Am J Cardiol (2004);94:9-13
Effect of intracoronary adenosine infusion during coronary intervention on myocardial reperfusion injury in patients with acute myocardial infarction
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Despite early recanalization of an occluded infarct artery, up to 33% of patients with acute myocardial infarction do not obtain complete myocardial reperfusion due to a process of reperfusion injury. This study assessed whether adjunctive therapy with adenosine might prevent or attenuate the phenomenon of myocardial reperfusion injury. Myocardial reperfusion was assessed in 79 consecutive patients receiving a 20-minute intracoronary infusion of adenosine during percutaneous coronary intervention (PCI) and in a historical cohort of 200 patients with acute myocardial infarction who were treated with PCI (controls). Myocardial reperfusion injury was defined as persistent (> or =50% of initial value) ST-segment elevation after successful recanalization. Its effect on infarct size was evaluated by calculating the Selvester QRS score before intervention and at follow-up. Myocardial reperfusion injury was present in 19% of patients receiving adenosine versus 35% of control patients (p = 0.004). Evaluation of infarct expansion over time showed almost no change in the QRS score in patients receiving adenosine (3.4 +/- 3.0 before PCI; 3.5 +/- 3.1 at follow-up). In contrast, infarct QRS score in the control group worsened from 3.1 +/- 2.7 before PCI to 4.5 +/- 3.2 at follow-up (p = 0.003 treatment with adenosine vs control). Multivariate analysis identified adjunctive therapy with adenosine as an independent protective determinant of myocardial reperfusion injury and of infarct expansion. The rate of major adverse cardiac events (death and myocardial infarction) at 1 month tended to be lower in patients receiving adenosine (4% vs 6.5%, p = 0.7) and was mainly observed in patients with evidence of myocardial reperfusion injury (cardiac event rate 2% in patients with ST-segment elevation of <50% vs 14% in patients with ST-segment elevation > or =50%, p = 0.003). Thus, impaired myocardial reperfusion is the most important determinant of clinical outcome in patients with acute myocardial infarction treated with PCI. Adjunctive therapy with intracoronary infusion of adenosine during PCI prevents the occurrence of severe myocardial reperfusion injury and is associated with less infarct expansion.
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Am Heart J (2004);148:E14
Adjunctive effect of hyperbaric oxygen treatment after thrombolysis on left ventricular function in patients with acute myocardial infarction
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BACKGROUND: The role of hyperbaric oxygen in patients with acute myocardial infarction is controversial, ranging from not beneficial to having a favorable effect. This randomized study was conducted to further assess the benefit of hyperbaric oxygen treatment after thrombolysis on left ventricular function and remodeling in patients with acute myocardial infarction. METHODS: Seventy-four consecutive patients with first acute myocardial infarction were randomly assigned to treatment with hyperbaric

oxygen treatment combined with streptokinase (HBO+) or streptokinase alone (HBO-). RESULTS: There was a significant decrease of end-systolic volume index from the first day to the third week in HBO+ patients compared with HBO- patients (from 30.40 to 28.18 vs from 30.89 to 36.68 mL/m2, P <.05) accompanied with no changes of end-diastolic volume index in HBO+ compared with increased values in HBO- (from 55.68 to 55.10 vs from 55.87 to 63.82 mL/m2, P <.05). Ejection fraction significantly improved in the HBO+ group and decreased in the HBO- group of patients after 3 weeks of acute myocardial infarction (from 46.27% to 50.81% vs from 45.54% to 44.05 %, P <.05). CONCLUSIONS: Adjunctive hyperbaric oxygen therapy after thrombolysis in acute myocardial infarction has a favorable effect on left ventricular systolic function and the remodeling process.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15459609

J Am Coll Cardiol (2004);43:1780-7
Impact of intravenous beta-blockade before primary angioplasty on survival in patients undergoing mechanical reperfusion therapy for acute myocardial infarction
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OBJECTIVES: We sought to examine the effect of intravenous beta-blockers administered before primary percutaneous coronary intervention (PCI) on survival and myocardial recovery after acute myocardial infarction (AMI). BACKGROUND: Studies of primary PCI but not thrombolysis have suggested that beta-blocker administration before reperfusion may enhance survival. Whether oral beta-blocker use before admission modulates this effect is unknown. METHODS: The Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial randomized 2082 AMI patients to either stenting or balloon angioplasty, each +/- abciximab. In accordance with the protocol, intravenous beta-blockers were administered before PCI in the absence of contraindications. RESULTS: A total of 1136 patients (54.5%, BB+ group) received beta-blockers before PCI, whereas 946 (45.5%, BB- group) did not. The 30-day mortality was significantly lower in the BB+ group than in the BB- group (1.5% vs. 2.8%, p = 0.03), an effect entirely limited to patients who had not been receiving beta-blockers before admission (1.2% vs. 2.9%, p = 0.007). In contrast, no survival benefit with pre-procedural beta-blockers was observed in patients receiving beta-blockers at home (3.3% vs. 1.9%, respectively, p = 0.47). By multivariate analysis, pre-procedural beta-blocker use was an independent predictor of lower 30-day mortality among patients without previous beta-blocker therapy (relative risk = 0.38 [95% confidence interval 0.17 to 0.87], p = 0.02). The improvement in left ventricular ejection fraction from baseline to seven months was also greater after intravenous beta-blockers (3.8% vs. 1.3%, p = 0.01), an effect limited to patients not receiving oral beta-blockers before admission. CONCLUSIONS: In patients with AMI undergoing primary PCI, myocardial recovery is enhanced and 30-day mortality is reduced with pre-procedural intravenous beta-blockade, effects confined to patients untreated with oral beta-blocker medication before admission.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15145099

Eur Heart J (2004);25:10-6
Acarbose reduces the risk for myocardial infarction in type 2 diabetic patients: meta-analysis of seven long-term studies
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AIMS: To assess if treatment with the alpha-glucosidase inhibitor acarbose can reduce cardiovascular events in type 2 diabetic patients. METHODS AND RESULTS: This meta-analysis included seven randomized, double-blind, placebo-controlled acarbose studies with a minimum treatment duration of 52 weeks. Type 2 diabetic patients valid for safety were randomized to either acarbose (n=1248) or placebo (n=932). The primary outcome measure was the time to develop a cardiovascular event. Primary analysis was conducted using Cox regression analysis. The effect of acarbose on metabolic parameters was also investigated. Acarbose therapy showed favourable trends towards risk reduction for all selected cardiovascular event categories. The treatment significantly reduced the risk for "myocardial infarction" (hazards ratio=0.36 [95% Cl 0.16-0.80], P=0.0120) and "any cardiovascular event" (0.65 [95% Cl 0.48-0.88], P=0.0061). Glycaemic control, triglyceride levels, body weight and systolic blood pressure also improved significantly during acarbose treatment. CONCLUSION: Intervention with acarbose can prevent myocardial infarction and cardiovascular disease in type 2 diabetic patients while most of them are already on intensive concomitant cardiovascular medication.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14683737

J Am Coll Cardiol (2004);43:1773-9
Does beta-blocker therapy improve clinical outcomes of acute myocardial infarction after successful primary angioplasty?
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OBJECTIVES: We sought to determine if beta-blocker therapy improves clinical

confidence interval [CI] 0.26 to 0.73, p = 0.0016). Beta-blocker therapy was an independent predictor of lower six-month events in high-risk subgroups: ejection fraction <or=50% (death: OR 0.34, 95% CI 0.19 to 0.60, p = 0.0002) or multi-vessel coronary artery disease (CAD) (death: OR 0.26, 95% CI 0.14 to 0.48, p < 0.0001; MACE: OR 0.57, 95% CI 0.41 to 0.80, p = 0.0011). CONCLUSIONS: Treatment with beta-blockers after successful primary PCI is associated with reduced six-month mortality, with the greatest benefit in patients with a low ejection fraction or multi-vessel CAD.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15145098

Jama (2005);293:437-46
Effect of glucose-insulin-potassium infusion on mortality in patients with acute ST-segment elevation myocardial infarction: the CREATE-ECLA randomized controlled trial
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CONTEXT: Glucose-insulin-potassium (GIK) infusion is a widely applicable, low-cost therapy that has been postulated to improve mortality in patients with acute ST-segment elevation myocardial infarction (STEMI). Given the potential global importance of GIK infusion, a large, adequately powered randomized trial is required to determine the effect of GIK on mortality in patients with STEMI. OBJECTIVE: To determine the effect of high-dose GIK infusion on mortality in patients with STEMI. DESIGN, SETTING, AND PARTICIPANTS: Randomized controlled trial conducted in 470 centers worldwide among 20,201 patients with STEMI who presented within 12 hours of symptom onset. The mean age of patients was 58.6 years, and evidence-based therapies were commonly used. INTERVENTION: Patients were randomly assigned to receive GIK intravenous infusion for 24 hours plus usual care (n = 10,091) or to receive usual care alone (controls; n = 10,110). MAIN OUTCOME MEASURES: Mortality, cardiac arrest, cardiogenic shock, and reinfarction at 30 days after randomization. RESULTS: At 30 days, 976 control patients (9.7%) and 1004 GIK infusion patients (10.0%) died (hazard ratio [HR], 1.03; 95% confidence interval [CI], 0.95-1.13; P =.45). There were no significant differences in the rates of cardiac arrest (1.5% [151/10 107] in control and 1.4% [139/10,088] in GIK infusion; HR, 0.93; 95% CI, 0.74-1.17; P =.51), cardiogenic shock (6.3% [640/10 107] vs 6.6% [667/10 088]; HR, 1.05; 95% CI, 0.94-1.17; P =.38), or reinfarction (2.4% [246/10,107] vs 2.3% [236/10,088]; HR, 0.98; 95% CI, 0.82-1.17; P =.81). The rates of heart failure at 7 days after randomization were also similar between the groups (16.9% [1711/10,107] vs 17.1% [1721/10,088]; HR, 1.01; 95% CI, 0.95-1.08; P =.72). The lack of benefit of GIK infusion on mortality was consistent in prespecified subgroups, including in those with and without diabetes, in those presenting with and without heart failure, in those presenting early and later after symptom onset, and in those receiving and not receiving reperfusion therapy (thrombolysis or primary percutaneous coronary intervention). CONCLUSION: In this large, international randomized trial, high-dose GIK infusion had a neutral effect on mortality, cardiac arrest, and cardiogenic shock in patients with acute STEMI.
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Statin therapy, LDL cholesterol, C-reactive protein, and coronary artery disease
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BACKGROUND: Recent trials have demonstrated better outcomes with intensive than with moderate statin treatment. Intensive treatment produced greater reductions in both low-density lipoprotein (LDL) cholesterol and C-reactive protein (CRP), suggesting a relationship between these two biomarkers and disease progression. METHODS: We performed intravascular ultrasonography in 502 patients with angiographically documented coronary disease. Patients were randomly assigned to receive moderate treatment (40 mg of pravastatin orally per day) or intensive treatment (80 mg of atorvastatin orally per day). Ultrasonography was repeated after 18 months to measure the progression of atherosclerosis. Lipoprotein and CRP levels were measured at baseline and follow-up. RESULTS: In the group as a whole, the mean LDL cholesterol level was reduced from 150.2 mg per deciliter (3.88 mmol per liter) at baseline to 94.5 mg per deciliter (2.44 mmol per liter) at 18 months (P<0.001), and the geometric mean CRP level decreased from 2.9 to 2.3 mg per liter (P<0.001). The correlation between the reduction in LDL cholesterol levels and that in CRP levels was weak but significant in the group as a whole (r=0.13, P=0.005), but not in either treatment group alone. In univariate analyses, the percent change in the levels of LDL cholesterol, CRP, apolipoprotein B-100, and non-high-density lipoprotein cholesterol were related to the rate of progression of atherosclerosis. After adjustment for the reduction in these lipid levels, the decrease in CRP levels was independently and significantly correlated with the rate of progression. Patients with reductions in both LDL cholesterol and CRP that were greater than the median had significantly slower rates of progression than patients with reductions in both biomarkers that were less than the median (P=0.001). CONCLUSIONS: For patients with coronary artery disease, the reduced rate of progression of atherosclerosis associated with intensive statin treatment, as compared with moderate statin treatment, is significantly related to greater reductions in the levels of both atherogenic lipoproteins and CRP.
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Early statin treatment in patients with acute coronary syndrome: demonstration of the beneficial effect on atherosclerotic lesions by serial volumetric intravascular ultrasound analysis during half a year after coronary event: the ESTABLISH Study
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BACKGROUND: Recent clinical trials have demonstrated that aggressive lipid lowering by statins could prevent recurrent events after acute coronary syndrome (ACS). We hypothesized that this efficacy was caused by a significant reduction in plaque volume by aggressive LDL cholesterol (LCL-C) lowering. The present study investigated the effect of early statin treatment on plaque volume of a nonculprit lesion by serial volumetric intravascular ultrasound in patients with ACS. METHODS AND RESULTS:

Seventy patients with ACS were enrolled. All patients underwent emergency coronary angiography and percutaneous coronary intervention (PCI). They were randomized to intensive lipid-lowering therapy (n=35; atorvastatin 20 mg/d) or control (n=35) groups after PCI. Volumetric intravascular ultrasound analyses were performed at baseline and 6-month follow-up for a non-PCI site in 48 patients (atorvastatin, n=24; control, n=24). LDL-C level was significantly decreased by 41.7% in the atorvastatin group compared with the control group, in which LDL-C was increased by 0.7% (P<0.0001). Plaque volume was significantly reduced in the atorvastatin group (13.1+/-12.8% decrease) compared with the control group (8.7+/-14.9% increase; P<0.0001). Percent change in plaque volume showed a significant positive correlation with follow-up LDL-C level (R=0.456, P=0.0011) and percent LDL-C reduction (R=0.612, P<0.0001), even in patients with baseline LDL-C <125 mg/dL. CONCLUSIONS: Early aggressive lipid-lowering therapy by atorvastatin for 6 months significantly reduced the plaque volume in patients with ACS. Percent change in plaque volume showed a significant positive correlation with percent LDL-C reduction, even in patients with low baseline LDL-C.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15326073

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Randomized trial of atorvastatin for reduction of myocardial damage during coronary intervention: results from the ARMYDA (Atorvastatin for Reduction of MYocardial Damage during Angioplasty) study
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