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

CLINICAL ABSTRACTS

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

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Background: In the treatment of patients with unstable angina and non-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-TI MI 18 trial, 22220 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 ratio 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 ratio of death or MI at 6 months was also significantly reduced (9.5% vs. 7.3% respectively, OR 0.74, p = 0.009). Conclusions: 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 in an angiographic, ambulatory ECG monitoring (ACEG) and major adverse cardiac events (MACE). Included were 540 patients (83% male, age 61 ± 11 yrs) with an acute myocardial infarction (43% anterior) and a cholesterol value <6.5 mmol/L (mean 5.4 ± 0.7). AECGs were performed during admission for MI, after 6 weeks and 12 months. Fluvastatin 80 mg/day or placebo were 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 ACEG was present in 12%, 8% and 6% of the patients on fluvastatin and on 13%, 6% and 10% of the patients on placebo (p = 0.04). On fluvastatin the ischemic burden [Mean ± SE] was 13.4 ± 5.2 and 13 ± 5.1 mm min⁻¹ on placebo 16 ± 6.5 ± 3 ± 13 ± 5.1 mm min⁻¹ (p = 0.04). At 12 months, MACE and residual AECG ischemia occurred in 30% of fluvastatin patients and in 36% of placebo patients (p = 0.04). For this combined endpoint, ischemia at baseline was highly predictive (OR 2.92, 95% CI 1.61–5.39, p = 0.0004). One-year mortality was 2.6% on fluvastatin and 4.9% on placebo (p = 0.22). Toward a beneficial clinical effect of fluvastatin on MACE, ischemia was observed, cardiac event was severe with ischemia at baseline (p = 0.08). Conclusion: Post-MI ischemia on ACEG was highly predictive for adverse outcome after one year. Fluvastatin had no beneficial effect on post-MI ischemia after 6 weeks or 12 months. Although not powered for this purpose, this study showed no effect of fluvastatin on MACE. A positive trend was observed in patients with severe ischemia at baseline.

The Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) Trial: Effects of Intensive Atorvastatin Treatment on Recent 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 3086 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 or non-fatal acute myocardial infarction, or ischemia 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. Of the other secondary endpoints, there were significantly fewer strokes in the atorvastatin group than in the placebo group (12 versus 24 events). In the atorvastatin group, mean LDL cholesterol declined from 123 to 72 mg/dL (3.2 to 1.9 mmol/L). Abnormal liver transaminases (≥3 times upper limit of normal) occurred in 2.5% and 6% of patients in atorvastatin and placebo groups, respectively. Conclusion: Early intensive lipid-lowering with atorvastatin reduces recurrent ischemic events in the first 16 weeks after an acute coronary syndrome.
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_Circulation_. 2000;102:2672
doi: 10.1161/01.CIR.102.21.2672-b
_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/102/21/2672.4

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