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

Christopher P. Cannon, William S. Weintraub, Laura Demopoulos, Debbie Robertson, Paul DeLucca, Carolyn H. McCabe, Eugene Braunwald, Brigham and Women's Hospital, Boston MA

Background: In the treatment of patients with unstable angina and non-ST-segment elevation myocardial infarction (UAINSTEMI), debate exists as to whether an early invasive vs. conservative strategy is optimal therapy. Methods: In the international TACTICS-TIMI 18 trial, 22220 patients with UAINSTEMI 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 within 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 < 0.05). Conclusion: In patients with UAINSTEMI 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 BlockerValsartan on Morbidity and Mortality in Heart Failure: the Valsartan Heart Failure Trial (Val-HeFT)

Jay N. Cohn and Gianni Tognoni for the Val-HeFT Investigators, Minneapolis, Minnesota and Milan, Italy

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 II (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) (labeled to 160 mg BID) 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+M), which 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 to first M = M event was significantly reduced by 13.3% by V (32% vs. 35% in P, p< 0.001). HF hospitalization was significantly reduced by 27.5% by V (18% in P, 13% in V, p < 0.003). The benefit of V on M = M was particularly prominent in patients not taking a beta blocker (37% vs. 30.8%, P < 0.001) and in those taking a beta blocker (42.9% to 24.9%, P < 0.001). The benefit on M = M was accompanied by significant improvements in NYHA class, quality of life, and EF. These data demonstrate clinical efficacy of valsartan in heart failure in patients already receiving standard HF therapy.

The Department of Veterans Affairs Aneurysm Detection and Management (ADAM) Study.

FA Lederer, SE Wilson, GR Johnson, for the ADAM VA Cooperative Study Group, VA Medical Centers, Minneapolis MN, West Haven CT, Long Beach CA.

Aortic aneurysm is the 13th leading cause of death in the US, and most of these deaths are due to rupture or elective repair of abdominal aortic aneurysm (AAA). Because AAA diameter is the strongest predictor of patient AAA rupture, a principal question in AAA management is the appropriate AAA diameter at which to offer elective repair to both prevent rupture and minimize deaths from elective surgery. The Society for Vascular Surgery has recommended the appropriate AAA diameter at which to offer elective repair to both prevent rupture and minimize deaths from elective surgery. The Society for Vascular Surgery has recommended that the appropriate AAA diameter at which to offer elective repair to both prevent rupture and minimize deaths from elective surgery. The Society for Vascular Surgery has recommended that, for intravenous support for worsening heart failure. Time to death was similar in the two groups but to first M = M event was significantly reduced by 13.3% by V (32% vs. 35% in P, p< 0.001). HF hospitalization was significantly reduced by 27.5% by V (18% in P, 13% in V, p < 0.003). The benefit of V on M = M was particularly prominent in patients not taking a beta blocker (37% vs. 30.8%, P < 0.001) and in those taking a beta blocker (42.9% to 24.9%, P < 0.001). The benefit on M = M was accompanied by significant improvements in NYHA class, quality of life, and EF. These data demonstrate clinical efficacy of valsartan in heart failure in patients already receiving standard HF therapy.

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

Gregory G. Schwartz, Anders G. Olsson, Michael D. Ezekowitz, Peter Ganz, Michael F. Oliver, David Waters, Andreas Zeiher, Bernard Chatman, Sally Leslie, and Theresa Stern for the MIRACL Investigators

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, 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 = 0.045). 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. On 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 0.6% 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.
The Department of Veterans Affairs Aneurysm Detection and Management (ADAM) Study. 
FA Lederle, SE Wilson and GR Johnson

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
Copyright © 2000 American Heart Association, Inc. All rights reserved.
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

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/