and 42% (n=36), 39% (n=49), 47% (n=47), and 80% (n=5; discontinued because of excessive bleeding and excess mortality) in the respective streptokinase-plus-abciximab groups. In the tPA-plus-abciximab groups, the incidence of TIMI 3 flow at 90 minutes was 53% (20-mg bolus; n=36), 38% (35-mg bolus; n=40), 62% (15-mg bolus, 20-mg infusion over 30 minutes; n=50), 54% (50-mg bolus; n=28), 61% (15-mg bolus, 35-mg infusion over 30 minutes; n=46), 79% (15-mg bolus, 35-mg infusion over 60 minutes; n=34), and 71% (15-mg bolus, 50-mg infusion over 60 minutes; n=31). A group that combined tPA (15-mg bolus, 35-mg infusion over 60 minutes) with higher-dose abciximab (and reduced heparin) had a 90-minute TIMI 3 flow rate of 69% (n=36). The incidence of major bleeding was 6% with tPA alone; 6% with abciximab alone; 5%, 8%, 14%, and 67% (discontinued arm) in the respective streptokinase groups; and 5%, 4%, 0%, 8%, 8%, 5%, and 0% in the respective tPA groups. The higher-dose abciximab group had a 15% incidence of major bleeding.

**Summary:** Abciximab alone achieves TIMI 3 flow rates comparable to streptokinase alone (in prior studies). The combination of reduced-dose thrombolytic therapy and abciximab augments the rate and extent of thrombolysis. With streptokinase plus abciximab, there appears to be a dose-related increased risk of major bleeding, and unacceptably high rates of bleeding and mortality occur with full-dose streptokinase plus abciximab. The combination of reduced-dose tPA (bolus plus infusion) with abciximab is a promising alternative to full-dose accelerated tPA.

PACT

**Presenter:** Allan Ross, MD, George Washington University Medical Center, Washington, DC.

**The study:** A randomized, placebo-controlled trial of preprocedure thrombolytic therapy in AMI patients treated with primary PTCA. AMI patients presenting within 6 hours of symptoms were randomized to receive either tPA (50-mg bolus; n=302) or placebo (n=304) and brought immediately to coronary angiography. If TIMI grade 3 flow was present at initial angiography, a second bolus of study medication was administered. If TIMI grade 0, 1, or 2 flow was present, the patient was treated with PTCA. A predischARGE follow-up angiogram was performed in all patients on day 5 to 7. The primary endpoint of the study was the ejection fraction on the predischARGE ventriculogram.

**The results:** On initial angiography, the 50-mg tPA group had higher rates of TIMI grade 2 (27.7% versus 19.5%) and grade 3 (32.8% versus 14.8%) flow than did the placebo group. There was no significant difference between groups in the final post-PTCA incidence of TIMI grade 3 flow. There was no significant increase in major bleeding events between groups. PredischARGE LVEF, the primary endpoint in the trial, was not significantly different between treatment groups. However, there was a significant difference in the entire population in mean predischARGE LVEF between patients who had TIMI grade 3 flow on arrival in the catheterization laboratory (mean LVEF, 62%), those who had grade 3 flow after PTCA (mean LVEF, 58%), and those who never achieved TIMI grade 3 flow (mean LVEF, 55%).

**Summary:** AMI patients treated with a 50-mg bolus of tPA had significant improvement in vessel patency before PTCA. Early patency in the entire patient population was associated with an improvement in ventricular function. There was no adverse effect of preprocedure thrombolytic therapy on procedural safety or outcome.
Selected Abbreviations and Acronyms
- AMI = acute myocardial infarction
- AR = atrial regurgitation
- ICD = implantable cardioverter defibrillator
- IL = interleukin
- LVEF = left ventricular ejection fraction
- MI = myocardial infarction
- MLD = minimum lumen diameter
- MR = mitral regurgitation
- QOL = quality of life
- rhVEGF = recombinant human vascular endothelial growth factor
- tPA = tissue plasminogen activator

ESSENCE (1-Year Results)
**Presenter:** Marc Cohen, MD, Allegheny University of the Health Sciences, Hahnemann Division, Philadelphia, Pa.

**The study:** A multicenter, randomized, double-blind, placebo-controlled, parallel group trial comparing low-molecular-weight heparin (enoxaparin) with unfractionated heparin in patients with unstable angina/non–Q-wave MI. A total of 3171 patients in 176 centers in 8 countries were randomized to enoxaparin 1 mg/kg every 12 hours plus aspirin versus standard intravenous unfractionated heparin (titrated to activated clotting times) plus aspirin. Prior reports indicated significant benefit of enoxaparin at 30 days in reducing the combined incidence of death, MI, or recurrent angina. The current data represent follow-up of these patients to 1 year.

**The results:** The composite incidence of death/MI/recurrent angina at 1 year was 32.0% in the enoxaparin group and 35.7% in the heparin group (P=0.022). The composite incidence of death/MI at 1 year was 11.5% in the enoxaparin group and 13.5% in the heparin group (P=0.08). By 1 year in the enoxaparin group, there were significantly fewer repeat diagnostic catheterizations (55.8% versus 59.4% with unfractionated heparin) and fewer repeat revascularizations (35.9% versus 41.2% with unfractionated heparin). Regarding new end-point events (repeat catheterization or revascularization), there were no significant differences between groups in the time period from day 31 to 1 year.

**Summary:** In patients with unstable angina/non–Q-wave MI, the early benefits of enoxaparin over unfractionated heparin are sustained at 1-year follow-up.

ARGAMI-2
**Presenter:** Elieser Kaplinsky, MD, Sheba Medical Center, Tel-Hashomer, Israel.

**The study:** A randomized, controlled trial comparing 2 different doses of the direct thrombin antagonist argatroban (60-μg bolus plus 2-μg·kg⁻¹·min⁻¹ infusion for 72 hours or 120-μg bolus plus 4-μg·kg⁻¹·min⁻¹ infusion for 72 hours) with heparin in patients with AMI treated with thrombolytic therapy (streptokinase or tPA). The primary end point of the trial was 30-day mortality. After an interim analysis of 609 patients, the lower-dose argatroban arm of the study was discontinued for lack of efficacy; the trial continued enrollment, and a total of 1001 patients were considered in the final analysis.

**The results:** There was no significant difference in 30-day mortality between the high-dose argatroban group (5.5%; n=494) and the heparin group (5.4%; n=507). Other secondary clinical event rates were also similar between groups. There was a trend toward less frequent major bleeding events in the argatroban group.

**Summary:** In patients with AMI treated with thrombolytic therapy, argatroban was comparable to heparin in terms of clinical efficacy and exhibited a trend toward fewer major bleeding events.

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Coronary Stenting

**EPI-STENT**
**Presenter:** Eric Topol, MD, Cleveland Clinic, Cleveland, Ohio.

**The study:** A multicenter, randomized, parallel group trial comparing stenting plus abciximab versus stenting alone versus PTCA plus abciximab in 2399 patients undergoing elective and emergent coronary intervention; all patients received aspirin. The procedural heparin dose in the group not receiving abciximab was 100 U/kg titrated to activated clotting times >300 seconds; in the 2 abciximab arms, the heparin dose was 70 U/kg, titrated to activated clotting times >200 seconds. The primary end point of the study was the 30-day composite of death/MI/urgent revascularization.

**The results:** The 30-day incidence of death/MI/revascularization was 10.8% in the stent-only group, 5.3% in the stent-plus-abciximab group, and 6.9% in the PTCA-plus-abciximab group. The differences between groups were well established by 24 hours after the procedure. A large component of the 30-day composite end point was the incidence of death or large non–Q-wave infarctions (5× elevation of creatine kinase with positive MB) infarctions: 7.8% in the stent-only group, 4.7% in the stent-plus-abciximab group, and 3.0% in the PTCA-plus-abciximab group. The incidence of major bleeding events tended to be lower in the 2 abciximab arms than in the stent-only study arm (higher-dose heparin). There was comparable benefit both in patients with stable angina and in higher-risk patients with acute coronary syndromes.

**Summary:** Abciximab was effective in reducing the composite 30-day incidence of death/MI/urgent revascularization in patients undergoing stent implantation. The use of balloon angioplasty with abciximab had a lower incidence of composite events at 30 days than stenting alone. Six-month follow-up data, including angiographic substudies and need for repeat target-vessel revascularization, will be forthcoming.

**STENT PAMI**
**Presenter:** Cindy Grines, MD, William Beaumont Hospital, Royal Oak, Mich.

**The study:** A multicenter, randomized, parallel group trial of primary PTCA versus implantation of a heparin-coated stent in patients with AMI. A total of 900 patients at 65 clinical centers worldwide were randomized to PTCA (n=448) or stent (n=452); 67 (15.1%) of the PTCA patients crossed over to stent. The primary end point of the trial was the composite incidence of death, recurrent MI, disabling
stroke, or ischemia-driven target-vessel revascularization at 6 months.

The results: The clinical and angiographic results during hospital stay and at 30 days were presented. The acute postprocedural MLD was significantly better in the stent group (mean, 2.55 versus 2.11 mm with PTCA). Angiographic success was high (97% to 99%) in both groups. The incidence of subsequent clinical end-point events at 30 days was low: death, 3.5% versus 1.8% (stents versus PTCA, \(P=NS\)); recurrent MI, 0.4% versus 1.1% (\(P=NS\)); disabling cerebrovascular accident, 0.2% versus 0% (\(P=NS\)); and ischemia-driven target-vessel revascularization, 0.6% versus 2.5% (\(P=0.006\)). The composite end point at 30 days was not significantly different between groups (4.2% for stent versus 5.4% for PTCA; \(P=NS\)). There was no difference in bleeding complications between groups. Complete 6-month data will be available in the fall of 1998.

Summary: Compared with primary PTCA in AMI, the use of a heparin-coated Palmaz-Schatz stent was associated with a larger immediate MLD, a comparable procedure success rate, a lower 30-day rate of ischemia-driven target-vessel revascularization, and a comparable composite rate of adverse clinical events at 30 days.

TOSCA
Presenter: Christopher Buller, MD, Vancouver General Hospital, Vancouver, Canada.

The study: A multicenter, randomized trial of primary stenting (with a heparin-coated Palmaz-Schatz stent) versus balloon angioplasty in 410 patients with symptomatic nonacute total occlusion (TIMI grade 0/1 flow) of native coronary arteries. Randomization was stratified by duration of occlusion (\(\leq6\) weeks versus \(>6\) weeks/unknown); patients were enrolled in the study after successful placement of a guidewire across the occlusion. The primary end point of the trial was failure of sustained patency, defined as presence of less than TIMI grade 3 flow within 6 months of the procedure, as confirmed by angiography.

The results: The target lesions were complex, with mean lesion work length of 35 mm and use of multiple stents in the majority of patients randomized to stent. A total of 10% of the patients crossed over from the PTCA to the stent arm of the trial during the initial procedure because of suboptimal results; 4% of the patients randomized to stent underwent balloon angioplasty instead, usually because of inability to deliver the stent. The follow-up incidence of TIMI grade 0 flow was 11% in the PTCA group and 6.8% in the stent group; the incidence of TIMI grade 1 flow was 2.5% in the PTCA group and 1.6% in the stent group; the incidence of TIMI grade 2 flow was 6% in the PTCA group and 2.6% in the stent group. The overall incidence of failure of sustained patency was 19.5% in the PTCA group and 10.9% in the stent group (\(P=0.024\)). The postprocedural initial MLD was 1.90 mm in the PTCA group and 2.45 mm in the stent group. The final follow-up MLD was 1.23 mm in the PTCA group and 1.48 mm in the stent group. The binary rate of restenosis (<50% diameter stenosis at follow-up) was 70% in the PTCA group and 56% in the stent group. However, the incidence of target-vessel revascularization was only 13.9% in the PTCA group and 7.4% in the stent group. The overall incidence of adverse clinical events did not differ between groups.

Summary: In patients with symptomatic occlusions of native coronary arteries, stenting resulted in a higher 6-month patency, larger follow-up MLDs, and a decreased need for target-vessel revascularization. There remains a high binary angiographic restenosis rate in this anatomically complex group of patients. Stenting, if feasible, appears to be the preferable therapy.

Intracoronary Radiation Therapy
BERT Feasibility Study
Presenter: Spencer King, MD, Emory University, Atlanta, Ga.

The study: A trial of adjunctive \(\beta\)-radiation therapy in patients undergoing coronary angioplasty for de novo lesions at 4 clinical centers. After successful PTCA, qualifying patients received 1 of 3 doses of radiation (12, 14, or 16 Gy) delivered via a \(^{90}\)Sr\(^{90}\)Y \(\beta\)-source advanced hydraulically through a closed-end delivery catheter. The primary end point of the trial was 6-month quantitative angiography. Data on the first 64 patients with de novo lesions and complete angiographic follow-up were presented.

The results: Mean MLD was 0.75 mm before intervention, 2.09 mm immediately after intervention, and 2.07 mm at 6-month follow-up, corresponding to mean percent diameter stenosis of 75%, 24%, and 26%, respectively. Overall, the dichotomous rate of restenosis was 14% (20% in the 12-Gy group and 11% in the 14- and 16-Gy groups). Target-lesion revascularization was 9%. On quantitative coronary angiography, it was noted that 38 of 64 patients had 6-month follow-up lumen sizes that were slightly larger than the immediate postprocedure lumen. No aneurysms or pseudoaneurysms were observed.

Summary: Adjunctive therapy with locally delivered \(\beta\)-irradiation appears to result in improved lesion geometry at 6-month angiographic follow-up. This technique shows very promising preliminary results, but additional large-scale follow-up data are warranted.

Coronary Artery Disease
Intracoronary rhVEGF
Presenter: Timothy Henry, MD, Hennepin County Medical Center, Minneapolis, Minn.

The study: A dose-ranging trial of rhVEGF in patients with severe coronary artery disease who are not optimal candidates for revascularization. A total of 15 patients received two 10-minute intracoronary infusions of 0.005, 0.017, 0.050, or 0.67 \(\mu\)g \(\cdot\) kg\(^{-1}\) \(\cdot\) min\(^{-1}\). Pharmacodynamic sampling and hemodynamic monitoring were performed for 24 hours; nuclear perfusion studies were done at baseline and 30 and 60 days after treatment. Follow-up 60-day angiograms were done in 7 patients who demonstrated improved nuclear perfusion studies.

The results: rhVEGF therapy was well tolerated. At maximal doses, there was a significant reduction (mean, 28%) in systolic blood pressure that appeared to be related to a local vasodilator effect. Nuclear perfusion studies showed improved perfusion in 7 of 15 subjects. From a symptomatic
standpoint, 13 of 15 patients had improvement of ≥1 anginal class. On core laboratory angiographic analysis, there were improved collateral arteries by visual assessment in 5 of 7 patients and improved collateral density counts in 7 of 7 patients.

**Summary:** rhVEGF is well tolerated. Maximal doses may cause a fall in blood pressure. Initial clinical results are encouraging and indicate improved collaterals, improved perfusion, and improved symptoms in a significant number of patients. However, these preliminary results will need larger-scale corroboration.

**ACADEMIC**

**Presenters:** Jeffrey L. Anderson, MD, and J. Brent Muhlstein, Latter Day Saints Hospital, University of Utah, Salt Lake City, Utah.

**The study:** A randomized, placebo-controlled trial of azithromycin in patients with evidence of coronary artery disease and positive titers to *Chlamydia pneumoniae*. A total of 447 patients with coronary artery disease were screened; 302 with positive *C pneumoniae* titers (≥1:16) were randomized to placebo (n = 152) or azithromycin (n = 150). Treatment was continued for 3 months. The primary end point of the study was the change in a composite of 4 inflammatory markers (C-reactive protein, IL-1, IL-6, and tumor necrosis factor) at 3 months. Additional follow-up was conducted at 6 months.

**The results:** At 3 months, there were no significant changes in the individual inflammatory markers or in the composite end point. There were also no significant changes in antichlamydial IgG levels or IgA levels at 3 or 6 months. At 6 months, the azithromycin group was noted to have a significant decrease in C-reactive protein and IL-6; IL-1 and tumor necrosis factor were unchanged in both groups. Only limited long-term clinical follow-up data are available; at present there are no significant differences between groups in clinical outcomes at 6 months. Azithromycin therapy was well tolerated.

**Summary:** In patients with coronary artery disease and positive *C pneumoniae* titers, azithromycin therapy did not significantly reduce serum markers of inflammation at 3 months; by 6 months, there were significant decreases in C-reactive protein and IL-6. Long-term clinical follow-up data will be forthcoming.

**Congestive Heart Failure**

**ATLAS**

**Presenter:** Milton Packer, MD, Columbia University College of Physicians and Surgeons, New York, NY.

**The study:** A multicenter, randomized, placebo-controlled trial of low-dose versus high-dose ACE-inhibitor therapy in patients with congestive heart failure. A total of 3164 patients with class II, III, or IV congestive heart failure at 287 clinical centers in 19 countries were randomized to either low-dose (2.5 to 5 mg/d) or high-dose (32.5 to 35 mg/d) lisinopril. To qualify for the study, patients had to be symptomatic, have an ejection fraction ≤30%, and be on therapy with digitalis, diuretics, and an ACE inhibitor. After initiation of study drug, therapy patients were followed up for 3.5 to 5 years. The primary end point of the study was all-cause mortality.

**The results:** By the time of study termination, 17% of patients were taking a nonstudy ACE inhibitor. Total mortality (44.9% with low-dose versus 42.5% with high-dose therapy) was not significantly different between groups. There was a nonsignificant trend toward lower cardiovascular mortality in the high-dose lisinopril group (37.2% with high-dose therapy versus 40.2% with low-dose therapy; *P* = 0.073). There was a significant decrease in the composite end point of mortality and recurrent hospitalization with high-dose lisinopril (79.8% versus 83.9% with low-dose therapy; *P* = 0.002); this effect was similar across all subgroups of patients. There was little difference between groups in the incidence of drug-related adverse effects.

**Summary:** Compared with low-dose therapy, high-dose lisinopril therapy did not result in a significant decrease in mortality but was associated with a significant reduction in the composite incidence of mortality and recurrent hospitalization.

**RESOLVD (Part II)**

**Presenter:** Jean-Lucien Rouleau, MD, Montreal Heart Institute, Montreal, Quebec, Canada.

**The study:** A multicenter, randomized, placebo-controlled trial of metoprolol CR in patients with congestive heart failure. Part I of the study compared candesartan, enalapril, and combination therapy. Part II took patients who had completed part I and randomized them to metoprolol CR (200 mg/d; n = 215) or placebo (n = 211). Treatment was continued for 24 weeks. The primary end point of the trial was functional status, as indicated by a 6-minute walk test, NYHA functional class, and a QOL assessment.

**The results:** The metoprolol CR group had a significant reduction in heart rate but no change in blood pressure. At follow-up, there was no significant difference between groups in 6-minute walk test results, NYHA class, or QOL scores. Metoprolol patients demonstrated a decline in angiotensin II and renin levels and an increase in brain natriuretic peptide and atrial natriuretic peptide levels. Over time, ejection fraction did not change in the placebo group but did increase significantly in the metoprolol group (*P* = 0.001). Ventricular volume increased in the placebo group but did not change in the metoprolol group. The overall number of clinical events was very small in both groups. Metoprolol therapy was very well tolerated.

**Summary:** Six-month treatment with metoprolol in patients with congestive heart failure is well tolerated but is not associated with any significant improvement in 6-minute walk testing, NYHA class, or QOL scores. There was a significant increase in ejection fraction and a prevention of ventricular dilatation with metoprolol therapy.

**Arrhythmias**

**CASH**

**Presenter:** Karl Kuck, MD, St. George Hospital, Hamburg, Germany.

**The study:** A multicenter, open-label, randomized trial comparing ICD therapy with pharmacological treatment in
survivors of sudden cardiac death. The study was initiated in 1987 and was originally designed to compare ICD with propafenone, amiodarone, and metoprolol. In July 1990, the protocol was modified to include the use of transvenously implanted defibrillators. In March 1992, an interim analysis (mean follow-up of 11 months at the time) indicated excess mortality in the propafenone arm of the study (compared with ICD), and the propafenone arm was dropped. The amiodarone and metoprolol arms of the trial continued, and follow-up for a minimum of 2 years after randomization was available for a total of 349 patients. The primary end point of the trial was total mortality.

The results: At follow-up, total 2-year mortality in the ICD group was 12.1% versus 19.6% in the combined drug therapy groups ($P=0.047$). There was no significant mortality difference between the 2 types of drug therapy.

Summary: In survivors of sudden cardiac death, ICD therapy is superior to propafenone in terms of 1-year total mortality. ICD therapy is also associated with a significantly lower 2-year total mortality than amiodarone or metoprolol. In this population, 2-year mortality did not appear to differ between amiodarone and metoprolol.

CIDS

Presenter: Stuart Connolly, MD, McMaster University, Hamilton, Ontario, Canada.

The study: A multicenter, randomized, parallel group trial comparing ICD therapy ($n=328$; using any currently available device) with amiodarone ($n=331$; 1200 mg/d for 1 week, 400 mg/d for 10 weeks, then 300 mg/d) in cardiac arrest survivors or patients with sustained, symptomatic ventricular tachycardia/fibrillation. The trial was initiated in 1990 and continued through December 1997. Patients were followed up for at least 1 year. The primary end point of the trial was all-cause mortality; a secondary end point was the incidence of arrhythmic death.

The results: By the end of 5 years, 22% of the amiodarone patients had received a subsequent crossover ICD and 30% of the ICD patients had received subsequent crossover amiodarone. In the ICD group, there was a higher 30-day mortality rate in patients with thoracotomy devices (3.3%, $n=33$) versus transvenous devices (0.36%, $n=227$). All-cause mortality was slightly but not significantly lower in the ICD group ($\approx 27\%$ at 4 years with ICD versus $\approx 33\%$ with amiodarone; $P=0.07$). Both forms of therapy were well tolerated.

Summary: In this population of patients with a history of sudden cardiac death or symptomatic sustained ventricular tachycardia/fibrillation, ICD therapy was associated with a modest, nonsignificant reduction in all-cause mortality.

ARCH

Presenter: Thomas Guarnieri, MD, Greater Baltimore Medical Center, Baltimore, Md.

The study: A multicenter, randomized, controlled clinical trial of amiodarone for the prevention of atrial fibrillation in patients after open-heart surgery. Patients undergoing CABG surgery, valve surgery, or combined procedures were randomized to amiodarone (2 g over 2 days; no loading dose; $n=158$) or placebo ($n=147$). Study drug infusions were begun in the surgical intensive care unit after surgery at the time of the first hemodynamic measurements. The primary end point of the study was the postoperative length of hospital stay.

The results: The amiodarone group had a significantly lower incidence of atrial fibrillation (35.4% versus 47.2% with placebo); this difference became apparent in the first 3 postoperative days. There was a nonsignificant trend toward shorter hospital lengths of stay in the amiodarone group (7.5 ± 5.9 versus 8.2 ± 6.2 days with placebo). In the overall population, the development of atrial fibrillation was associated with a significantly longer length of stay (9.1 ± 5.3 versus 7.1 ± 6.6 days in patients without atrial fibrillation). Amiodarone therapy was well tolerated. The incidence of major morbidity events in this population was very low.

Summary: A low-dose, short course of intravenous amiodarone reduced the incidence of postoperative atrial fibrillation but did not significantly reduce postoperative hospital lengths of stay in this study.

Dexfenfluramine

Randomized Redux Study

Presenter: Neil Weissman, MD, Georgetown University Medical Center, Washington, DC.

The study: A prospective, double-blind, randomized, placebo-controlled trial of 2 doses of dexfenfluramine (Redux) in patients with obesity. The trial was stopped when Redux was withdrawn from the market in response to concerns about valvular abnormalities. As part of the trial, echocardiograms were obtained in all patients after a median of $\approx 77$ days of drug therapy. Echocardiograms were reviewed independently and any valvular abnormalities noted and categorized. Baseline echos were not routinely performed. The primary end point of this substudy was the Food and Drug Administration’s definition of significant valvular regurgitation, ie, the incidence of MR ($\approx$ moderate) or AR ($\approx$ mild).

The results: There was a trend toward less valvular regurgitation in the placebo group ($n=330$, AR 3.6%, MR 1.2%, composite 4.5%) than in the 2 Redux groups (Redux: $n=342$, AR 5.0%, MR 1.7%, composite 6.5%; Redux SR [a sustained release formulation that has not been commercially available]: $n=329$, AR 5.8%, MR 1.8%, composite 7.3%). However, this difference did not achieve statistical significance. There was a high incidence ($\approx 75\%$) of any regurgitation (including physiological and trivial) in the study population. Estimated pulmonary artery pressures were not different between groups. Redux patients were noted to have slightly more frequent physiological or mild MR and some minor restriction of the motion of the posterior leaflet of the mitral valve.

Summary: In this short-term Redux therapy trial, Redux was not associated with a significant increase in clinically meaningful valvular regurgitation. There may be an increase in physiological or mild MR and some minor restriction of the posterior mitral leaflet. The incidence of significant valvular abnormalities in this study was much lower than in previous early reports.
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James J. Ferguson

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