Am J Cardiol (2005);95:383-6
Angiographic and clinical outcomes associated with direct versus conventional stenting among patients treated with fibrinolytic therapy for ST-elevation acute myocardial infarction
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The present study reports outcomes of direct stenting versus conventional stenting, which was performed during adjunctive/rescue percutaneous coronary intervention (n = 556) in the Integrilin and Tenecteplase in Acute Myocardial Infarction trial, the Enoxaparin as Adjunctive Antithrombin Therapy for ST-Elevation Myocardial Infarction-Thrombolysis in Myocardial Infarction 23 trial, and the Fibrinolytic and Aggrastat ST-Elevation Resolution trial of fibrinolytic therapy in ST-elevation myocardial infarction. Direct stenting was associated with a lower rate of death, myocardial infarction, or congestive heart failure during hospitalization and at 30 days and was independently associated with improved in-hospital outcomes (odds ratio 0.44, 95% confidence interval 0.23 to 0.85, p = 0.014).
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15670549

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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Department of Medicine, Beth Israel Deaconess Medical Center.
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 stetting 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

Am J Cardiol (2005);95:100-1
Comparison of mortality rates in acute myocardial infarction treated by percutaneous coronary intervention versus fibrinolysis
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We studied the relation between angioplasty-related time delay and the effectiveness of the intervention in decreasing death compared with fibrinolysis in patients who had acute myocardial infarction. The absolute survival benefit of angioplasty compared with fibrinolysis decreased by 0.24% for every additional 10-minute delay. Regression analysis showed that percutaneous coronary intervention remained superior to fibrinolysis when a time delay related to percutaneous coronary intervention extended to 110 minutes.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15619401

J Am Coll Cardiol (2004);44:287-96
A randomized trial of rescue angioplasty versus a conservative approach for failed fibrinolysis in ST-segment elevation myocardial infarction: the Middlesbrough Early Revascularization to Limit INfarction (MERLIN) trial
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OBJECTIVES: We sought to compare emergency coronary angiography with or without rescue percutaneous coronary intervention (PCI) with conservative treatment in patients with failed fibrinolysis complicating ST-segment elevation myocardial infarction (STEMI). BACKGROUND: Most patients with STEMI receive fibrinolytic therapy and aspirin. The management of failed fibrinolysis is unclear. METHODS: A total of 307 patients with STEMI and failed fibrinolysis were randomized to emergency coronary angiography with or without rescue PCI or conservative treatment. RESULTS: Thirty-day all-cause mortality was similar in the rescue and conservative groups (9.8% vs. 11%, p = 0.7, risk difference [RD] 1.2%, 95% confidence interval [CI] -5.8 to 8.3). The composite secondary end point of death/re-infarction/stroke/subsequent revascularization/heart failure occurred less frequently in the rescue group (37.3% vs. 50%, p = 0.02, RD 12.7%, 95% CI 1.6 to 23.5), driven by less subsequent revascularization (6.5% vs. 20.1%, p < 0.01, RD 13.6%, 95% CI 6.2 to 21.4). Re-infarction and clinical heart failure were less common in the rescue group (7.2% vs. 10.4%, p = 0.3, RD 3.2%, 95% CI -3.3 to 9.9; and 24.2% vs. 29.2%, p = 0.3, RD 5.7%, 95% CI -4.3 to 15.6, respectively). Strokes and transfusions were more common in the rescue group (4.6% vs. 0.6%, p = 0.03, RD 3.9%, 95% CI 0.5 to 8.6; and 11.1% vs. 1.3%, p < 0.001, RD 9.8%, 95% CI 4.9 to 19.9, respectively). Left ventricular function at 30 days was the same in the two groups. CONCLUSIONS: Rescue angioplasty did not improve survival by 30 days, but

improved event-free survival, almost completely due to a reduction in subsequent revascularization. Rescue angioplasty was associated with more strokes and more transfusions and did not result in preservation of left ventricular systolic function at 30 days.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15261920

Chest (2004);126:600S-608S
Antithrombotic therapy in patients with saphenous vein and internal mammary artery bypass grafts: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy
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This chapter about prevention of coronary artery bypass occlusion is part of the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence Based Guidelines. Grade 1 recommendations are strong and indicate that the benefits do, or do not, outweigh risks, burden, and costs. Grade 2 suggests that individual patients' values may lead to different choices (for a full understanding of the grading see Guyatt et al, CHEST 2004; 126:179S-187S). Among the key recommendations in this chapter are the following: For patients undergoing coronary artery bypass grafting (CABG), we recommend aspirin, 75 to 162 mg/d, starting 6 h after operation over preoperative aspirin (Grade 1A). In patients in whom postoperative bleeding prevents the administration of aspirin at 6 h after CABG, we recommend starting aspirin as soon as possible thereafter (Grade 1C). For patients undergoing CABG, we recommend against addition of dipyridamole to aspirin therapy (Grade 1A). For patients with coronary artery disease undergoing CABG who are allergic to aspirin, we recommend clopidogrel, 300 mg, as a loading dose 6 h after operation followed by 75 mg/d p.o. (Grade 1C+). In patients who undergo CABG for non-ST-segment elevation acute coronary syndrome (ACS), we recommend clopidogrel, 75 mg/d for 9 to 12 months following the procedure in addition to treatment with aspirin (Grade 1A). For patients who have received clopidogrel for ACS and are scheduled for CABG, we recommend discontinuing clopidogrel for 5 days prior to the scheduled surgery (Grade 2A). For patients undergoing CABG who have no other indication for vitamin K antagonists (VKAs), we suggest clinicians to not administer VKAs (Grade 2B). For patients undergoing CABG in whom oral anticoagulants are indicated, such as those with heart valve replacement, we suggest clinicians administer VKA in addition to aspirin (Grade 2C). For all patients with coronary artery disease who undergo internal mammary artery (IMA) bypass grafting,

Thrombolytic-3 (ASSENT-3) randomized trial in acute myocardial infarction
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BACKGROUND: In the ASsessment of the Safety of a New Thrombolytic 3 (ASSENT-3) study, full-dose tenecteplase plus enoxaparin or half-dose tenecteplase plus abciximab reduced the frequency of ischemic complications of acute myocardial infarction, when compared to full-dose tenecteplase plus unfractionated heparin. The aim of the present study was to determine the effect of these fibrinolytic regimens on 1-year mortality. METHODS AND RESULTS: Vital status at 1 year was available for 5942 patients (97.5%) of the 6095 initially enrolled in the study. At 1 year, 515 patients (8.7%) had died. Elderly or female patients and patients with low body weight, previous myocardial infarction, anterior wall myocardial infarction, and diabetes were at increased risk for death at 1 year. Mortality at 1 year was 7.9 % (n = 161) in the heparin group, 8.1% (n = 166) in the enoxaparin group, and 9.3% (n = 188) in the abciximab group (P =.226). Overall, pairwise comparisons did not show a significant difference among treatment regimens: relative risk 1.03 (95% CI 0.82-1.30) for enoxaparin versus heparin (P =.794) and relative risk 1.18 (95% CI 0.95-1.47) for abciximab versus heparin (P =.144). However, 1-year outcome tended to be worse with abciximab in diabetic patients. CONCLUSION: Mortality at 1 year after acute myocardial infarction remains high. Despite a reduction in ischemic complications after acute myocardial infarction with the use of full-dose tenecteplase plus enoxaparin or half-dose tenecteplase plus abciximab, mortality at 1 year was similar in these treatment groups.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15199346

J Am Coll Cardiol (2004);44:2073-9
A randomized trial of coronary stenting versus balloon angioplasty as a rescue intervention after failed thrombolysis in patients with acute myocardial infarction
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OBJECTIVES: This study was conducted to assess whether coronary stenting produces better results compared with balloon angioplasty in patients with acute myocardial infarction (AMI) after failed thrombolysis. BACKGROUND: Little evidence exists on the value of rescue mechanical reperfusion after failed thrombolysis. METHODS: This open-label, randomized study enrolled 181 patients with AMI referred for failed thrombolysis performed within the previous 24 h. The patients had to have a Thrombolysis In Myocardial Infarction (TIMI) flow grade of <or=2 in coronary angiography. Patients were randomly assigned to coronary stenting (90 patients) or coronary balloon angioplasty (91 patients). Salvage index (proportion of initial perfusion defect salvaged by rescue intervention), which was obtained by paired scintigraphic studies performed 7 to 10 days apart, was the primary end point of the trial. One-year clinical follow-up was assessed. RESULTS: Myocardial salvage index (median [25th, 75th percentiles]) was significantly greater in the stent group than in the angioplasty group (0.35 [0.24, 0.56] vs. 0.25 [0.04, 0.43]; p = 0.005). Major bleeding occurred in four patients (4%) in the stent group and four patients (4%) in the angioplasty group. One-year mortality was 8% (7 patients) in the stent group versus 12% (11 patients) in

the angioplasty group (relative risk, 0.6; 95% confidence interval 0.2 to 1.6; p = 0.35). CONCLUSIONS: Patients with AMI and failed thrombolysis benefit from rescue mechanical reperfusion in terms of myocardial salvage. Coronary stenting is associated with a greater myocardial salvage in this setting compared with coronary balloon angioplasty.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15542294

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 of 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 separated by 10 min, 2.0 microg/kg/min infusion) was compared with full-dose tenecteplase (0.53 microg/kg). RESULTS: The dose-confirmation regimen of reduced-dose tenecteplase plus high-dose eptifibatide was associated with a faster 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

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This chapter about antithrombotic therapy during percutaneous coronary intervention (PCI) is part of the seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence Based Guidelines. Grade 1 recommendations are strong and indicate that the benefits do, or do not, outweigh risks, burden, and costs. Grade 2 suggests that individual patients' values may lead to different choices (for a full understanding of the grading, see Guyatt et al, CHEST 2004;126:179S-187S). Among the key recommendations in this chapter are the following: For patients undergoing PCI, we recommend pretreatment with aspirin, 75 to 325 mg (Grade 1A). For long-term treatment after PCI, we recommend aspirin, 75 to 162 mg/d (Grade 1A). For long-term treatment after PCI in patients who receive antithrombotic agents such as clopidogrel or warfarin, we recommend lower-dose aspirin, 75 to 100 mg/d (Grade 1C+). For patients who undergo stent placement, we recommend the combination of aspirin and a thienopyridine derivative (ticlopidine or clopidogrel) over systemic anticoagulation therapy (Grade 1A). We recommend clopidogrel over ticlopidine (Grade 1A). For all patients undergoing PCI, particularly those undergoing primary PCI, or those with refractory unstable angina or other high-risk features, we recommend use of a glycoprotein (GP) IIb-IIIa antagonist (abciximab or eptifibatide) [Grade 1A]. In patients undergoing PCI for ST-segment elevation MI, we recommend abciximab over eptifibatide (Grade 1B). In patients undergoing PCI, we recommend against the use of tirofiban as an alternative to abciximab (Grade 1A). In patients after uncomplicated PCI, we recommend against routine postprocedural infusion of heparin (Grade 1A). For patients undergoing PCI who are not treated with a GP IIb-IIIa antagonist, we recommend bivalirudin over heparin during PCI (Grade 1A). In PCI patients who are at low risk for complications, we recommend bivalirudin as an alternative to heparin as an adjunct to GP IIb-IIIa antagonists (Grade 1B). In PCI patients who are at high risk for bleeding, we recommend that bivalirudin over heparin as an adjunct to GP IIb-IIIa antagonists (Grade 1B). In patients who undergo PCI with no other indication for systemic anticoagulation therapy, we recommend against routine use of vitamin K antagonists after PCI (Grade 1A).
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15383485

Am J Cardiol (2004);94:772-4
Primary percutaneous coronary intervention versus fibrinolytic therapy in acute myocardial infarction: does the choice of fibrinolytic agent impact on the importance of time-to-treatment?
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The mortality benefit associated with primary percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction may be lost if door-to-balloon time is delayed by >1 hour compared with tissue plasminogen activator therapy door-to-needle time. When a substantial delay in initiating primary PCI is likely, reperfusion therapy with second- or third-generation fibrinolytic agents should be strongly considered.
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n&list_uids=15374785

Am J Cardiol (2004);93:195-8
Effect of abciximab on prothrombin activation and thrombin generation in patients with acute myocardial infarction also receiving reteplase
P. A. Merlini*, et al.*
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Fibrinolysis in acute myocardial infarction activates blood coagulation and may favor reocclusion or ischemic complications. The aim of the GUSTO V Italian Hematologic Substudy was to compare the effects of full-dose reteplase on coagulation activation markers with those of half-dose reteplase combined with full-dose abciximab, a platelet glycoprotein IIb/IIIa receptor antagonist, during the early phase after acute myocardial infarction.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14715345

Am J Cardiol (2004);93:822-5
Activation of the contact system and inflammation after thrombolytic therapy in patients with acute myocardial infarction
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Thrombolytic therapy activates the contact system, and factor XII activation may activate the coagulation cascade and inflammation. It is not known whether an early inflammatory response is induced by thrombolytic therapy in patients with acute myocardial infarction (AMI). We prospectively measured the plasma levels of activated factor XII, cleaved kininogen, prothrombin fragment 1 + 2 (as indexes of the contact phase and coagulation activation), and interleukin-6 and C-reactive protein (CRP) (as indexes of inflammation) in 39 patients hospitalized for AMI within 12 hours of symptom onset: 26 receiving thrombolytic therapy and 13 heparin alone. Blood samples were collected at baseline and after 90 minutes and 24 hours. Patients undergoing thrombolysis had a significant early increase in activated factor XII (from 2.2 ng/ml at baseline to 4.7 ng/ml after 90 minutes; p = 0.0001), cleaved kininogen (from 26% to 37%; p = 0.001), and fragment 1 + 2 (from 1.4 to 2.1 nmol/L; p = 0.0001), whereas the 24-hour levels were similar to baseline levels. The levels of interleukin-6 significantly increased during the first 90 minutes (from 3.9 to 6.3 microg/ml; p = 0.001), and were even higher afte9 4fr3 alsost 90 receivingst 90 1), even hgrhefMerliand 2(6.)19.8evein67(ghe),1),7(et1)

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BACKGROUND: Few data exist from a community-based perspective on the relative effectiveness of primary percutaneous coronary intervention (PCI) as compared with thrombolytic therapy (TT) in elderly patients with ST-elevation myocardial infarction (STEMI), particularly in the current era of coronary stents and newer antithrombotic agents. METHODS: We evaluated data from patients, aged > or =70 years, with STEMI who were enrolled in the Global Registry of Acute Coronary Events study between April 1999, and September 2002. RESULTS: Of the 2975 elderly patients eligible for reperfusion therapy, 365 (12.7%) underwent primary PCI and 769 (26.7%) received TT. The median delay from hospital arrival to therapy was 105 minutes for primary PCI and 40 minutes for TT. Inhospital complications for primary PCI versus TT included mortality (13.5% vs 14.8%), reinfarction (1.1% vs 5.7%), composite of death or reinfarction (14.3% vs 18.7%), cardiogenic shock (11.3% vs 11.6%), major bleeding (8.6% vs 5.9%), and stroke (1.1% vs 2.8%). After adjustment for baseline differences and propensity score, patients receiving primary PCI showed a lower rate of reinfarction (odds ratio [OR], 0.15; 95% CI, 0.05-0.44) and mortality (OR, 0.62; 95% CI, 0.39-0.96) and the composite of reinfarction or death (OR, 0.53; 95% CI, 0.35-0.79), with no difference in other outcome measures. CONCLUSION: Our data suggest that, compared with TT, primary PCI is associated with a decrease in reinfarction and mortality, with no change in other outcome measures, in elderly patients with STEMI. These findings from an observational registry require further confirmation in future randomized clinical trial assessing the optimal reperfusion strategy in the elderly cohort with STEMI.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14760322

Jama (2004);291:947-54
Early administration of reteplase plus abciximab vs abciximab alone in patients with acute myocardial infarction referred for percutaneous coronary intervention: a randomized controlled trial
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CONTEXT: The optimal pharmacological strategy for bridging the delay between admission and performance of percutaneous coronary intervention (PCI) in patients with acute myocardial infarction (MI) is not known. OBJECTIVE: To assess whether early administration of reteplase plus abciximab produces better results compared with abciximab alone in patients with acute MI referred for PCI. DESIGN, SETTING, AND PATIENTS: Open-label, randomized controlled study conducted from May 3, 2001, through June 2, 2003, of 253 patients who were admitted to 13 community hospitals without catheterization facilities (n = 186) and to 5 hospitals with catheterization facilities (n = 67), with the diagnosis of an ST-segment elevation acute MI within 12 hours from onset of symptoms. INTERVENTIONS: Patients received intravenously either the combination of a half-dose reteplase (two 5-U boluses, 30 minutes apart) with a standard dose of abciximab (0.25 mg/kg bolus, 0.125 microg/kg per minute infusion [maximum 10 microg/min for 12 hours]) or the standard dose of abciximab alone; all patients were then transferred for PCI. MAIN OUTCOME MEASURE: Final infarct size

according to a single-photon emission computed tomography study with technetium Tc 99m sestamibi performed between 5 and 10 days after randomization in 228 patients (90.1% of entire sample). RESULTS: Of the 253 patients enrolled, 125 were assigned to reteplase plus abciximab and 128 to abciximab alone. The median (interquartile range) of the final infarct size of the left ventricle was 13.0% (3.0%-28.0%) in the reteplase plus abciximab group and 11.5% (3.0%-26.3%) in the abciximab-alone group (P =.81). The mean difference in final infarct size of left ventricle between the reteplase plus abciximab group and the abciximab group was 1.3% (95% confidence interval [CI], -3.1% to 5.7%). Within 6 months after randomization, the composite secondary end point of death, recurrent MI, or stroke occurred in 8 patients (6.4%) in the reteplase plus abciximab group and 6 patients (4.7%) in the abciximab group (relative risk, 1.4; 95% CI, 0.5-3.9; log-rank P =.56). Major bleeding complications were observed in 7 patients (5.6%) in the reteplase plus abciximab group and 2 patients (1.6%) in the abciximab group (P =.16). CONCLUSION: Early administration of reteplase plus abciximab does not lead to a reduction of infarct size compared with abciximab alone in patients with acute MI referred for PCI.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14982910

Am J Cardiol (2004);93:458-61
Risk factors for intracranial hemorrhage and nonhemorrhagic stroke after fibrinolytic therapy (from the GUSTO-i trial)
D. E. Kandzari*, et al.*
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Of 592 patients in the Global Utilization of Streptokinase and tPA for Occluded Arteries-I trial who had a stroke during initial hospitalization, the risk for intracranial hemorrhage was significantly greater in those with recent facial or head trauma (odds rai .ur-0.0001 Tw[rAn5(odds.
99m sestamibi performed between 5 and 10 days after randomization in 228 patients (90.1% of entire sample). RESULTS: Of the 253 patients enrolled, 125 were assigned to reteplase plus abciximab and 128 to abciximab alone. The median (interquartile range) of the final infarct size of the left ventricle was 13.0% (3.0%-28.0%) in the reteplase plus abciximab group and 11.5% (3.0%-26.3%) in the abciximab-alone group (P =.81). The mean difference in final infarct size of left ventricle between the reteplase plus abciximab group and the abciximab group was 1.3% (95% confidence interval [CI], -3.1% to 5.7%). Within 6 months after randomization, the composite secondary end point of death, recurrent MI, or stroke occurred in 8 patients (6.4%) in the reteplase plus abciximab group and 6 patients (4.7%) in the abciximab group (relative risk, 1.4; 95% CI, 0.5-3.9; log-rank P =.56). Major bleeding complications were observed in 7 patients (5.6%) in the reteplase plus abciximab group and 2 patients (1.6%) in the abciximab group (P =.16). CONCLUSION: Early administration of reteplase plus abciximab does not lead to a reduction of infarct size compared with abciximab alone in patients with acute MI referred for PCI.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14982910

Am J Cardiol (2004);93:458-61
Risk factors for intracranial hemorrhage and nonhemorrhagic stroke after fibrinolytic therapy (from the GUSTO-i trial)
D. E. Kandzari*, et al.*
Department of Medicine, Duke University Medical Center, Durham, North Carolina 27710, USA.
Of 592 patients in the Global Utilization of Streptokinase and tPA for Occluded Arteries-I trial who had a stroke during initial hospitalization, the risk for intracranial hemorrhage was significantly greater in those with recent facial or head trauma (odds ratio 13.0,

involving 111 Canadian hospitals. Trained medical personnel recorded admission, treatment, and discharge data on patients admitted with acute coronary syndromes. RESULTS: From January 1, 1998, to December 31, 2000, 12,739 patients received fibrinolytic therapy for acute myocardial infarction. Of these, 146 patients (1.15%) sustained strokes and 82 patients (0.65%) had an ICH. Advanced age, female sex, history of cerebrovascular event, and systolic hypertension on arrival (systolic blood pressure >160 mm Hg) were identified with a multivariate logistic regression model to be important independent risks factors for ICH. Patients receiving streptokinase had a lower risk of ICH. Among the patients at high risk for ICH, the ICH rates remained low, ranging from 0.7% to 1.8%. CONCLUSION: ICH is an infrequent event after fibrinolytic therapy in ST-elevation MI; this low rate supports broad penetration of this therapy. Simple clinical characteristics are useful in predicting the risk of ICH and allow a clinician to individualize the risk-benefit assessment of this therapy.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15215796

Chest (2004);126:513S-548S
Antithrombotic therapy for coronary artery disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy
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This chapter about antithrombotic therapy for coronary artery disease (CAD) is part of the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence Based Guidelines. Grade 1 recommendations are strong and indicate that the benefits do, or do not, outweigh risks, burden, and costs. Grade 2 suggests that individual patients' values may lead to different choices (for a full understanding of the grading see Guyatt et al, CHEST 2004; 126:179S-187S). Among the key recommendations in this chapter are the following: For patients presenting with non-ST-segment elevation (NSTE) acute coronary syndrome (ACS), we recommend immediate and then daily oral aspirin (Grade 1A). For patients with an aspirin allergy, we recommend immediate treatment with clopidogrel, 300-mg bolus po, followed by 75 mg/d indefinitely (Grade 1A). In all NSTE ACS patients in whom diagnostic catheterization will be delayed or when coronary bypass surgery will not occur until > 5 days, we recommend clopidogrel as bolus therapy (300 mg), followed by 75 mg/d for 9 to 12 months in addition to aspirin (Grade 1A). In NSTE ACS patients in whom angiography will take place within 24 h, we suggest beginning clopidogrel after the coronary anatomy has been determined (Grade 2A). For patients who have received clopidogrel and are scheduled for coronary bypass surgery, we recommend discontinuing clopidogrel for 5 days prior to the scheduled surgery (Grade 2A). In moderate- to high-risk patients presenting with NSTE ACS, we recommend either eptifibatide or tirofiban for initial (early) treatment in addition to treatment with aspirin and heparin (Grade 1A). For the acute treatment of NSTE ACS, we recommend low molecular weight heparins over unfractionated heparin (UFH) [Grade 1B] and UFH over no heparin therapy use with antiplatelet therapies (Grade 1A). We recommend against the direct thrombin inhibitors as routine initial antithrombin therapy (Grade 1B). For patients after myocardial infarction, after ACS, and with stable CAD, we recommend aspirin in doses from 75 to 325 mg as initial therapy and in doses

of 75 to 162 mg as indefinite therapy (Grade 1A). For patients with contraindications to aspirin, we recommend long-term clopidogrel (Grade 1A). For primary prevention in patients with at least moderate risk for a coronary event, we recommend aspirin, 75 to 162 mg/d, over either no antithrombotic therapy or vitamin K antagonist (VKA) [Grade 2A]; for patients at particularly high risk of events in whom the international normalized ratio (INR) can be monitored without difficulty, we suggest low-dose VKA (target INR, 1.5) [Grade 2A].
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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=14975461

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 association of symptom-to-treatment times with impaired Thrombolysis In Myocardial Infarction myocardial perfusion grades (TMPGs). BACKGROUND: Prolonged symptom 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

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 J Cardiol (2004);94:178-81
Effect of rescue or adjunctive percutaneous coronary intervention of the culprit artery after fibrinolytic administration on epicardial flow in nonculprit arteries
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We hypothesized that blood flow in noninfarct arteries would improve after percutaneous coronary intervention of the culprit artery in the setting of ST-elevation myocardial infarction (STEMI). The corrected Thrombolysis In Myocardial Infarction (TIMI) frame count was measured in 94 patients (102 arteries) enrolled in the INTEGRITI, ENTIRE, and FASTER trials of reduced dose fibrinolytic and glycoprotein IIb/IIIa inhibition. The corrected TIMI frame count in nonculprit arteries improved by 3.4 +/- 13.4 frames after percutaneous coronary intervention but remained significantly slower than flow in normal arteries.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15246895

Lancet (2004);364:1045-53
Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided

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.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15380963

Circulation (2004);110:1909-15
Impact of prehospital thrombolysis for acute myocardial infarction on 1-year outcome: results from the French Nationwide USIC 2000 Registry
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BACKGROUND: Limited data are available on the impact of prehospital thrombolysis (PHT) in the "real-world" setting. METHODS AND RESULTS: Of 443 intensive care units in France, 369 (83%) prospectively collected all cases of infarction (< or =48 hours 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

ST-elevation myocardial infarction has been hypothesized to enhance microvascular perfusion. Resolution of ST-segment elevation after thrombolytic therapy is believed to be a marker of myocardial reperfusion and to predict mortality rate. Among 16,588 patients enrolled in the Fifth Global Use of Strategies to Open Occluded Arteries in Acute Myocardial Infarction trial, 1,764 consecutive patients from selected centers had their study electrocardiograms evaluated by a core laboratory for ST-segment deviation resolution 60 minutes after treatment. Patients were categorized into 4 groups: complete resolution (>70%), partial resolution (<70% to 30%), no resolution (<30%), and worsening ST-segment deviation. Patients treated with reteplase or a combination of reteplase plus abciximab had similar rates of complete resolution (32% vs 34%), partial resolution (29% vs 27%), no resolution (15% vs 16%), and worsening ST-segment elevation (23 vs 23%; $p = 0.59$). The 30-day mortality rates in these 4 groups were 2.1%, 5.2%, 5.5%, and 8.1% ($p < 0.001$). Even after accounting for baseline variables, incomplete ST-segment resolution (<70%) was associated with an increased risk of death within 30 days (adjusted hazard ratio 2.41, 95% confidence interval 1.25 to 4.63, $p < 0.008$). Thus, ST-segment resolution at 60 minutes was no

CONCLUSIONS: The adjusted 1-year mortality rate was twice as high in patients treated with fibrinolytic agents and not enrolled in a clinical trial compared with those enrolled. One major reason for the difference in outcome appeared to be the selection of less critically ill patients to the trial.
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Am J Cardiol (2004);93:1465-8
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

Am J Cardiol (2004);94:415-20
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

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 < or =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

Circulation (2004);109:2480-6
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

Am J Cardiol (2004);93:76-80
Influence of conduction disturbances on clinical outcome in patients with acute myocardial infarction receiving thrombolysis (results from the ARGAMI-2 study)
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Right bundle branch block and complete atrioventricular (AV) block are conduction disorders (CDs) that have been observed in 14% of patients admitted with ST-elevation acute myocardial infarction. CDs carry a poor prognosis, with a threefold increase in the mortality rate, mainly due to cardiogenic shock and recurrent fatal myocardial infarction at 1-year follow-up. According to multivariable analysis, CD was the second strongest predictor of death, after high Killip class. Compared with patients without CD, the 1-year outcome of patients with CD was identically worse, irrespective of whether CD appeared during admission, disappeared, or remained constant. Similar adverse outcomes were seen in patients with complete AV block and right bundle branch block.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14697471