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Clinically unrecognized Q-wave myocardial infarction in patients with diabetes mellitus, systemic hypertension, and nephropathy

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During the Irbesartan Diabetic Nephropathy Trial, 1,387 participants with type 2 diabetes mellitus, hypertension, and nephropathy underwent serial electrocardiograms for the identification of Q-wave myocardial infarction (MI). During a mean follow-up of 2.5 years, 14 of 99 first nonfatal MIs in this group were clinically unrecognized, accounting for 14% of all first nonfatal MIs.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15276098

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Newly diagnosed and previously known diabetes mellitus and 1-year outcomes of acute myocardial infarction: the VALsartan In Acute myocardial iNfarcTion (VALIANT) trial

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BACKGROUND: A prior diagnosis of diabetes mellitus is associated with adverse outcomes after acute myocardial infarction (MI), but the risk associated with a new diagnosis of diabetes in this setting has not been well defined. **METHODS AND RESULTS:** We assessed the risk of death and major cardiovascular events associated with previously known and newly diagnosed diabetes by studying 14,703 patients with acute MI enrolled in the VALsartan In Acute myocardial iNfarcTion (VALIANT) trial. Patients were grouped by diabetic status: previously known diabetes (insulin use or diagnosis of diabetes before MI, n=3400, 23%); newly diagnosed diabetes (use of diabetic therapy or diabetes diagnosed at randomization [median 4.9 d after infarction], but no known diabetes at presentation, n=580, 4%); or no diabetes (n=10,719). Patients with newly diagnosed diabetes were younger and had fewer comorbid conditions than did patients with previously known diabetes. At 1 year after enrollment, patients with previously known and newly diagnosed diabetes had similarly increased adjusted risks of mortality (hazard ratio [HR] 1.43; 95% confidence interval [CI], 1.29 to 1.59 and HR, 1.50; 95% CI, 1.21 to 1.85, respectively) and cardiovascular events (HR, 1.37; 95% CI, 1.27 to 1.48 and HR, 1.34; 95% CI, 1.14 to 1.56). **CONCLUSIONS:** Diabetes mellitus, whether newly diagnosed or previously known, is associated with poorer long-term outcomes after MI in high-risk patients. The poor prognosis of patients with newly diagnosed diabetes, despite having baseline characteristics similar to those of patients without diabetes, supports the idea that metabolic abnormalities contribute to their adverse outcomes.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15364810

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Classification of systemic therapies for potential stabilization of the vulnerable plaque to prevent acute myocardial infarction

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In this editorial, a classification of systemic therapies for potential plaque stabilization of vulnerable plaque to prevent acute myocardial infarction is proposed based on both biologic plausibility (a potential mechanism to explain the effect) and clinical evidence (i.e., whether the agent reduced acute myocardial infarction in well-designed clinical trials). All therapies possess biologic plausibility but are classified into groups I to IV based on clinical data.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15670548

J Am Coll Cardiol (2004);44:671-719

ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction--executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction)

E. M. Antman, *et al.*

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ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction)

E. M. Antman, *et al.*

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ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction--executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction)

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ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction; A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction)

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Pharmacoinvasive therapy: the future of treatment for ST-elevation myocardial infarction
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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15173037

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Abciximab-supported infarct artery stent implantation for acute myocardial infarction and long-term survival: a prospective, multicenter, randomized trial comparing infarct artery stenting plus abciximab with stenting alone

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BACKGROUND: The impact on survival of routine use of abciximab as adjunctive treatment to routine infarct artery stenting for acute myocardial infarction is not defined. We sought to determine the effect of abciximab on 1-year survival and other major adverse cardiac events of patients with acute myocardial infarction undergoing routine infarct artery stenting. **METHODS AND RESULTS:** The Abciximab and Carbostent Evaluation (ACE) Trial is an unblinded, randomized, controlled trial that compared abciximab with placebo in patients undergoing routine infarct artery stent implantation for acute myocardial infarction. At 1 year, the survival rate was 95+/-2% in the abciximab group and 88+/-2% in the stent-alone group (P=0.017). The reinfarction rate was 1% in the abciximab group and 6.0% in the stent-alone group, whereas there were no differences between groups in target vessel revascularization rate (16.5% in the abciximab group, 17.5% in the stent-alone group). **CONCLUSIONS:** Abciximab as adjunctive treatment to routine infarct artery stenting for acute myocardial infarction resulted in improved 1-year survival and lower reinfarction rates.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15066943

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Therapeutic delay and reduced functional status six months after thrombolysis for acute myocardial infarction

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Thrombolytic therapy decreases the mortality rate in patients with acute myocardial infarction (AMI), and the timing of thrombolysis has proved to be critical for decreasing the short-term mortality rate. Much less is known about the longer term consequences of delays in thrombolysis, particularly for outcomes other than the mortality rate. We assessed the effect of time to thrombolysis and other clinical predictors on cardiac functional status 6 months after AMI. We used InTIME II, a multicenter trial, to test the efficacy of alteplase and lanoteplase. This component of the trial was conducted in 147

North American centers. Patients were ≥ 18 years of age with ST-elevated AMI. Functional status was measured by the Duke Activity Status Index, which was administered 6 months after AMI. After multivariate adjustment for baseline characteristics, delay in presentation to hospital and delay in initiation of thrombolysis were significantly and independently associated with decreased cardiac functional status 6 months later. Each additional hour from symptom onset to hospital presentation was associated with a 16% increase (95% confidence interval 3% to 31%) in the likelihood of functional impairment (Duke Activity Status Index score ≤ 30). In addition, each additional delay of 1 hour from hospital presentation to thrombolysis independently increased the probability of functional impairment by 38% (12% to 71%). Thus, in patients with AMI, earlier presentation to the hospital and more rapid initiation of thrombolysis could prevent significant decreases in functional status months after the initial infarct.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15325921

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Long-term prognostic significance of left atrial volume in acute myocardial infarction
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OBJECTIVES: The aim of this study was to evaluate the significance of increased left atrial (LA) volume determined within the first 48 h of admission as a long-term predictor of outcome in patients with acute myocardial infarction (MI). **BACKGROUND:** The LA volume reflects left ventricular (LV) diastolic properties. Whereas other LV Doppler diastolic characteristics are influenced by acute changes in LV function, LA volume is stable and reflects diastolic properties before MI. **METHODS:** Clinical and echocardiographic parameters were prospectively collected in 395 consecutive patients with acute MI. Patients with LA volume index (LAVI) >32 ml/m² (normal + 2 standard deviations) were compared with those with LAVI ≤ 32 ml/m². Independent clinical and echocardiographic prognostic risk factors for five years' mortality were determined by the Cox proportional hazard model. **RESULTS:** Left atrial volume index >32 ml/m² was found in 63 patients (19%) who had a higher incidence of congestive heart failure on admission (24% vs. 12%, $p < 0.01$), a higher incidence of mitral regurgitation, increased LV dimensions, and reduced LV ejection fraction when compared with patients with LAVI ≤ 32 ml/m². Their five-year mortality rate was 34.5% versus 14.2% ($p < 0.001$). Significant independent risk predictors of five years' mortality were age (10 years) (odds ratio [OR] 1.45; 95% confidence interval [CI] 1.14 to 1.86), Killip class ≥ 2 on admission (OR 2.30; 95% CI 1.29 to 4.09), LAVI >32 ml/m² (OR 2.22; 95% CI 1.25 to 3.96), diabetes (OR 1.94; 95% CI 1.15 to 3.28), and LV restrictive filling pattern (OR 1.89; 95% CI 1.09 to 3.31). **CONCLUSIONS:** In patients with acute MI, increased LA volume, determined within the first 48 h of admission, is an independent predictor of five-year mortality with incremental prognostic information to clinical and echocardiographic data.

Comparison of rapidity of coronary recanalization in men with tenecteplase versus alteplase in acute myocardial infarction

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To determine whether tenecteplase (TNK-t-PA), a bioengineered variant of tissue-type plasminogen activator (t-PA) designed to accelerate thrombolysis, exhibits favorable properties compared with those of alteplase, 266 men were studied ≤ 6 hours after the onset of symptoms and signs of acute myocardial infarction. The primary end point was the rapidity of recanalization as judged from analysis of serial changes in the concentrations in blood of isoforms of creatine kinase-MM in serially obtained blood samples. Additional end points included enzymatically estimated infarct size and mortality. Patients were treated quite promptly after the onset of symptoms. The interval from the onset of chest pain to recanalization seen with TNK-t-PA was 208 ± 10 (SE) minutes compared with 237 ± 9 minutes seen with alteplase ($p = 0.04$). Thirty-day mortality was low with the use of the 2 agents (2%). TNK-t-PA appears to induce recanalization more rapidly than alteplase, and thrombolysis initiated early after the onset of symptoms is associated with remarkably low mortality.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15194014

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Anti-inflammatory and profibrinolytic effect of insulin in acute ST-segment-elevation myocardial infarction

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BACKGROUND: The clinical benefits of insulin previously observed in acute ST-segment-elevation myocardial infarction (STEMI) may be partially explained by an anti-inflammatory effect. We assessed this potential effect of insulin in STEMI patients treated with fibrinolytics. **METHODS AND RESULTS:** Thirty-two patients receiving reteplase were randomly assigned infusions of either insulin at 2.5 U/h, dextrose, and potassium (GIK) or normal saline and potassium (C) for 48 hours. Plasma concentrations of high-sensitivity C-reactive protein (CRP), serum amyloid A (SAA), plasminogen activator inhibitor-1 (PAI-1), creatine kinase (CK), and CK-MB were measured at baseline and sequentially for 48 hours. Total p47phox protein in mononuclear cells was measured in a subgroup of 13 subjects. Baseline CRP and SAA were significantly increased (2- to 4-fold) at 24 and 48 hours in each group ($P < 0.01$). However, in the insulin group, there was a significant ($P < 0.05$) attenuation of the absolute rise in concentration of CRP and SAA from baseline. The absolute increase of CRP and SAA was reduced by 40% (CRP) and 50% (SAA) at 24 hours and at 48 hours compared with the control group. The absolute increase in PAI-1 from baseline and the percentage increase in p47phox over 48 hours were significantly ($P < 0.05$) lower in the insulin-treated group. CK-MB peaked earlier and tended to be lower in insulin-treated subjects, especially in patients with inferior MI. **CONCLUSIONS:** Insulin has an anti-inflammatory and profibrinolytic effect in patients with acute MI. These effects may contribute to the clinical benefits of insulin in STEMI.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15194014

n&list_uids=14757687

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In-hospital and long-term outcomes of multivessel percutaneous coronary revascularization after acute myocardial infarction

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Multivessel percutaneous coronary intervention (PCI) early after acute myocardial infarction (AMI) is discouraged because of the potential for increased complications. However, with recent advances in PCI, the safety and long-term outcomes of multivessel PCI are unknown. We evaluated the outcomes of multivessel PCI early after AMI (ST-elevation and non-ST-elevation AMI). We identified all patients who had multivessel disease and underwent PCI within 7 days after an AMI from 1997 to 2002. Clinical outcomes were compared between patients who underwent multivessel PCI (n = 239) and patients who underwent treatment of the infarct-related artery alone (n = 1,145). The primary end point was cumulative survival at 6, 12, and 36 months. Secondary end points included a composite of mortality, recurrent infarction, coronary artery bypass graft, or target vessel revascularization at the same time points. There were 138 deaths and 351 occurrences of the composite end point during follow-up. The multivessel PCI group had a significantly higher prevalence of adverse prognostic indicators. Despite this, observed event rates were similar between the multivessel PCI and 1-vessel PCI groups. The Kaplan-Meier estimated 1-year survival was 0.91 (95% confidence interval [CI] 0.87 to 0.95) for the multivessel PCI group and 0.93 (95% CI 0.92 to 0.95) for the 1-vessel PCI group (p = 0.43). Similarly, 1-year survival free of recurrent infarction and target vessel revascularization rates were similar between the 2 groups: multivessel PCI 0.78 (95% CI 0.73 to 0.84) and 1-vessel PCI 0.78 (95% CI 0.75 to 0.81). Multivessel PCI in patients with multivessel coronary artery disease after AMI compared with 1-vessel PCI was not associated with an excess risk of death or of combined death, myocardial infarction, coronary artery bypass graft, or target vessel revascularization.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15670543

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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.

=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 $\geq 50\%$, $p = 0.003$). 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.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15219500

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Multivessel percutaneous coronary intervention in patients with multivessel disease and acute myocardial infarction

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BACKGROUND: The optimal percutaneous interventional strategy for dealing with significant non-culprit lesions in patients with multivessel disease (MVD) with acute myocardial infarction (AMI) at presentation remains controversial. **METHODS:** A total of 820 patients treated with primary angioplasty for AMI between 1998 and 2002 were classified in groups of patients with single vessel disease (SVD) or MVD ($\geq 70\%$ stenosis of ≥ 2 coronary arteries). Patients with MVD were subdivided in 3 groups on the basis of the revascularization strategy: 1) patients undergoing percutaneous coronary intervention (PCI) of the infarct-related artery (IRA) only; 2) patients undergoing PCI of both the IRA and non-IRA(s) during the initial procedure; and 3) patients undergoing PCI of the IRA followed by staged, in-hospital PCI of the non-IRA(s). Procedural, 30-day, and 1-year outcomes are reported. **RESULTS:** At 1 year, compared with patients with SVD, patients with MVD had a higher incidence of re-infarction (5.9% vs 1.6%, $P = .003$), revascularization (18% vs 9.6%, $P < .001$), mortality (12% vs 3.2%, $P < .001$), and major adverse cardiac events (MACEs; 31% vs 13%, $P < .001$). In patients with MVD, compared with PCI restricted to the IRA only, multivessel PCI was associated with higher rates of re-infarction (13.0% vs 2.8%, $P < .001$), revascularization (25% vs 15%, $P = .007$), and MACEs (40% vs 28%, $P = .006$). Multivessel PCI was an independent predictor of MACEs at 1 year (odds ratio = 1.67, $P = .01$). **CONCLUSIONS:** These data suggest that in patients with MVD, PCI should be directed at the IRA only, with decisions about PCI of non-culprit lesions guided by objective evidence of residual

ischemia at late follow-up. Further studies are needed to confirm these findings.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15389238

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Eptifibatide provides additional platelet inhibition in non-ST-elevation myocardial infarction patients already treated with aspirin and clopidogrel. Results of the platelet activity extinction in non-Q-wave myocardial infarction with aspirin, clopidogrel, and eptifibatide (PEACE) study

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OBJECTIVES: The present study hypothesis was that eptifibatide offered further antiplatelet efficacy above clopidogrel in non-ST-elevation myocardial infarction (NSTEMI) patients before an expeditive coronary intervention. **BACKGROUND:** Although thienopyridines and glycoprotein (GP) IIb/IIIa antagonists are often co-prescribed in the context of NSTEMI, the antiplatelet interaction of these agents is poorly described and the superiority of GP IIb/IIIa antagonists above thienopyridine treatment alone is not clear. **METHOD:** Thirty-two NSTEMI patients treated with aspirin and enoxaparin were studied using flow cytometry to define parameters of platelet activation with a panel of agonists before clopidogrel, after clopidogrel, and during an eptifibatide infusion following the clopidogrel load. **RESULTS:** After platelet activation with adenosine diphosphate, thrombin receptor-activating peptide, or U46-619, relative reductions in conformationally activated GP IIb/IIIa receptor expression (evaluated with PAC-1) of 48%, 43%, and 33%, respectively (all $p < 0.0001$), were seen with clopidogrel, but further 80%, 78%, and 72% (all $p < 0.0001$) reductions were seen with eptifibatide. With the same agonists, fibrinogen binding was significantly reduced after clopidogrel by 70%, 64%, and 81% (all $p < 0.0001$) and again further reduced with eptifibatide by 90%, 95%, and 69% (all $p < 0.0001$). The total number of GP IIb/IIIa receptors (measured as P2 expression) and P-selectin expression fell after clopidogrel, after *ex vivo* stimulation with the same agonists; however, both parameters increased slightly during the eptifibatide infusion. **CONCLUSIONS:** The activated GP IIb/IIIa expression and fibrinogen binding findings indicate that eptifibatide provides significant potent antiplatelet activity above aspirin and clopidogrel, suggesting additive immediate protection in the treatment of NSTEMI. The P2 and P-selectin findings suggest the

of symptom onset) in November 2000; 1922 patients (median age, 67 years; 73% men) with ST-segment-elevation infarction were included, of whom 180 (9%) received intravenous thrombolysis before hospital admission (PHT). Patients with PHT were younger than those with in-hospital thrombolysis, primary percutaneous interventions, or no reperfusion therapy. Median time from symptom onset to hospital admission was 3.6 hours for PHT, 3.5 hours for in-hospital lysis, 3.2 hours for primary percutaneous interventions, and 12 hours for no reperfusion therapy. In-hospital death was 3.3% for PHT, 8.0% for in-hospital lysis, 6.7% for primary percutaneous interventions, and 12.2% for no reperfusion therapy. One-year survival was 94%, 89%, 89%, and 79%, respectively. In a multivariate analysis of predictors of 1-year survival, PHT was associated with a 0.49 relative risk of death (95% CI, 0.24 to 1.00; $P=0.05$). When the analysis was limited to patients receiving reperfusion therapy, the relative risk of death for PHT was 0.52 (95% CI, 0.25 to 1.08; $P=0.08$). In patients with PHT admitted in $<$ or $=3.5$ hours, in-hospital mortality was 0% and 1-year survival was 99%. **CONCLUSIONS:** The 1-year outcome of patients treated with PHT compares favorably with that of patients treated with other modes of reperfusion therapy; this favorable trend persists after multivariate adjustment. Patients with PHT admitted very early have a very high 1-year survival rate.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15451803

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Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts

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BACKGROUND: Although the relationship between mortality and time delay to treatment has been demonstrated in patients with acute ST-segment elevation myocardial infarction (STEMI) treated by thrombolysis, the impact of time delay on prognosis in patients undergoing primary angioplasty has yet to be clarified. The aim of this report was to address the relationship between time to treatment and mortality as a continuous function and to estimate the risk of mortality for each 30-minute delay.

METHODS AND RESULTS: The study population consisted of 1791 patients with STEMI treated by primary angioplasty. The relationship between ischemic time and 1-year mortality was assessed as a continuous function and plotted with a quadratic regression model. The Cox proportional hazards regression model was used to calculate relative risks (for each 30 minutes of delay), adjusted for baseline characteristics related to ischemic time. Variables related to time to treatment were age >70 years ($P<0.0001$), female gender ($P=0.004$), presence of diabetes mellitus ($P=0.002$), and previous revascularization ($P=0.035$). Patients with successful reperfusion had a significantly shorter ischemic time ($P=0.006$). A total of 103 patients (5.8%) had died at 1-year follow-up. After adjustment for age, gender, diabetes, and previous revascularization, each 30 minutes of delay was associated with a relative risk for 1-year mortality of 1.075 (95% CI 1.008 to 1.15; $P=0.041$). **CONCLUSIONS:** These results suggest that every minute of delay in primary angioplasty for STEMI affects 1-year mortality, even after adjustment for baseline characteristics. Therefore, all efforts

also for primary angioplasty.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15007008

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

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Combined Abciximab REteplase Stent Study in acute myocardial infarction (CARESS in AMI)

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BACKGROUND: Most patients with acute myocardial infarction (AMI) are admitted to hospitals without percutaneous transluminal coronary angioplasty (PTCA) facilities or are initially managed in a prehospital mobile unit. Thrombolysis remains the most readily available reperfusion treatment in those settings, but the optimal subsequent strategy in those patients is unclear. If a mechanical recanalization is likely to be performed in an emergency, it is probably desirable that the patient receives abciximab, the glycoprotein IIb/IIIa antagonist with the strongest evidence of benefit for angioplasty in AMI. **OBJECTIVE:** The aim of this trial is to compare the effects on clinical outcome and cost-effectiveness of 2 strategies after immediate treatment with abciximab and half-dose reteplase for ST-elevation AMI: to manage the patients conservatively (referring them for rescue PTCA only if needed) or to immediately send all patients for emergency coronary angioplasty. **METHODS:** The Combined Abciximab RE-teplase

Stent Study in Acute Myocardial Infarction (CARESS in AMI) is an open, prospective, randomized, multicenter clinical trial conducted in patients with high-risk ST-segment elevation AMI treated within 12 hours from symptom onset in hospitals without PTCA facilities or in a prehospital mobile intensive care unit. Apart from contraindications to thrombolysis, the main exclusion criteria are age > or =75 years and a past history of CABG surgery or a percutaneous coronary intervention procedure involving the infarct-related artery. Enrollment will be performed in hospitals without PTCA facilities or directly in the ambulance if a dedicated system is in place for prehospital diagnosis and treatment of AMI. Patients will receive half-dose reteplase and full-dose abciximab and will subsequently be randomized to conventional medical therapy (with referral for emergency rescue PTCA allowed in selected cases) or emergency angioplasty. The primary end point is the 30-day combined incidence of mortality, reinfarction, and refractory ischemia. In order to obtain a 95% power (2-sided) to detect a 42% reduction in the primary end point, 900 patients are required in each arm of the study. Secondary end points include the 1-year composite end point of mortality, reinfarction, refractory ischemia, and hospital readmission because of heart failure; resource use at 30 days and 1 year; and the incidence of in-hospital stroke and bleeding complications in the 2 groups. RESULTS: Seventy-four patients have been randomized (as of March 10, 2004); results are expected in June 2005. CONCLUSION: This study will establish whether angioplasty must be started as soon as possible in all patients who receive combined pharmacologic reperfusion with the glycoprotein IIb/IIIa inhibitor abciximab and half-dose thrombolysis or whether it can be postponed or skipped in patients with signs of successful reperfusion, with obvious organizational advantages.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15389222

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Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial

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BACKGROUND: In patients with ST-segment elevated myocardial infarction (STEMI), early post-thrombolysis routine angioplasty has been discouraged because of its association with high incidence of events. The GRACIA-1 trial was designed to reassess the benefits of an early post-thrombolysis interventional approach in the era of stents and new antiplatelet agents. METHODS: 500 patients with thrombolysed STEMI (with recombinant tissue plasminogen activator) were randomly assigned to angiography and intervention if indicated. RESULTS: Primary end point was mortality at 30 days. Secondary end points were reinfarction, refractory ischemia, and hospital readmission because of heart failure. CONCLUSIONS: In patients with STEMI, routine angioplasty within 24 hours of thrombolysis was not superior to a conservative approach. The results of this trial support the use of a conservative approach in patients with STEMI who have received thrombolysis within 24 hours.

endpoint (23 [9%] vs 51 [21%], risk ratio 0.44 [95% CI 0.28-0.70], $p=0.0008$), and they tended to have reduced rate of death or reinfarction (7% vs 12%, 0.59 [0.33-1.05], $p=0.07$). Index time in hospital was shorter in the invasive group, with no differences in major bleeding or vascular complications. At 30 days both groups had a similar incidence of cardiac events. In-hospital incidence of revascularisation induced by spontaneous recurrence of ischaemia was higher in patients in the conservative group than in those in the invasive group. INTERPRETATION: In patients with STEMI, early post-thrombolysis catheterisation and appropriate intervention is safe and might be preferable to a conservative strategy since it reduces the need for unplanned in-hospital revascularisation, and improves 1-year clinical outcome.

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Infarct resorption, compensatory hypertrophy, and differing patterns of ventricular remodeling following myocardial infarctions of varying size

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OBJECTIVES: We sought to identify advantages of contrast-enhanced magnetic resonance imaging (MRI) in studying postinfarction ventricular remodeling.

BACKGROUND: Although sequential measurements of ventricular volumes, internal dimensions, and total ventricular mass have provided important insights into

postinfarction left ventricular remodeling, it has not been possible to define serial, directionally opposite changes in resorption of infarcted tissue and hypertrophy of viable myocardium and effects of these changes on commonly used indices of remodeling.

METHODS: Using gadolinium-enhanced MRI, the time course and geometry of changes in infarcted and noninfarcted regions were assessed serially in dogs subjected to coronary occlusion for 45 min, 90 min, or permanently. RESULTS: Infarct mass decreased progressively between three days and four to eight weeks following coronary occlusion; terminal values averaged 24 +/- 3% of those at three days. Radial infarct thickness also decreased progressively, whereas changes in circumferential and longitudinal extent of infarction were variable. The ability to define the circumferential endocardial and epicardial extents of infarction allowed radial thinning without epicardial expansion to be distinguished from true infarct expansion. The mass of noninfarcted myocardium increased by 15 +/- 2% following 90-min or permanent occlusion. However, the time course of growth of noninfarcted myocardium differed systematically from that of infarct resorption. Measurements of total ventricular mass frequently failed to reflect concurrent changes in infarcted and noninfarcted regions. Reperfusion accelerated infarct resorption. Histologic reductions in nucleus-to-cytoplasm ratios corresponded with increases in noninfarcted ventricular mass. CONCLUSIONS: Concurrent directionally opposite changes in infarcted and noninfarcted myocardium can be defined serially, noninvasively, and with high spatial resolution and full ventricular coverage following myocardial infarction.

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Value of electrocardiographic algorithm based on "ups and downs" of ST in assessment of a culprit artery in evolving inferior wall acute myocardial infarction

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Acute myocardial infarction (AMI) of the inferoposterior wall is due to occlusion of the right coronary artery (RCA) or the left circumflex (LCx) coronary artery. The outcome of patients depends mainly on the culprit artery. Therefore, the presumptive prediction of a culprit artery based on the electrocardiogram recorded at admission is of clinical importance. The aim of this study was to develop a sequential algorithm based on the "ups and downs" of the ST segment in different leads to predict the culprit artery (RCA vs LCx) in cases of inferoposterior AMI. We analyzed electrocardiographic and angiographic findings of 63 consecutive patients with an evolving AMI with ST elevation in the inferior leads (II, III, and aVF) and a single-vessel occlusion. Specificity, sensitivity, and positive and negative predictive values of different electrocardiographic criteria (ups and downs of the ST segment) were studied individually and in combination to find an algorithm that would best predict the culprit artery. The following electrocardiographic criteria were included in the 3-step algorithm: (1) ST changes in lead I, (2) the ratio of ST elevation in lead III to that in lead II, and (3) the ratio of the sum of ST depression in precordial leads to the sum of ST elevation in inferior leads [(summation operator downward arrow ST in leads V(1) to V(3))/(summation operator upward arrow ST in leads II, III, and aVF)]. Application of this sensitive algorithm suggested the location of the culprit coronary artery (RCA vs LCx) in 60 of 63 patients (>95%). The few patients in whom this algorithm did not work were those with a very dominant LCx that presented ST depression of > or =0.5 mm in lead I. In conclusion, careful sequential analysis of an electrocardiogram of an inferoposterior AMI with ST elevation may lead to the identification of a culprit artery.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15374771

Am Heart J (2004);148:306-11

Too little aspirin for secondary prevention after acute myocardial infarction in patients at high risk for cardiovascular events: Results from the MITRA study

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enzyme inhibitors: 65.6% vs 70.2%, $P = .06$; statins: 12.2% vs 15.1%, $P = .10$). Patients who were not given aspirin were at high risk for vascular events. They were more likely to have a history of prior AMI (OR, 1.34; 95% CI, 1.02-1.79), were in critical clinical condition at admission more often (cardiogenic shock: OR, 1.98; 95% CI, 1.09-3.56; overt heart failure: OR, 1.6; 95% CI, 1.05-2.3), and received acute revascularization less often (OR, 1.32; 95% CI, 1.05-1.67). The 1-year mortality was 2-times higher in patients who did not receive aspirin than in patients who did receive aspirin (16.5% vs 8.3%, $P < .001$). A significant association of withheld aspirin at discharge with a higher long-term mortality rate was confirmed with multivariate analysis (OR, 1.62; 95% CI, 1.15-2.29). CONCLUSIONS: Ten percent of patients who sustained an AMI did not receive aspirin at the time of hospital discharge. Most of these patients were at high risk for cardiovascular events. Withheld aspirin was significantly associated with higher mortality rate during follow up.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15309001

Circulation (2004);110:1392-7

Platelet function predicts myocardial damage in patients with acute myocardial infarction
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BACKGROUND: Platelet activation is a hallmark of acute coronary syndromes.

Numerous lines of evidence suggest a mechanistic link between von Willebrand factor or platelet hyperfunction and myocardial damage in patients with acute coronary syndromes. Thus, we assessed whether platelet function under high shear rates (collagen adenosine diphosphate closure times [CADP-CTs]) measured with the platelet function analyzer (PFA-100) may be enhanced in patients with myocardial infarction (MI) and whether it may predict the extent of myocardial damage as measured by creatine kinase (CK-MB) or troponin T (TnT) levels. METHODS AND RESULTS: Patients with acute chest pain or symptoms suggestive of acute coronary syndromes ($n=216$) were prospectively examined at an emergency department. CADP-CT was significantly shorter in patients with MI, particularly in those with an ST-segment-elevation MI (STEMI) compared with the other patient groups (unstable angina, stable coronary artery disease, or controls). Furthermore, CADP-CT and collagen epinephrine-CT at presentation were independent predictors of myocardial damage as measured by CK-MB or TnT. Patients with MI whose CADP-CT values fell in the first quartile had 3-fold higher CK-MB and TnT levels than those in the fourth quartile. CONCLUSIONS: Patients with STEMI have significantly enhanced platelet function when measured under high shear rates. CADP-CT is an independent predictor of the severity of MI, as measured by markers of cardiac necrosis. Measurement of platelet function with the PFA-100 may help in the risk stratification of patients presenting with MI.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15313953

Am J Cardiol (2004);94:108-11

Association of lesion complexity following fibrinolytic administration with mortality in ST-elevation myocardial infarction

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Greater lesion complexity, according to the American College of Cardiology and American Heart Association, has been associated with decreased success rates of percutaneous coronary intervention. We hypothesized that greater lesion complexity after fibrinolytic administration for ST-segment elevation myocardial infarction would similarly be associated with increased mortality and other adverse events at 30 days. We studied 2,605 patients from the Thrombolysis In Myocardial Infarction 10B and 14, Integrilin and Tenecteplase in Acute Myocardial Infarction, ENTIRE, and FASTER studies. For all studies, angiographic outcomes were assessed immediately after fibrinolytic administration and clinical outcomes were assessed at 30 days. Greater lesion complexity was associated with poorer epicardial flow and decreased myocardial perfusion at 60 minutes and after percutaneous coronary intervention and with a higher risk of shock and mortality within 30 days. In a multivariate model, type C lesion complexity remained associated with an increased 30-day mortality rate.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15219518

Am Heart J (2004);147:847-52

Association of the timing of ST-segment resolution with TIMI myocardial perfusion grade in acute myocardial infarction

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BACKGROUND: More complete ST-segment resolution (ST res) in acute myocardial infarction (MI) has been associated with better epicardial and myocardial reperfusion as assessed with the Thrombolysis in Myocardial Infarction (TIMI) flow grade (TFG) and

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after thrombolytic administration.

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J Am Coll Cardiol (2004);43:1170-6

Association of a pulsatile blood flow pattern on coronary arteriography and short-term clinical outcomes in acute myocardial infarction

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OBJECTIVES: We hypothesized that recognition of systolic flow reversal (pulsatile flow) after thrombolytic administration on coronary angiography is associated with

angiographic and electrocardiogram findings reflecting impaired myocardial perfusion, as well as poorer clinical outcomes. **BACKGROUND:** Reversal of systolic flow on

Doppler velocity wire recordings has been associated with impaired tissue perfusion on myocardial contrast echocardiography in the setting of myocardial infarction (MI).

METHODS: Patients (n = 1,062) with a patent infarct-related artery were drawn from the Thrombolysis In Myocardial Infarction (TIMI) 10, TIMI 14, and Integrilin and

Tenecteplase acute MI trials. **RESULTS:** Pulsatile flow (systolic flow reversal with

cessation of antegrade contrast-dye motion or frank reversal of contrast-dye motion during systole) at 60 min after fibrinolytic administration was present in 11.0% of

patients. Pulsatile flow was associated with higher corrected TIMI frame counts (slower epicardial flow) (median 40.1 frames, IQ 30 of 63 vs. 30 frames, interquartile 22 of 42, p

< 0.0001), a closed microvasculature (TIMI myocardial perfusion grades 0 of 1, 57.1% vs. 37.8%, p = 0.03) and less complete (> or =70%) ST-segment resolution (23.5% vs.

58.9%, p = 0.008). Patients with pulsatile flow had a higher risk of death or reinfarction at 30 days (10.3% vs. 5.0%, p = 0.019). After controlling for age, pulse, blood pressure,

anterior MI location, epicardial flow, and creatine kinase, pulsatile flow remained associated with an increased risk of death/MI (odds ratio 3.1, p = 0.006).

CONCLUSIONS: A pulsatile pattern of flow is associated with impaired myocardial perfusion and poorer clinical outcomes independent of the velocity of antegrade flow in the epicardial artery. This simple and easily identifiable angiographic flow pattern may be useful in clinical risk stratification.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15063425

J Am Coll Cardiol (2004);44:980-7

Association of duration of symptoms at presentation with angiographic and clinical outcomes after fibrinolytic therapy in patients with ST-segment elevation myocardial infarction

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OBJECTIVES: We sought to determine if an underlying mechanism of the association between prolonged symptom-to-treatment times and adverse outcomes may be an

duration among ST-segment elevation myocardial infarction (STEMI) patients undergoing fibrinolytic therapy is associated with adverse outcomes. **METHODS:** Angiography was performed 60 min after fibrinolytic administration in 3,845 Thrombolysis In Myocardial Infarction (TIMI) trial patients. **RESULTS:** The median time from symptom onset to treatment was longer among patients with impaired myocardial perfusion (3.0 h for TMPG 0/1 vs. 2.7 h for TMPG 2/3; $p = 0.001$). In a multivariate model, impaired tissue perfusion (TMPG 0/1) remained associated with increased time to treatment (odds ratio 1.14 per hour of delay; $p = 0.007$) even after adjusting for Thrombolysis In Myocardial Infarction flow grade (TFG) 3, left anterior descending infarct location, and baseline clinical characteristics. Impaired myocardial perfusion after rescue/adjunctive percutaneous coronary intervention (PCI) was associated with longer median times to treatment (3.0 h for TMPG 2/3 vs. 2.7 h for TMPG 0/1; $p = 0.017$), as was abnormal epicardial flow after rescue/adjunctive PCI (3.3 h for TFG 0/1/2 vs. 2.8 h for TFG 3; $p = 0.005$). Thirty-day mortality was associated with longer time from onset of symptoms to treatment (6.6% mortality for time to treatment >4 h vs. 3.3%; $p < 0.001$), even among patients undergoing rescue PCI. **CONCLUSIONS:** A prolonged symptom to treatment time among STEMI patients is associated with impaired myocardial perfusion independent of epicardial flow both immediately after fibrinolytic administration and after rescue/adjunctive PCI. These data provide a pathophysiologic link between prolonged symptoms due to vessel occlusion, impaired myocardial perfusion, and poor clinical outcomes.

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Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs: nested case-control study

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BACKGROUND: Controversy has surrounded the question about whether high-dose rofecoxib increases or naproxen decreases the risk of serious coronary heart disease. We sought to establish if risk was enhanced with rofecoxib at either high or standard doses compared with remote non-steroidal anti-inflammatory drug (NSAID) use or celecoxib use, because celecoxib was the most common alternative to rofecoxib.

METHODS: We used data from Kaiser Permanente in California to assemble a cohort of all patients age 18-84 years treated with a NSAID between Jan 1, 1999, and Dec 31, 2001, within which we did a nested case-control study. Cases of serious coronary heart disease (acute myocardial infarction and sudden cardiac death) were risk-set matched with four controls for age, sex, and health plan region. Current exposure to cyclo-oxygenase 2 selective and non-selective NSAIDs was compared with remote exposure to any NSAID, and rofecoxib was compared with celecoxib. **FINDINGS:** During 2302029 person-years of follow-up, 8143 cases of serious coronary heart disease occurred, of which 2210 (27.1%) were fatal. Multivariate adjusted odds ratios versus celecoxib were: for rofecoxib (all doses), 1.59 (95% CI 1.10-2.32, $p=0.015$); for rofecoxib 25 mg/day or less, 1.47 (0.99-2.17, $p=0.054$); and for rofecoxib greater than

25 mg/day, 3.58 (1.27-10.11, p=0.016). For naproxen versus remote NSAID use the adjusted odds ratio was 1.14 (1.00-1.30, p=0.05). INTERPRETATION: Rofecoxib use increases the risk of serious coronary heart disease compared with celecoxib use.

Naproxen use does not protect against serious coronary heart disease.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15705456

J Am Coll Cardiol (2004);43:542-8

Outcome of acute ST-segment elevation myocardial infarction in diabetics treated with fibrinolytic or combination reduced fibrinolytic therapy and platelet glycoprotein IIb/IIIa inhibition: lessons from the GUSTO V trial

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OBJECTIVES: We studied the outcome of diabetics enrolled in the Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) V trial to assess whether the combination of half-dose reteplase and abciximab provides any propitious benefits over standard fibrinolytic therapy in diabetic patients. **BACKGROUND:** Diabetics with acute ST-segment elevation myocardial infarction (MI) have a worse outcome compared with nondiabetics. Higher-risk patients are usually more likely to benefit from advances in medical therapy. **METHODS:** We analyzed diabetic patients enrolled in the GUSTO V trial to assess the outcome of those randomized to the combination of half-dose reteplase and abciximab versus those randomized to reteplase. We also evaluated whether any differences existed in presentation and outcome of MI among the diabetics versus the nondiabetics enrolled in the study. **RESULTS:** The trial enrolled 13782 nondiabetics and 2633 diabetics. Compared to nondiabetics, diabetics had a significantly higher mortality at 30 days (8.5% vs. 5.1%, $p < 0.001$) and at 1 year (12.7% vs. 7.5%, $p < 0.001$). Among the diabetic subset, no significant difference existed in the incidence of 30-day (8.8% vs. 8.2%, $p = 0.52$) or 1-year mortality (13.0% vs. 12.4%, $p = 0.62$) among patients randomized to reteplase compared to those receiving combination of abciximab and reteplase. The incidence of reinfarction (2.5% vs. 4.3%, $p = 0.013$), recurrent ischemia (11.8% vs. 14.9%, $p = 0.017$), and urgent revascularization (10.9% vs. 13.3%, $p = 0.055$) at seven days was lower in diabetics treated with the combination therapy. **CONCLUSIONS:** Compared to nondiabetics, diabetics continue to have a worse outcome with MI. Although combination therapy did not provide a survival benefit, nonfatal ischemic outcomes, including reinfarction, recurrent ischemia, and urgent revascularization, were substantially reduced.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15705456

plaque instability and plasma levels of biomarkers was determined in patients with unstable angina and non-ST-segment elevation myocardial infarction (UA/NSTEMI). METHODS: Fifty-two patients underwent coronary angiography and IVUS 8 +/- 5 hours after the onset of chest pain. IVUS analysis included plaque morphology, disruption, thrombi and eccentricity, lumen, external elastic membrane, and plaque plus media areas of culprit lesion and reference segments and arterial remodeling. Plasma levels of the thrombin activation system (thrombin-antithrombin complex [TAT], tissue factor pathway inhibitor [TFPI], and prothrombin fragments 1+2 [F1+2]) and plasmin activation system (tissue and urokinase-type plasminogen activator [t-PA and u-PA], plasminogen activator inhibitor-1 [PAI-1], and D-dimer) were measured with enzyme-linked immunosorbent assay kits before angiography. RESULTS: Elevated levels of TAT (7.2 +/- 6.0 microg/L), F1+2 (1.8 +/- 1.0 nmol/L), TFPI (179.1 +/- 131.0 ng/mL), PAI-1 (95.4 +/- 54.6 ng/mL), t-PA (10.6 +/- 8.8 ng/mL), and u-PA (2.6 +/- 0.9 ng/mL) were found in patients with UA/NSTEMI. The serum levels of D-dimer (40.0 +/- 39.5 ng/mL) remained in reference range. Expansive and constrictive remodeling were found in 18 (35%) and 12 (23%) patients, respectively. Expansive remodeling of the culprit lesion was associated with significantly higher plasma levels of PAI-1 (121.6 +/- 55.0 vs 87.7 +/- 61.5 and 77.4 +/- 42.8 ng/ml, P =.039), and u-PA (3.0 +/- 1.2 vs 2.2 +/- 0.5 and 2.5 +/- 0.7 ng/mL, P =.026) as compared with constrictive and neutral remodeling. Increased plasma levels of u-PA were associated with plaque rupture (3.0 +/- 0.7 vs 2.5 +/- 0.9 ng/mL, P =.062). Plasma levels of PAI-1 and u-PA correlated positively with plaque plus media (P =.0297 and P =.0093) and external elastic membrane areas (P =.010 and P =.0002). CONCLUSIONS: Elevated levels of biomarkers of plasmin activation system are associated with signs of plaque instability of culprit lesion in UA/NSTEMI and might therefore serve as non-invasive determinants of the population that is at high risk for subsequent adverse events.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14691435

Heart (2004);90:1404-10

Management and in-hospital outcome of patients with acute myocardial infarction admitted to intensive care units at the turn of the century: results from the French nationwide USIC 2000 registry

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OBJECTIVE: To assess actual practices and in-hospital outcome of patients with acute myocardial infarction on a nationwide scale. METHODS: Of 443 intensive care units in France, 369 (83%) prospectively collected data on all cases of infarction (within < 48 hours of symptom onset) in November 2000. RESULTS: 2320 patients (median age 68 years, 73% men) were included, of whom 83% had ST segment elevation infarction (STEMI). Patients without STEMI were older and had a more frequent history of cardiovascular disease. Median time to admission was 5.0 hours for patients with and 6.5 hours for those without STEMI. Reperfusion therapy was used for 53% of patients with STEMI (thrombolysis 28%, primary angioplasty 25%). In-hospital mortality was 8.7% (5.5% of patients without and 9.3% of those with STEMI). Multivariate analysis found that age, Killip class, lower blood pressure, higher heart rate on admission, anterior location of infarct, STEMI, diabetes mellitus, previous stroke, and no current

smoking independently predicted in-hospital mortality. At hospital discharge, 95% received antiplatelet agents, 75% received beta blockers, and over 60% received statins. Angiotensin converting enzyme inhibitors were prescribed for 40% of the patients without and 52% of those with ST elevation. CONCLUSIONS: This nationwide registry, including all types of centres irrespective of their size and experience, shows continued improvement in patient care and outcomes. Time from symptom onset to admission, however, has not improved in recent years and reperfusion therapy is used for just over 50% of patients with STEMI, with an increasing use of primary angioplasty.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15547013

Eur Heart J (2004);25:232-9

Effect of fixed low-dose warfarin added to aspirin in the long term after acute myocardial infarction; the LoWASA Study

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AIM: To evaluate whether long-term treatment with a fixed low dose of warfarin in combination with aspirin improves the prognosis compared with aspirin treatment alone after an acute myocardial infarction (AMI). METHODS: Patients who were hospitalized for AMI were randomized to either 1.25mg of warfarin plus 75mg of aspirin (n=1659) daily or 75mg of aspirin alone (n=1641). The study was performed according to the PROBE (Prospective Open Treatment and Blinded End Point Evaluation) design and was conducted at 31 hospitals in Sweden. The median follow-up time was 5.0 years. In the aspirin+warfarin group, 30.2% were permanently withdrawn as opposed to 14.0% in the aspirin group (P<0.0001). Analyses were performed on an intention-to-treat basis. RESULTS: The combination of cardiovascular death, reinfarction or stroke was registered in 28.1% in the aspirin+warfarin group versus 28.8% in the aspirin group (NS). Cardiovascular deaths occurred in 14.2% in the aspirin+warfarin group vs 15.7% in the aspirin group (NS). Whereas no difference was found with regard to total mortality or reinfarction, those randomized to aspirin+warfarin had a reduced occurrence of stroke (4.7% vs 7.1%; P=0.004). The percentage of patients who suffered a serious bleed was

This retrospective, nonrandomized analysis evaluated the effect of initiating statin or beta-blocker treatment early in the course of heart failure developed during acute myocardial infarction compared with the effect of neither or both treatments. Early initiation of statins or beta blockers alone was associated with improved event-free survival, and the benefits of the combined treatment were additive.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14996587

Am J Cardiol (2004);94:632-6, A9

Comparison of mortality rates after acute myocardial infarction in smokers versus nonsmokers

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Patients who smoke paradoxically have favorable outcomes after acute myocardial infarctions compared with nonsmokers. However, after adjustment for age only, the decrease in all-cause mortality in the smoker population is explained by the smokers' generally younger age, with better prognoses due to their age.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15342296

Am Heart J (2004);147:457-62

Improved clinical outcomes with abciximab therapy in acute myocardial infarction: a systematic overview of randomized clinical trials

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BACKGROUND: Investigations of glycoprotein (GP) IIb/IIIa inhibition in primary percutaneous coronary intervention (PCI) have suggested the efficacy of abciximab in improving clinical and angiographic outcomes, but sample-size limitations and variability in trial design preclude the ability to generalize these results to a broader patient population. **METHODS:** Meta-analytic techniques were used to evaluate clinical outcomes from randomized trials comparing GP IIb/IIIa inhibition with placebo or control therapy in primary PCI for acute myocardial infarction (MI). **RESULTS:** In 3266 patients, treatment with abciximab significantly reduced the 30-day composite end point of death, reinfarction, or ischemic or urgent target-vessel revascularization (TVR; odds ratio [OR], 0.54; 95% CI, 0.40-0.72), with trends toward reduced 30-day death and death or reinfarction. Abciximab resulted in an increased likelihood of major bleeding (OR, 1.74; 95% CI, 1.11-2.72). By 6 months, abciximab significantly reduced the occurrence of death, reinfarction, or any TVR (OR, 0.80; 95% CI, 0.67-0.97), and there were positive trends favoring a decrease in mortality alone and the composite of death or reinfarction. **CONCLUSIONS:** Treatment with abciximab significantly reduces early adverse ischemic events, a clinical benefit that is maintained at 6-month follow-up. These findings support the use of adjunctive GP IIb/IIIa inhibition in primary PCI.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14999194

Circulation (2004);110:1754-60

Long-term mortality of patients with acute myocardial infarction in the United States and Canada: comparison of patients enrolled in Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO)-I

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BACKGROUND: In a previous substudy of the GUSTO-I trial, we observed better functional and quality-of-life outcomes among patients in the United States (US patients) compared with patients in Canada. Rates of invasive therapy were significantly higher in the United States and were associated with a small mortality benefit (0.4%, adjusted $P=0.02$). We sought to determine whether Canadian-US differences in practice patterns in GUSTO-I had an impact on 5-year mortality. **METHODS AND RESULTS:** Mortality data for 23,105 US and 2898 Canadian patients enrolled in GUSTO-I were obtained from national mortality databases. Median follow-up was 5.46 years in the US and 5.33 years in the Canadian cohort. Five-year mortality rate was 19.6% among US and 21.4% among Canadian patients ($P=0.02$). After baseline adjustment, enrollment in Canada was associated with a higher hazard of death (1.17; 95% confidence interval, 1.07 to 1.28, $P=0.001$). Revascularization rates during the index hospitalization in the United States were almost 3 times those in Canada: 30.5% versus 11.4% for angioplasty and 13.1% versus 4.0% for bypass surgery ($P<0.01$ for both). After accounting for revascularization status as a time-dependent covariate, country was no longer a significant predictor of long-term mortality. These results were confirmed in a propensity-matched analysis. **CONCLUSIONS:** Our results suggest, for the first time, that the more conservative pattern of care with regard to early revascularization in Canada for ST-segment elevation acute myocardial infarction may have a detrimental effect on long-term survival. Our results have important policy implications for cardiac care in countries and healthcare systems wherein use of invasive procedures is similarly conservative.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15381645

Am J Cardiol (2005);95:337-42

Association of culprit lesion calcium with angiographic and clinical outcomes in patients with ST-elevation myocardial infarction treated with fibrinolytic therapy

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Coronary artery calcium has been associated with a greater extent of angiographically significant coronary artery stenoses, but the angiographic and clinical outcomes associated with culprit lesion calcium (CLC) have not been fully evaluated, particularly in the setting of ST-elevation myocardial infarction. We hypothesized that CLC would be associated with adverse angiographic and clinical outcomes in patients who had ST-elevation myocardial infarction. Data were evaluated in 3,292 patients from 6 trials of fibrinolytic therapy for ST-elevation myocardial infarction; 243 culprit lesions (7.4%) were calcified. CLC was associated with advanced age, history of hypertension, previous coronary artery disease, greater extent of disease, angiographically evident residual thrombus, smaller minimum luminal diameter, and larger percent residual

stenosis after fibrinolytic therapy. CLC was associated with lower rates of arterial patency after fibrinolytic therapy (63.3% vs 81.3% $p < 0.001$), lower rates of Thrombolysis In Myocardial Infarction grade 3 flow (41.5% vs 57.2%, $p < 0.001$), and higher (slower) Thrombolysis In Myocardial Infarction frame counts (52 vs 36 frames, $p < 0.0001$, multivariate $p = 0.02$). CLC was also associated with increased 30-day mortality rates (6.2% vs 3.4%, $p = 0.028$) and 30-day rates of death, myocardial infarction, or congestive heart failure (16.5% vs 8.9%, $p < 0.001$) and independently associated with 30-day rates of death, myocardial infarction, or congestive heart failure (odds ratio 1.6, $p = 0.016$) after multivariate adjustment for baseline clinical and lesion characteristics, epicardial flow, and performance of rescue/adjunctive percutaneous coronary intervention. In a model restricted to patients who had successful restoration of epicardial patency after fibrinolytic therapy, CLC was independently associated with 30-day mortality (odds ratio 2.2, $p = 0.045$). CLC is independently associated with indexes of poorer epicardial flow and a higher incidence of adverse clinical outcomes after fibrinolytic administration in patients who have ST-elevation myocardial infarction. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15670541

J Am Coll Cardiol (2004);44:276-86

Cardiac protection during acute myocardial infarction: where do we stand in 2004?

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Despite better outcomes with early coronary artery reperfusion for the treatment of acute ST-elevation myocardial infarction (MI), morbidity and mortality from acute myocardial infarction (AMI) remain significant, the incidence of congestive heart failure continues to increase, and there is a need to provide better cardioprotection (therapy that reduces the amount of necrosis that may be coupled with better clinical outcome) in the setting of AMI. Since the introduction of the concept of cardiac protection over a quarter of a century ago, various interventions have been investigated to reduce myocardial infarct size. Intravenous beta-blockers administered in the early hours of infarction were clearly shown to be of benefit. Intravenous adenosine appeared promising for anterior wall AMIs, as did cariporide in some studies.

Glucose-insulin-potassium infusion was beneficial in certain subgroups of patients, particularly diabetics. A variety of other medications were studied with negative or marginal results. The best strategy to limit infarct size is early reperfusion with percutaneous coronary stenting or thrombolytic therapy. Stenting is superior and should be adopted whenever there is a qualified laboratory available. Available resources should focus on decreasing time from onset of symptoms to start of reperfusion and maintaining vessel patency. Future studies powered to better assess clinical outcome are needed for adjunctive therapy with adenosine, K(ATP) channel openers, Na(+)/H(+) exchange inhibitors, and hypothermia.

Effects of percutaneous coronary arterial thrombectomy during acute myocardial infarction on left ventricular remodeling

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The benefit of primary angioplasty for acute myocardial infarction (AMI) is limited by the no-reflow phenomenon, resulting in chronic left ventricular (LV) remodeling. The aim of this study was to evaluate the impact of thrombectomy with the Rescue percutaneous thrombectomy catheter on LV function after AMI. We performed a retrospective study comparing conventional angioplasty with the combination of angioplasty and thrombectomy using the Rescue catheter. The study population was comprised of 109 consecutive patients with AMI who underwent angioplasty and thrombectomy and 86 controls treated with conventional angioplasty. Baseline clinical and lesion characteristics were similar in the 2 groups. Postprocedural restoration of normal flow (Thrombolysis In Myocardial Infarction grade 3) was more frequent in the thrombectomy group (82% vs 69%, $p = 0.03$). No differences were observed in cardiac events, including death, reinfarction, and target vessel revascularization (thrombectomy vs controls, 27% vs 33%; $p = 0.44$) or changes in ejection fraction ($p = 0.22$) during 6-month follow-up. The incidence of LV remodeling, defined as an increase in LV end-diastolic volume index of $>20\%$, was significantly lower in the thrombectomy group (22% vs 44%; $p = 0.01$). Multiple logistic regression analysis revealed that thrombectomy with the Rescue catheter contributed significantly to reduction of both no-reflow and LV remodeling. In the setting of primary angioplasty, adjunctive pretreatment with a rescue catheter reduces the no-reflow phenomenon and protects against LV remodeling.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14996573

Circulation (2004);110:e533-9

Clinical utility of serial and continuous ST-segment recovery assessment in patients with acute ST-elevation myocardial infarction: assessing the dynamics of epicardial and myocardial reperfusion

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15611375

Am Heart J (2004);147:281-6

Change of multiple complex coronary plaques in patients with acute myocardial infarction: a study with coronary angiography

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BACKGROUND: Patients with acute myocardial infarction (AMI) may have multiple complex coronary plaques that are not limited to the culprit lesions. However, it is unknown whether they tend to progress in severity, regress, or remain stable. The aim

of this angiographic study is to evaluate the natural history of these lesions. **METHODS:** We consecutively enrolled 229 patients who underwent coronary angiography at the time of their hospitalization to treat AMI with primary angioplasty. Baseline and follow-up (mean follow-up duration, 192 +/- 33 days) coronary angiographic data in patients with multiple complex coronary plaques characterized by thrombus, ulceration, plaque irregularity, and impaired flow were compared. **RESULTS:** Single complex coronary plaques were identified in 167 patients (73%), and multiple complex plaques were identified in the other 62 patients (27%). Among the patients with multiple complex plaques (62 patients, 83 non-culprit complex plaques), the angiographic examinations were reviewed simultaneously in 43.5% (27 patients, 35 non-culprit complex plaques). Of 35 non-culprit complex lesions, 29 lesions (82%) remained complex without changing into smooth lesions, 1 lesion became totally occluded, and 4 lesions regressed. The severity of non-culprit complex lesions between baseline and follow-up angiography is equal (maximal diameter stenosis, 74% +/- 15% vs 72% +/- 15%, P = .4). Long-term cardiac events after discharge were more likely to develop in patients with multiple complex plaques than in patients with single complex plaques (24% vs 10%, respectively; P <.01). **CONCLUSIONS:** In patients with AMI, little angiographic change occurred during 6 months of follow-up in the non-culprit complex plaques.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14760326

J Am Coll Cardiol (2004);43:704-8

Short- and long-term clinical benefit of sirolimus-eluting stents compared to conventional bare stents for patients with acute myocardial infarction

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OBJECTIVES: This study investigated the clinical outcomes of patients with ST-segment elevation myocardial infarction (MI) treated with sirolimus-eluting stents (SESs) or with conventional bare stents. **BACKGROUND:** The clinical impact of SES implantation for patients with ST-segment elevation MI is currently unknown. **METHODS:** Primary angioplasty was performed with SESs in 186 consecutive patients with acute MI who were compared with 183 patients treated with bare stents. The incidence of death, reinfarction, and repeat revascularization was assessed at 30 and 300 days. **RESULTS:** Postprocedure vessel patency, enzymatic release, and the incidence of short-term adverse events were similar in both the sirolimus and the bare stents (30-day rate of death, reinfarction, or repeat revascularization: 7.5% vs. 10.4%, respectively; p = 0.4). Stent thrombosis was not diagnosed in any patient in the sirolimus group and occurred in 1.6% of patients treated with bare stents (p = 0.1). At 300 days, treatment with SESs significantly reduced the incidence of combined adverse events (9.4% vs. 17%; hazard ratio [HR] 0.52 [95% confidence interval (CI) 0.30 to 0.92]; p = 0.02), mainly due to a marked reduction in the risk of repeat intervention (1.1% vs. 8.2%; HR 0.21 [95% CI 0.06 to 0.74]; p = 0.01). **CONCLUSIONS:** Compared to conventional bare stents, the SESs were not associated with an increased risk of stent thrombosis and were effective in reducing the incidence of adverse events at 300 days in unselected patients with ST-segment elevation acute MI referred for primary

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J Am Coll Cardiol (2004);44:1510-20

Effect of granulocyte-macrophage colony-stimulating factor inducer on left ventricular remodeling after acute myocardial infarction

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OBJECTIVES: We sought to determine the influence of granulocyte-macrophage colony-stimulating factor (GM-CSF) induction on post-myocardial infarction (MI) remodeling, especially in relation to the inflammatory response and myocardial fibrosis.

BACKGROUND: Granulocyte-macrophage colony-stimulating factor modifies wound healing by promoting monocytopoiesis and infiltration of monocytes and macrophages into injured tissue; however, the effect of GM-CSF induction on the infarct healing process and myocardial fibrosis is unclear. **METHODS:** A model of MI was produced in Wistar rats by ligation of the left coronary artery. The MI animals were randomized to receive GM-CSF inducer (romurtide 200 microg/kg/day for 7 consecutive days) (MI/Ro) or saline (MI/C). **RESULTS:** Echocardiographic and hemodynamic studies on day 14 revealed increased left ventricular (LV) end-diastolic dimension, decreased fractional shortening, elevated LV end-diastolic pressure, and decreased LV maximum rate of isovolumic pressure development in MI/Ro compared with MI/C. Immunoblotting showed that expression of transforming growth factor (TGF)-beta1 in the infarcted site on day 3 after MI was decreased in MI/Ro compared with MI/C. In the infarcted site, TGF-beta1, collagen type I and type III messenger ribonucleic acid (mRNA) expression on day 3, and collagen content on day 7 were reduced in MI/Ro compared with MI/C, in association with marked infarct expansion. In MI/Ro, monocyte chemoattractant protein-1 mRNA level and the degree of infiltration of monocyte-derived macrophages (ED-1-positive) were greater in the infarcted site on day 7 than those in MI/C.

CONCLUSIONS: The GM-CSF induction by romurtide facilitated infarct expansion in association with the promotion of monocyte recruitment and inappropriate collagen synthesis in the infarcted region during the early phase of MI.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15464336

Circulation (2004);109:3171-5

Clopidogrel resistance is associated with increased risk of recurrent atherothrombotic events in patients with acute myocardial infarction

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BACKGROUND: Although clopidogrel reduces the risk of cardiovascular episodes after coronary events and stenting, a substantial number of incidents continue to occur.

METHODS AND RESULTS: The antiplatelet effect of clopidogrel was studied prospectively in 60 consecutive patients who underwent primary angioplasty (percutaneous coronary intervention [PCI]) with stenting for acute ST-segment-elevation myocardial infarction (STEMI) to determine whether variability in response to clopidogrel affects clinical outcomes. Patients were stratified into 4 quartiles according to the percentage reduction of ADP-induced platelet aggregation. Although patients in the first

quartile were resistant to the effects of clopidogrel (ADP-induced platelet aggregation at day 6, 103+/-8% of baseline), ADP-induced aggregation was reduced to 69+/-3%, 58+/-7%, and 33+/-12% of baseline, respectively, in patients in quartiles 2 through 4 (P<0.01 for all). In addition, epinephrine-induced platelet aggregation and platelet aggregation under flow conditions, assessed by the cone-and-plate(let) analyzer method, were reduced significantly less in the first quartile than in quartiles 2 through 4. Whereas 40% of patients in the first quartile sustained a recurrent cardiovascular event during a 6-month follow-up, only 1 patient (6.7%) in the second quartile and none in the third and fourth quartiles suffered a cardiovascular event (P=0.007). CONCLUSIONS: Up to 25% of STEMI patients undergoing primary PCI with stenting are resistant to clopidogrel and therefore may be at increased risk for recurrent cardiovascular events. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15184279

J Am Coll Cardiol (2004);44:335-9

B-type natriuretic peptide at presentation and prognosis in patients with ST-segment elevation myocardial infarction: an ENTIRE-TIMI-23 substudy

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OBJECTIVES: We sought to evaluate B-type natriuretic peptide (BNP), alone and in comparison to cardiac troponin I (cTnI) and high-sensitivity C-reactive protein (hs-CRP), for risk assessment at initial presentation with ST-segment elevation myocardial infarction (STEMI). BACKGROUND: Elevated levels of BNP drawn two to four days after acute myocardial infarction are associated with higher mortality. Sparse data are available on its use at first presentation with STEMI. METHODS: We obtained samples from 438 patients presenting within 6 h of STEMI enrolled in the Enoxaparin Tenecteplase-Tissue-Type Plasminogen Activator With or Without Glycoprotein IIb/IIIa Inhibitor as Reperfusion Strategy in ST-Segment Elevation Myocardial Infarction (ENTIRE)-Thrombolysis In Myocardial Infarction (TIMI)-23 trial. Outcomes were assessed through 30 days. RESULTS: Median BNP was higher in patients who died (89 pg/ml, 25th to 75th percentile: 40 to 192), compared with survivors (15 pg/ml, 25th to 75th percentile: 8.8 to 32, $p < 0.0001$). Patients with BNP >80 pg/ml were at significantly higher risk of death (17.4% vs. 1.8%, $p < 0.0001$). Cardiac troponin established a gradient of mortality between the highest and lowest quartile (7.9% vs. 0%, $p = 0.007$). C-reactive protein was not associated with outcome. After adjustment for cTnI, hs-CRP, and major clinical predictors, including age, heart failure, anterior myocardial infarction location, heart rate, and blood pressure, a BNP level >80 pg/ml was associated with a seven-fold higher mortality risk (odds ratio 7.2, 95% CI 1.1 to 40.0, $p < 0.0001$).

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.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15671428

Am Heart J (2004);147:897-904

Prevalence of resistance against activated protein C resulting from factor V Leiden is significantly increased in myocardial infarction: investigation of 507 patients with myocardial infarction

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BACKGROUND: A point mutation in the gene encoding coagulation factor V is a cause of resistance against activated protein C. The presence of factor V Leiden is linked to

50% of congenital defects causing venous thrombosis. Its relationship to arterial thrombosis, particularly to myocardial infarction, has not been defined. Therefore, we performed a study on the role of factor V Leiden in patients with myocardial infarction. The study was carried out in Bavarians of German origin, a relatively homogeneous population. METHODS AND RESULTS: The study group consisted of 507 patients with documented myocardial infarction (77.5% (393/507) men, 22.5% (114/507) women), with a mean age of 56.1 (range 18-86) years. Strict criteria for patient selection and highly sensitive and specific functional tests for factor V Leiden were used. In addition, all patients with pathological test results were genotyped. The prevalence of factor V Leiden in patients with myocardial infarction was 8.7% (44/507), a significant increase in the prevalence of this mutation compared with the control group (3.7%, $P = .0025$). The odds ratio was 2.46 (95% CI 1.35-4.50). CONCLUSIONS: A significantly increased prevalence of factor V Leiden in patients with documented myocardial infarction was seen. Patients with this mutation appear to have a predisposition for myocardial infarction.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15131548

Am Heart J (2004);148:e3

A randomized evaluation of the effects of glucose-insulin-potassium infusion on myocardial salvage in patients with acute myocardial infarction treated with reperfusion therapy

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BACKGROUND: Intravenous glucose-insulin-potassium (GIK) may have a positive metabolic influence in patients with acute myocardial infarction (AMI) who receive reperfusion therapy. The objective of this randomized trial was to assess for the first time whether GIK improves myocardial salvage in patients with AMI. METHODS: The Reevaluation of Intensified Venous Metabolic Support for Acute Infarct Size Limitation (REVIVAL) trial is a randomized, open-label study conducted among 312 patients with AMI. Patients were randomly assigned to either the GIK therapy group ($n = 155$) or the control group ($n = 157$). All patients were intended to receive reperfusion treatment, which was given in all but 5 patients (1.6%). The primary end point of the study was salvage index, measured as the proportion of initial perfusion defect (acute technetium-99m sestamibi scintigraphy) salvaged by therapy (follow-up scintigraphy performed after 7 to 14 days). RESULTS: The primary end point of the study, the salvage index, was in median 0.50 (25th, 75th percentiles: 0.18, 0.87) in the GIK group and 0.48 (25th, 75th percentiles: 0.27, 0.78) in the control group ($P = .96$). By 6 months, the mortality rate was 5.8% in the GIK group and 6.4% in the control group ($P = .85$; relative risk, 0.92; 95% CI, 0.37 to 2.26). Subgroup analyses showed that GIK therapy was associated with increased salvage index only among diabetic patients (mean difference, 0.19; 95% CI, 0.01 to 0.37). CONCLUSIONS: The routine use of GIK therapy in patients with AMI is not associated with enhanced myocardial salvage. This therapy appears to improve myocardial salvage only among diabetic patients.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15215812

Am Heart J (2004);147:841-6

Obesity and the risk of death after acute myocardial infarction

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BACKGROUND: In the general population, obesity is associated with an increased risk of all-cause death. However, the importance of obesity in patients with established coronary heart disease is less well defined. **METHODS:** As part of the Determinants of Myocardial Infarction Onset Study, we performed a prospective cohort study of 1898 patients hospitalized with confirmed acute myocardial infarction between 1989 and 1994, with a median follow-up of 3.8 years. We assessed all-cause death through December 1995, using the National Death Index. We categorized patients according to WHO criteria for body mass index (BMI). We compared long-term death according to BMI (kg/m²) by using Cox proportional hazards regression. **RESULTS:** Of the 1898 eligible patients, 607 (32%) were normal weight (18.5 to 24.9 kg/m²), 832 (44%) were overweight (25.0 to 29.9 kg/m²), 331 (17%) were class I obese (30.0 to 34.9 kg/m²), and 128 (7%) were class II or more obese (> or =35.0 kg/m²). A total of 311 patients died during follow-up. After adjustment for potentially confounding risk factors and excluding patients with noncardiac comorbidity, the risk for death appeared to increase linearly, with increasing BMI across all categories (P for trend =.08). The relative risk of death in all obese patients (> or =30 kg/m²) was 1.46, compared with those with normal weight (95% CI, 0.98 to 2.17). **CONCLUSIONS:** We found that BMI appeared to have a positive, graded relation with post-myocardial infarction death. Whether weight reduction and secondary prevention strategies would reverse this effect in obese population remains to be seen.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15131540

J Am Coll Cardiol (2004);43:549-56

Improved speed and stability of ST-segment recovery with reduced-dose tenecteplase and eptifibatide compared with full-dose tenecteplase for acute ST-segment elevation myocardial infarction

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OBJECTIVES: This sub-study of the Integrilin and Tenecteplase in Acute Myocardial Infarction (INTEGRITI) trial evaluated the impact of combination reperfusion therapy with reduced-dose tenecteplase plus eptifibatide on continuous ST-segment recovery and angiographic results. **BACKGROUND:** Combination therapy with reduced-dose fibrinolytics and glycoprotein IIb/IIIa inhibitors for ST-segment elevation myocardial infarction improves biomarkers of reperfusion success but has not reduced mortality when compared with full-dose fibrinolytics. **METHODS:** We evaluated 140 patients enrolled in the INTEGRITI trial with 24-h continuous 12-lead ST-segment monitoring and angiography at 60 min. The dose-combination regimen of 50% of standard-dose tenecteplase (0.27 microg/kg) plus high-dose eptifibatide (2 boluses of 180 microg/kg separate

median time to stable ST-segment recovery (55 vs. 98 min, $p = 0.06$), improved stable ST-segment recovery by 2 h (89.6% vs. 67.7%, $p = 0.02$), and less recurrent ischemia (34.0% vs. 57.1%, $p = 0.05$) when compared with full-dose tenecteplase. Continuously updated ST-segment recovery analyses demonstrated a modest trend toward greater ST-segment recovery at 30 min (57.7% vs. 40.6%, $p = 0.13$) and 60 min (82.7% vs. 65.6%, $p = 0.08$) with this regimen. These findings correlated with improved angiographic results at 60 min. **CONCLUSIONS:** Combination therapy with reduced-dose tenecteplase and eptifibatid leads to faster, more stable ST-segment recovery and improved angiographic flow patterns, compared with full-dose tenecteplase. These findings question the relationship between biomarkers of reperfusion success and clinical outcomes.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14975462

Circulation (2004);110:1896-902

Comorbidity and myocardial dysfunction are the main explanations for the higher 1-year mortality in acute myocardial infarction with left bundle-branch block

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BACKGROUND: The purpose of this study was to assess the independent contribution of left bundle-branch block (LBBB) on cause-specific 1-year mortality in a large cohort with acute myocardial infarction (MI). **METHODS AND RESULTS:** We studied a prospective cohort of 88,026 cases of MI from the Register of Information and Knowledge about Swedish Heart Intensive care Admissions in 72 hospitals in 1995 to 2001. Long-term mortality was calculated by Cox regression analysis, adjusted for multiple covariates that affect mortality by calculation of a propensity score. LBBB was present in 9% (8041 of 88,026) of the MI admissions. Patients with LBBB were older and had a higher prevalence of comorbid conditions than patients with no LBBB. The unadjusted relative risk of death within 1 year was 2.16 (95% CI, 2.08 to 2.24; $P < 0.001$) for LBBB (42%, 3350 of 8041) compared with those with no LBBB (22%, 17,044 of 79,011). After adjustment for a propensity score that takes into account differences in risk factors and acute intervention, LBBB was associated with a relative risk of death of 1.19 (95% CI, 1.14 to 1.24; $P < 0.001$). In a subgroup of 11,812 patients for whom left ventricular ejection fraction was available and could be added to the analysis, the contributing relative risk of LBBB for death was only 1.08 (95% CI, 0.93 to 1.25; $P = 0.33$). The most common cause of death in both groups was ischemic heart disease.

CONCLUSIONS: MI patients with LBBB have more comorbid conditions and an increased unadjusted 1-year mortality. When adjusted for age, baseline characteristics, concomitant diseases, and left ventricular ejection fraction, LBBB does not appear to be an important independent predictor of 1-year mortality in MI.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15451802

Circulation (2004);110:1387-91

Plasma level of B-type natriuretic peptide as a prognostic marker after acute myocardial infarction: a long-term follow-up analysis

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BACKGROUND: Circulating levels of B-type natriuretic peptide (BNP), a cardiac hormone, reflect the severity of cardiac dysfunction. Because the plasma BNP level changes dramatically during the period after the onset of acute myocardial infarction (AMI), identification of a suitable sampling time is problematic. There have been several reports indicating that the plasma BNP level obtained in the acute phase of AMI can be used as a prognostic marker. We examined whether the plasma BNP level measured 3 to 4 weeks after the onset of AMI represents a reliable prognostic marker for patients with AMI. **METHODS AND RESULTS:** We analyzed 145 consecutive patients with AMI. Plasma BNP levels were measured during the 3 to 4 weeks after onset of AMI. Of those patients, 23 experienced fatal cardiac events during this study. The mean follow-up period was 58.6 months. Log BNP, left ventricular end-diastolic pressure, and pulmonary vascular resistance were all significantly higher in the cardiac death group, and there were more men and more patients with a history of heart failure in the cardiac death group. A Cox proportional hazards model analysis showed that log BNP was an independent predictor of cardiac death. The survival rate was significantly higher in patients with log BNP <2.26 (180 pg/mL) than in those with log BNP ≥2.26.

CONCLUSIONS: The plasma BNP level obtained 3 to 4 weeks after the onset of AMI can be used as an independent predictor of cardiac death in patients with AMI.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15353502

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Aborted myocardial infarction in patients with ST-segment elevation: insights from the Assessment of the Safety and Efficacy of a New Thrombolytic Regimen-3 Trial Electrocardiographic Substudy

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OBJECTIVES: The investigators undertook a systematic, comprehensive analysis of the therapeutic response and clinical outcomes of reperfusion therapy for acute ST-segment elevation myocardial infarction (STEMI) in 5,470 patients from the Assessment of the Safety and Efficacy of a New Thrombolytic Regimen (ASSENT)-3 trial. **BACKGROUND:** Prompt effective reperfusion therapy for acute STEMI may attenuate major myocardial necrosis. **METHODS:** We prospectively collected sequential electrocardiographs and clinical data. Aborted myocardial infarction (MI) was defined as maximal creatine kinase < or =2x upper limit of normal coupled with typical evolutionary

0.70, 95% CI 0.50 to 0.98, $p = 0.035$ for one year). A very low-risk subset was identified with $\geq 70\%$ ST-segment resolution at 60 min whose 30-day and 1-year mortality was 1.0% and 2.7%, respectively, compared with 5.9% and 9.3% in aborted MI patients with $< 70\%$ ST-segment resolution at 60 min (all $p < 0.002$). CONCLUSIONS: Prompt fibrinolytic treatment improved the likelihood of aborted MI. The subgroup with complete 60-min ST-segment resolution had the best clinical outcomes.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15234403

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Circadian variation of plaque rupture in acute myocardial infarction

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Studies have reported a circadian variation in the onset of acute myocardial infarction (AMI). Pathologic studies have revealed that plaque rupture is 1 of the major causes of AMI, but none of these has looked specifically at the circadian variation of plaque rupture. The aim of this study was to use intravascular ultrasound (IVUS) to investigate the circadian variation of plaque rupture in AMI. This study included 174 consecutive patients with AMI who underwent preinterventional IVUS. All patients were assigned to either a rupture group or a nonrupture group according to the preinterventional IVUS. In the 81 patients (47%) in the rupture group, the frequency of the onset of AMI increased significantly in the period from 6 A.M. to 12 P.M. compared with all other time periods ($p < 0.05$). The clinical features of AMI in the rupture group were characterized as occurring significantly more at rest (67% vs 31%, $p < 0.01$) and after significantly less preinfarction angina (22% vs 57%, $p < 0.01$) compared with the nonrupture group. A different circadian variation was identified in the nonrupture group, characterized as a significant nocturnal nadir (12 to 6 A.M. compared with all other periods, $p < 0.05$). The circadian variation of AMI is the result of a morning increase in incidence of plaque rupture.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14697456

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Effect of pravastatin compared with placebo initiated within 24 hours of onset of acute myocardial infarction or unstable angina: the Pravastatin in Acute Coronary Treatment (PACT) trial

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BACKGROUND: The efficacy of statin drugs after an acute coronary event is now well established, but the evidence for statin use in the early treatment of acute coronary events remains unclear. METHODS: We tested the effects of administering pravastatin within 24 hours of the onset of symptoms in patients with unstable angina, non-ST-segment elevation myocardial infarction, or ST-segment elevation myocardial infarction. Patient recruitment of 10,000 with 1200 end points was planned, but the trial was stopped early. A total of 3408 patients were randomly assigned to treatment with pravastatin (1710 patients) or matching placebo (1698 patients). Treatment was continued for 4 weeks. The primary end point of the study was a composite of death,

recurrence of myocardial infarction, or readmission to hospital for unstable angina within 30 days of random assignment. RESULTS: The primary end point occurred in 199 of patients allocated to pravastatin (11.6%) and in 211 patients allocated to placebo (12.4%). A relative risk reduction of 6.4% favored allocation to pravastatin but was not statistically significant (95% CI, -13.2% to 27.6%). No adverse effects were seen. CONCLUSIONS: We conclude that 20 to 40 mg of pravastatin can be safely administered within 24 hours of the onset of symptoms of an acute coronary event, with a favorable but not significant trend in outcome at 30 days compared with placebo. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15215811

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Detection of increased temperature of the culprit lesion after recent myocardial infarction: the favorable effect of statins

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BACKGROUND: Increased thermal heterogeneity has been demonstrated in atherosclerotic plaques, with the higher temperature recorded in acute myocardial infarction (MI). Dietary or treatment interventions reduce heat production. The purpose of the present study was to investigate whether increased plaque temperature is maintained for a prolonged period after MI and the role of statin administration.

METHODS: We enrolled 55 patients, 29 with recent MI and 26 with chronic stable angina (CSA). Total cholesterol, C-reactive protein (CRP), interleukin-6 (IL-6) and soluble adhesion molecules were measured in the study population. All patients underwent coronary plaque temperature measurements. Temperature difference (DeltaT) was designated as the temperature of the culprit atherosclerotic plaque minus the temperature of the proximal healthy vessel wall. RESULTS: Under treatment with statins were 19 patients with recent MI and 14 with CSA. In patients with recent MI DeltaT was 0.19 +/- 0.18 degrees C, while in patients with CSA was 0.10 +/- 0.08 degrees C (P =.03). Patients treated with statins had lower DeltaT compared to untreated patients (0.10 +/- 0.11 versus 0.20 +/- 0.18 degrees C, P =.01). Treated patients with recent MI had similar DeltaT compared to CSA patients treated with statins (0.13 +/- 0.13 versus 0.10 +/- 0.11 degrees C, P =.31). In patients with recent MI treated with statins, DeltaT was significantly lower compared to untreated patients (0.13 +/- 0.13 versus 0.20 +/- 0.18 degrees C, P =.01).

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BACKGROUND: It has been shown that transient increase in left ventricular stiffness, assessed by Doppler-derived early filling deceleration time, occurs during the first 24 to 48 hours after myocardial infarction but returns to normal within several days. It has been reported that hyperbaric oxygen treatment has a favorable effect on left ventricular systolic function in patients with acute myocardial infarction treated with thrombolysis. However, there are no data on the effects of hyperbaric oxygen on diastolic function after myocardial infarction. **METHODS:** To assess acute and short-term effects of hyperbaric oxygen on left ventricular chamber stiffness, we studied 74 consecutive patients with first acute myocardial infarction who were randomly assigned to treatment with hyperbaric oxygen combined with streptokinase or streptokinase alone. After thrombolysis, patients in the hyperbaric oxygen group received 100% oxygen at 2 atm for 60 minutes in a hyperbaric chamber. All patients underwent 2-dimensional and Doppler echocardiography 1 (after thrombolysis), 2, 3, 7, 21, and 42 days after myocardial infarction. **RESULTS:** Patient characteristics, including age, sex, risk factors, adjunctive postinfarction therapy, infarct location, and baseline left ventricular volumes and ejection fraction, were similar between groups ($P > .05$ for all). For both groups, deceleration time decreased nonsignificantly from day 1 to day 3 and increased on day 7 ($P < .001$, for both groups), increasing nonsignificantly subsequently. The E/A ratio increased in the entire study group throughout the time of study ($P < .001$, for both groups). The pattern of changes of deceleration time was similar in both groups ($P > .05$ by analysis of variance), as was in subgroups determined by early reperfusion success. **CONCLUSIONS:** These data in a small clinical trial do not support a benefit of hyperbaric oxygen on left ventricular diastolic filling in patients with acute myocardial infarction treated with thrombolysis.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15215810

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Different treatments and outcomes of consecutive patients with non-ST-elevation myocardial infarction depending on initial electrocardiographic changes (results of the Acute Coronary Syndromes [ACOS] Registry)

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Of 6,302 consecutive patients with acute non-ST-elevation myocardial infarction, 42.8% presented with ST depression, 31.9% showed no significant electrocardiographic changes, and 25.3% presented with T inversion. In comparison with patients with T inversion or no significant electrocardiographic changes, patients with ST depression more often had 3-vessel coronary disease, received less acute therapy despite a strong benefit in a subgroup analysis, and had a worse clinical outcome even after adjustment in a multivariate analysis. Patients with T inversion received a high rate of acute therapy and had a better outcome than did patients without significant electrocardiographic changes and patients with ST depression.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15194032

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Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study

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BACKGROUND: Although more than 80% of the global burden of cardiovascular disease occurs in low-income and middle-income countries, knowledge of the importance of risk factors is largely derived from developed countries. Therefore, the effect of such factors on risk of coronary heart disease in most regions of the world is unknown. **METHODS:** We established a standardised case-control study of acute myocardial infarction in 52 countries, representing every inhabited continent. 15152 cases and 14820 controls were enrolled. The relation of smoking, history of hypertension or diabetes, waist/hip ratio, dietary patterns, physical activity, consumption of alcohol, blood apolipoproteins (Apo), and psychosocial factors to myocardial infarction are reported here. Odds ratios and their 99% CIs for the association of risk factors to myocardial infarction and their population attributable risks (PAR) were calculated. **FINDINGS:** Smoking (odds ratio 2.87 for current vs never, PAR 35.7% for current and former vs never), raised ApoB/ApoA1 ratio (3.25 for top vs lowest quintile, PAR 49.2% for top four quintiles vs lowest quintile), history of hypertension (1.91, PAR 17.9%), diabetes (2.37, PAR 9.9%), abdominal obesity (1.12 for top vs lowest tertile and 1.62 for middle vs lowest tertile, PAR 20.1% for top two tertiles vs lowest tertile), psychosocial factors (2.67, PAR 32.5%), daily consumption of fruits and vegetables (0.70, PAR 13.7% for lack of daily consumption), regular alcohol consumption (0.91, PAR 6.7%), and regular physical activity (0.86, PAR 12.2%), were all significantly related to acute myocardial infarction ($p < 0.0001$ for all risk factors and $p = 0.03$ for alcohol). These associations were noted in men and women, old and young, and in all