Late Breaking Science: Linking Genes to Function in the Heart and Vasculature

CLINICAL ABSTRACTS

Results of the Treat Angina With Aggrastat and Determine the Cost of Therapy With an Invasive or Conservative Strategy (TACTICS-TIMI 18) Trial: A Comparison of Invasive Versus Conservative Strategy in Patients With Unstable Angina and Non–ST-Segment Elevation Myocardial Infarction

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Background: In the treatment of patients with unstable angina and non-ST-segment elevation myocardial infarction (UA/NSTEMI), debate exists as to whether an early invasive vs. a conservative strategy is optimal therapy. Methods: In the international TACTICS-TIMI 18 trial, 2222 patients with UA/NSTEMI who had either electrocardiographic changes, elevated cardiac markers or a history of prior coronary artery disease, were immediately treated with aspirin, heparin and the glycoprotein (GP) IIb/IIIa inhibitor tirofiban. They were randomized to an early invasive strategy with routine catheterization and revascularization as appropriate between 4–48 hours, or to a conservative, “selective invasive” strategy, with catheterization performed only if the patient had objective evidence of recurrent ischemia or a positive stress test. The primary endpoint was a composite of death, myocardial infarction or rehospitalization for acute coronary syndromes at 6 months. Results: The rate of the primary endpoint was significantly reduced with the invasive strategy compared to the conservative strategy, 15.9% vs. 19.4%, odds ratio (OR) 0.78, p = 0.025. The rate of death or MI at 6 months was also significantly reduced (9.5% vs. 7.3%, respectively, OR 0.74, p = 0.005). Conclusion: In patients with UA/NSTEMI treated with the GP IIb/IIIa inhibitor tirofiban, an early invasive strategy resulted in a significant reduction in major cardiac events. These data suggest a need to update the ACC/AHA Unstable angina guidelines, and to modify the clinical approach to managing unstable angina with broader use of an early invasive strategy with upstream GP IIb/IIIa inhibition.

Effect of the Angiotensin Receptor Blocker Valsartan on Morbidity and Mortality in Heart Failure: the Valsartan Heart Failure Trial (Val-HeFT)

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In order to assess the efficacy of the angiotensin receptor blocker valsartan in the treatment of heart failure (HF), 5010 patients were studied in 16 countries on 4 continents. Patients with chronic HF (NYHA III (62%), III (36%) and IV (2%), ejection fraction (EF) <40% and left ventricular diastolic transverse diameter (LVDD) >2.9 cm/m2 were randomly assigned to receive placebo (P) or valsartan (V) titrated to 160 mg BIQ in addition to all other appropriate therapy including ACE inhibitors (93%), beta blockers (68%), diuretics (86%) and digoxin (67%). Primary end-points were all-cause mortality (M) and mortality plus morbidity (M+). This included hospitalization for heart failure (adjudicated), cardiac arrest with resuscitation, or need for intravenous support for worsening heart failure. Time to death was similar in the two groups but time to first M+ event was significantly reduced by 13.3% by V (32.1% in P, 28.8% in V; P = 0.001). The benefit of V on M+ event was significantly reduced by 13.3% by V (32.1% in P, 28.8% in V; P = 0.001). The benefit of V on M was particularly prominent in patients not taking an ACE inhibitor (42.5% to 10.1%, p = 0.001), with the greatest effect of V on placebo 16.3% vs. 6.3%, p = 0.001. Consequently, in patients with UA/NSTEMI treated with the GP IIb/IIIa inhibitor tirofiban, an early invasive strategy resulted in a significant reduction in major cardiac events. These data suggest a need to update the ACC/AHA Unstable angina guidelines, and to modify the clinical approach to managing unstable angina with broader use of an early invasive strategy with upstream GP IIb/IIIa inhibition.

Fluvastatin in Acute Myocardial Infarction: Effects on Early and Late Ischemia and Events: the FLORIDA Trial

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In post-myocardial infarction (MI) patients, residual ischemia is related to an adverse clinical outcome. Thus, early initiation of statin treatment may be particularly beneficial after MI. The “Fluvastatin On Risk Diminishing after Acute myocardial infarction” (FLORIDA) trial is a prospective, placebo-controlled multicenter trial, designed to study the effect of Fluvastatin 80 mg per day on post-MI ischemia and adverse cardiac events. MI patients were randomized to Fluvastatin 80 mg/day or placebo administered during admission and for one year. Events were adjudicated by a blinded monitoring committee. After 12 months treatment, fluvastatin lowered LDL cholesterol from 3.5 to 2.7 mmol/L and placebo from 3.6 to 3.9 mmol/L (p < 0.001). At baseline, 6 weeks and 12 months ischemia on AECG was present in 12%, 8% and 6% of the patients on fluvastatin and in 13%, 6% and 10% of the patients on placebo (p = 0.03). On fluvastatin the ischemic burden ( ischemia was reduced from 13.1% ± 5.2% to 5.1% ± 4.4% and on placebo 16.6 ± 6.3, ± 5.3 and 3.1 ± 4.6 (p < 0.03). At baseline, 6 months and 12 months ischemia on AECG was present in 12%, 8% and 6% of the patients on fluvastatin and in 13%, 6% and 10% of the patients on placebo (p = 0.03). A trend toward a beneficial effect of fluvastatin on MACE was observed, cardiac arrest with resuscitation, or worsening angina with new objective evidence of ischemia requiring emergency rehospitalization, analyzed by time to first event. Secondary endpoints included the components of the primary endpoint as well as stroke, coronary revascularization, worsening congestive heart failure, and worsening angina without new objective evidence of ischemia.

The Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) Trial: Effects of Intensive Atorvastatin Treatment on Early Recurrent Events After an Acute Coronary Syndrome

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Background: Previous trials have demonstrated that treatment with conventional doses of statins, initiated in patients with stable coronary heart disease, reduces death and non-fatal ischemic events over periods of years. The Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) trial tested the hypothesis that intensive treatment with atorvastatin, initiated immediately after an acute coronary syndrome, reduces death and non-fatal ischemic events in the ensuing 16 weeks. Methods: We conducted a randomized, double-blind trial comparing atorvastatin (80 mg daily) with placebo in 3006 patients with unstable angina or non-Q-wave acute myocardial infarction. Treatment was initiated 24 to 96 hours after hospitalization and continued for 16 weeks. The primary combined endpoint was death, non-fatal acute myocardial infarction, cardiac arrest with resuscitation, or worsening angina with new objective evidence of ischemia requiring emergency rehospitalization, analyzed by time to first event. Secondary endpoints included the components of the primary endpoint as well as stroke, coronary revascularization, worsening congestive heart failure, and worsening angina without new objective evidence of ischemia.

Results: A primary endpoint event occurred in 228 patients in the atorvastatin group (14.8%) and 269 patients in the placebo group (17.4%) (relative risk 0.84; 95% confidence interval 0.70 to 1.00; P = 0.048). The greatest effect of atorvastatin was on worsening angina with new objective evidence of ischemia requiring emergency rehospitalization (relative risk 0.74; 95% confidence interval 0.57 to 0.95; P = 0.02). Death, non-fatal myocardial infarction, and cardiac arrest were less frequent in the atorvastatin group than in the placebo group, but the differences were not statistically significant.

Conclusion: Early, intensive lipid-lowering with atorvastatin reduces recurrent ischemic events in the first 16 weeks after an acute coronary syndrome.
The Department of Veterans Affairs Aneurysm Detection and Management (ADAM) Study.
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Circulation. 2000;102:2672
doi: 10.1161/01.CIR.102.21.2672-c

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/102/21/2672.5

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