Most Important Papers in ST-Elevation Myocardial Infarction

The Editors

The following are highlights from the series, Circulation: Cardiovascular Interventions Topic Review. This series summarizes the most important manuscripts, as selected by the editors, that have published in the Circulation portfolio. The studies included in this article represent the most noteworthy research in the area of ST-elevation myocardial infarction. (Circ Cardiovasc Interv. 2011;4:e55-e66.)

Systems of Care

Prehospital 12-Lead ECG to Triage ST-Elevation Myocardial Infarction and Emergency Department Activation of the Infarct Team Significantly Improves Door-to-Balloon Times: Ambulance Victoria and MonashHEART Acute Myocardial Infarction (MonAMI) 12-Lead ECG Project

Summary: The MonashHEART acute myocardial infarction project adds to the growing body of evidence supporting the use of prehospital triage to improve patient care in the management of ST-elevation myocardial infarction. It supports initiatives aimed at incorporating a multidisciplinary approach to minimize door-to-balloon time. Furthermore, these system improvements do not shift the burden of care or significantly consume resources of individual stakeholders who provide the various components of optimal ST-elevation myocardial infarction management.

Conclusions: The performance of prehospital 12-lead ECG triage and emergency department activation of the infarct team significantly improves door-to-balloon time and results in a greater proportion of patients achieving guideline recommendations.

Editor’s Comment: Door-to-balloon time has been shown to predict outcomes after primary percutaneous coronary intervention, and American Heart Association/American College of Cardiology guidelines recommend the time from first encounter to balloon dilation of >90 minutes. Unfortunately, this is not achieved by the majority of hospitals. Efforts to understand the factors leading to a delay have shown that prehospital ECG and triage is highly effective. This study demonstrates the feasibility of this approach that resulted in a significant reduction in door-to-balloon times and ability to meet the goal in more than 90% of patients.1

Outcomes for Patients With ST-Elevation Myocardial Infarction in Hospitals With and Without Onsite Coronary Artery Bypass Graft Surgery: The New York State Experience

Summary: The benefit of primary percutaneous coronary interventions (P-PCI) for patients with ST-elevation myocardial infarction (STEMI) has been well documented. However, controversy still exists as to whether PCI should be expanded to hospitals without coronary artery bypass graft surgery. In this study, patients who were discharged after PCI for STEMI between January 1, 2003, and December 12, 2006, in P-PCI centers (hospitals with no coronary artery bypass graft surgery and PCI only for patients with STEMI) were propensity-matched with patients in full-service centers, and mortality and subsequent revascularization rates were compared. There were no differences for in-hospital/30-day mortality (2.3% for P-PCI centers versus 1.9% for full-service centers, P=0.40), emergency coronary artery bypass graft surgery (0.06% versus 0.35%, P=0.06), in 3-year mortality (7.1% versus 5.9%, P=0.07), or subsequent revascularization (23.8% versus 21.5%, P=0.52). P-PCI centers had a lower same/next-day coronary artery bypass graft rate (0.23% versus 0.69%, P=0.046) and higher repeat target vessel PCI rates (12.1% versus 9.0%, P=0.003). For patients with STEMI who did not undergo PCI, P-PCI centers had higher in-hospital mortality (28.5% versus 22.3%; adjusted odds ratio, 1.38; 95% confidence interval, 1.08–1.75). In conclusion, no differences between P-PCI centers and full-service centers were found in in-hospital/30-day mortality, the need for emergency surgery, 3-year mortality, or subsequent revascularization, but P-PCI centers had higher repeat target vessel PCI rates and higher mortality rates for patients who did not undergo PCI. P-PCI centers should be monitored very closely, including the monitoring of patients with STEMI who did not undergo PCI.

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Editor’s Comment: Primary PCI is the reperfusion strategy of choice for STEMI. The guidelines have recommended that primary PCI be done in hospitals with surgical backup, but many hospitals do not have surgical programs. In New York State, 11 hospitals were allowed to have primary PCI programs without on-site surgery. This study compared the outcome of these 2 settings and found many outcomes were similar with propensity-adjusted mortality, but the need for repeat target vessel PCI in follow-up was significantly greater in those without on-site surgery. Fewer patients underwent primary PCI, and those who did not had a worse outcome The reason for this difference was not clear, but it emphasizes the differences in practice and outcomes that require continued monitoring.2

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e55
Association Between Prehospital Time Intervals and ST-Elevation Myocardial Infarction System Performance

Summary: Currently, there is little guidance on how emergency medical services should optimize their time before hospital arrival when caring for ST-elevation myocardial infarction patients. This study analyzed the association between 5 prehospital system time intervals and achieving a goal time to percutaneous coronary intervention of ≤90 minutes. The findings imply that developing prehospital time benchmarks for important patient care–related variables may further enhance quality improvement for ST-elevation myocardial infarction care systems. It is important to recognize that not all of the individual prehospital time components may be feasible for implementation in any emergency medical service system. Focusing on individual components with an overall design for implementation may prove beneficial for emergency medical service systems attempting to improve ST-elevation myocardial infarction care. Although an ST-elevation myocardial infarction care system includes many more components than the benchmarks included in this study, these benchmarks may serve as plausible starting points for emergency medical service systems process improvement in ST-elevation myocardial infarction care.

Conclusions: In this patient population, prehospital timing benchmarks were associated with system performance. Although meeting all 5 benchmarks may be an ideal goal, this model may be more useful for identifying areas for system improvement that will have the greatest clinical impact.

Editor’s Comment: Over the past several years, there has been a substantial effort to improve hospital-based systems to limit the time from first medical contact to percutaneous coronary intervention (PCI) to ≤90 minutes. This study adds significant vital information toward achieving this goal by evaluating prehospital systems and care. This study analyzed the overall time period from the 911 call to the cardiac catheterization laboratory table, using data obtained from a regional system in North Carolina. These data identified critical time periods and time intervals that should not be exceeded to achieve the 90-minute goal, including the emergency call to scene time (<10 minutes), total scene time (<15 minutes), and scene to table time (<30 minutes). Although the study derived these benchmarks using data from a single emergency medical services group and was not able to adjust for patient clinical characteristics, it still provides an excellent example of the functionality of a regional system for primary PCI care. It also provides other centers with a blueprint to analyze their own systems and identify areas for improvement to decrease the time interval from first medical contact to primary PCI.

Therapy—Reperfusion

Impact of Thrombus Aspiration on Myocardial Tissue Reperfusion and Left Ventricular Functional Recovery and Remodeling After Primary Angioplasty

Summary: Mounting interest has emerged regarding the role of mechanical devices for thrombus removal for improving reperfusion and survival after primary percutaneous coronary intervention. Whether observed improvements in myocardial reperfusion and clinical outcome with thrombus aspiration are directly connected to better follow-up left ventricular function and geometry has not yet been clarified. In this study, the authors evaluated the effect of manual thrombus aspiration on tissue-level perfusion, as assessed using ST-segment resolution, Thrombolysis In Myocardial Infarction myocardial perfusion grade, and myocardial contrast enhancement by intracoronary myocardial contrast echocardiography and on the time course of changes in regional and global left ventricular function and volumes in patients with ST-segment elevation myo-

Cardioprotective Effects of Ischemic Postconditioning in Patients Treated With Primary Percutaneous Coronary Intervention, Evaluated by Magnetic Resonance

Summary: Acute restoration of myocardial blood flow with primary percutaneous coronary intervention in itself jeopardizes the cardiomyocytes. In some cases, this phenomenon accounts for 50% of the final size of the myocardial infarction. Therefore, it is important to look for means to protect the myocardium during reperfusion. Ischemic postconditioning has been suggested as such a method. Few small studies have demonstrated a beneficial effect of ischemic postconditioning, but the effect on the final infarct size only has been assessed in 38 patients with perfusion defect index measured by scintigraphy as a surrogate measurement for the infarct size. Ischemic postconditioning is simple, cheap, not time-consuming, and a safe adjuvant to primary percutaneous coronary intervention, and the method can be introduced in the catheterization laboratories almost overnight. However, the possible introduction of this modality in our view should be demonstrated in a substantial number of patients before taken into consideration. With the use of cardiac magnetic resonance to measure final infarct size in 86 patients, this article demonstrates a decrease in infarct size of 18% with ischemic postconditioning. Being the first to evaluate effect of ischemic postconditioning by cardiac magnetic resonance, we believe that this study makes an important contribution. Furthermore, it is the first, to our knowledge, to suggest an effect on functional status evaluated by New York Heart Association classification.

Conclusions: Mechanical postconditioning reduces infarct size in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention. The impact of mechanical postconditioning seems to be independent of the size of myocardium at risk.

Editor’s Comment: Postconditioning is another novel therapeutic approach that might reduce reperfusion injury. The paper reports a randomized clinical trial demonstrating that simple, repetitive intracoronary balloon inflations can reduce relative myocardial infarct size. Additional trials of larger sample size capable of detecting improvement in clinical outcomes will be required to recommend this strategy.

Adjunctive Thrombectomy for Acute Myocardial Infarction: A Bayesian Meta-Analysis

Summary: Device-based removal of thrombus from the infarct-related artery (adjunctive thrombectomy) during primary percutane-
ous coronary intervention for acute myocardial infarction (MI) has been the object of increasing interest. Devices can be classified on the basis of their mechanism of action. Suction of the thrombus into a catheter is termed aspiration thrombectomy, whereas mechanical thrombectomy refers to clot fragmentation before aspiration of debris. Aspiration thrombectomy is more simple to perform, and a recent pooled analysis suggested that these less bulky devices have a mortality benefit compared with mechanical devices. In this Bayesian meta-analysis, the authors tested whether thrombectomy with any device or with an aspiration device leads to better myocardial perfusion and clinical outcomes. Bayesian methods, unlike standard methods, are able to provide inferences of direct clinical utility, such as the probability that one intervention is better than another. The authors found that thrombectomy yielded substantially less no-reflow, more ST-segment resolution ≥50%, and more Thrombolysis In Myocardial Infarction myocardial perfusion grade 3. Thrombectomy may be one of the few preventive measures against no-reflow, for which treatments are limited once it is established. However, there was no evidence for a decrease in 30-day post-MI death, death, recurrent MI, or stroke. Moreover, aspiration thrombectomy devices did not lead to substantially better results. It remains possible that a benefit from thrombectomy emerges ≥6 months after MI. Further data on long-term clinical effects of thrombectomy are needed to justify a liberal use of these costly devices in primary percutaneous coronary intervention. The superiority of aspiration devices remains controversial.

Conclusions: In this Bayesian meta-analysis, adjunctive thrombectomy improves early markers of reperfusion but does not substantially affect 30-day post-MI mortality, reinfarction, and stroke. The use of aspiration thrombectomy devices is not associated with a reduction in post-MI clinical outcomes. Thrombectomy is one of the rare effective preventive measures against no-reflow.

Editor’s Comment: Although at least 1 randomized clinical trial has demonstrated a lower 1-year rate of death among primary percutaneous coronary intervention patients treated with thrombus aspiration, several other trials have had negative findings or had follow-up limited to 30 days. Using Bayesian meta-analysis, this report did not demonstrate that either mechanical or aspiration thrombectomy favorably affected clinical outcome, although thrombectomy patients typically had less no-reflow, better flow grades, and more ST-segment resolution. Follow-up was limited to 30 days. Given the consistent findings of benefit using these indirect markers and recognizing that “patient-centered” effects might not be detected until at least 1 year of follow-up, routine use of aspiration thrombectomy should still be considered when performing primary PCI.

A Comparison of Abciximab and Small-Molecule Glycoprotein Ib/IIIa Inhibitors in Patients Undergoing Primary Percutaneous Coronary Intervention: A Meta-Analysis of Contemporary Randomized, Controlled Trials

Summary: Although current guidelines support the use of abciximab in patients undergoing primary percutaneous coronary intervention, small-molecule glycoprotein Ib/IIIa inhibitors are more commonly used in contemporary clinical practice. Small, randomized trials evaluating predominantly angiographic end points have demonstrated no difference between small-molecule glycoprotein Ib/IIIa inhibitors and abciximab in patients undergoing primary percutaneous coronary intervention (PCI), although none of these trials were powered for clinical end points. The authors report a systematic evaluation of clinical outcomes of studies comparing small-molecule glycoprotein Ib/IIIa inhibitors with abciximab in patients undergoing primary PCI. The meta-analysis included 2138 patients from 5 randomized controlled trials. There were no differences in 30-day mortality (odds ratio, 0.84; P=0.38), reinfarction (odds ratio, 1.22; P=0.69), or major bleeding (odds ratio, 1.21; P=0.61) between the 2 adjunctive strategies. Similarly, there was no significant difference in the incidence of death (odds ratio, 0.77; P=0.43) or reinfarction on intermediate-term follow-up. The findings provide further support for the widespread current use of small-molecule glycoprotein Ib/IIIa inhibitors in patients undergoing primary PCI.

Conclusions: In patients undergoing primary PCI for ST-segment elevation myocardial infarction (STEMI), no difference in outcome could be identified in patients treated with small-molecule glycoprotein Ib/IIIa inhibitor or abciximab.

Editor’s Comment: In patients undergoing primary PCI, the administration of glycoprotein Ib/IIIa receptor inhibitors provides rapid periprocedural antiplatelet activity. This may be especially beneficial during the periprocedural period, when simultaneously given oral antiplatelet agents are being converted to their active metabolites. The majority of studies supporting the efficacy of glycoprotein Ib/IIIa inhibitors in STEMI have been performed with abciximab; however, the small-molecule glycoprotein Ib/IIIa inhibitors are used more commonly in daily clinical practice. Despite this, there has been no adequately powered, randomized, head-to-head study of abciximab and the small-molecule glycoprotein Ib/IIIa inhibitors in STEMI patients. This meta-analysis, which includes data from 5 randomized trials of the small-molecule inhibitors tirofiban or eptifibatide versus abciximab in primary PCI, found no difference in mortality or other adverse cardiovascular events at 30 days or 8 months between the treatment groups. Thus, this meta-analysis provides the best evidence to date to demonstrate that there is no difference in clinical outcomes between abciximab and the small-molecule inhibitors in STEMI patients undergoing primary PCI.

Primary Angioplasty Versus Fibrinolysis in Acute Myocardial Infarction: Long-Term Follow-Up in the Danish Acute Myocardial Infarction 2 Trial

Summary: The Danish Acute Myocardial Infarction 2 (DANAMI-2) study was a randomized, multicenter investigation comparing fibrinolytic treatment and primary percutaneous coronary intervention (pPCI) in patients with ST-segment elevation myocardial infarction. It consisted of 2 substudies: a substudy of patients randomized at noninvasive referral hospitals where the pPCI arm included transfer for pPCI and a substudy of patients randomized at hospitals with interventional facilities. The study was terminated prematurely when the third interim analysis showed a significant benefit of pPCI in the referral hospital substudy. The present study investigated the long-term outcome. The primary end point consisted of death and reinfarction, with a median follow-up of 7.8 years. In the overall cohort, pPCI reduced the composite end point from 41.3% in the fibrinolytic arm to 34.8% (P=0.003), reduced reinfarction by an absolute 6.8% (P<0.001), and reduced death by an absolute 3.5% (P=0.14). In the referral hospital substudy, pPCI reduced reinfarction by 5.5% (P=0.006) and mortality by 6.6% (P=0.03). In the smaller invasive hospital substudy, which was terminated after inclusion of only half of the planned number of patients, reinfarction was reduced by 10.2% (P=0.002). The results indicate that transfer from noninvasive referral hospitals to invasive hospitals is associated with a significant improvement in long-term clinical outcome.

Conclusions: The benefit of pPCI over fibrinolysis was maintained at a long-term follow-up. pPCI reduced the risk of reinfarction in the overall cohort and reduced reinfarction and mortality among patients randomized at referral hospitals. This result reinforces that pPCI should be offered to ST-segment elevation myocardial infarction patients when interhospital transport to an invasive hospital can be completed within 120 minutes.

Editor’s Comment: The landmark DANAMI-2 trial found that patients with ST-segment elevation myocardial infarction who were treated with pPCI had fewer adverse events at 30 days and a 45% relative risk reduction compared with patients treated with fibrinolysis. This beneficial effect was seen even in patients who had to be transferred to a PCI center from an outside hospital as long as
transport could be accomplished within 120 minutes. The observed decrease in adverse events was durable at 3 years; the present study extends these earlier findings by following patients for a median of 7.8 years and as long as 10.2 years in some cases. At these later follow-up periods, assignment to primary PCI was associated with a decrease in reinfarction and death, even in the transfer group. Interestingly, this study may underestimate the true long-term benefits of primary PCI, as the study was done prior to the routine implementation of manual thrombectomy and bivalirudin, both of which have been shown to decrease mortality, and before it was recognized that operator experience and hospital volume influenced PCI outcomes.9

Diagnostic Ultrasound Combined With Glycoprotein IIb/IIIa–Targeted Microbubbles Improves Microvascular Recovery After Acute Coronary Thrombotic Occlusions

Summary: Coronary thrombosis on a ruptured coronary plaque is the main pathophysiological event that leads to acute coronary syndromes. Although current pharmacological therapies and interventional techniques have improved the prognosis of patients with acute coronary syndromes, each of these therapeutic interventions has significant limitations. In the present study, the authors demonstrate that diagnostic ultrasound and intravenous microbubbles can improve both microcirculatory and epicardial recanalization rates in acute coronary thromboses. After acute left anterior descending thrombotic occlusions, intravenous platelet-targeted microbubbles combined with brief high–mechanical index diagnostic transthoracic ultrasound transducer guided by a low–mechanical index pulse sequence scheme improved microvascular flow to the risk area and increased epicardial recanalization rates. The improvement in microvascular flow was observed even when epicardial recanalization did not occur and correlated with improvements in wall thickening within the risk area. The addition of ultrasound and microbubbles may permit lower doses of fibrinolytic agents to be administered while still achieving an equivalent pharmacological effect. Furthermore, the enhanced thrombolytic effects would be targeted to just the region being isonified, which would reduce the risk of bleeding at remote locations. Because the ultrasound pressures and frequencies used in this study are already within Food and Drug Administration limits, this supplemental treatment regimen could be tested in ST-segment elevation myocardial infarction to determine whether guided diagnostic ultrasound and intravenous microbubbles will result in improved regional function and better clinical outcomes compared with treatment regimens focused only on recanalizing the epicardial vessel.

Conclusions: Intravenous platelet-targeted microbubbles combined with brief high–mechanical index diagnostic ultrasound impulses guided by contrast pulse sequencing improve both epicardial recanalization rates and microvascular recovery.

Editor’s Comment: Reperfusion therapy with primary percutaneous coronary intervention or fibrinolysis is the mainstay of treatment for ST-elevation myocardial infarction but is limited by time delays and reperfusion microvascular injury. This study examined the ability of therapeutic ultrasound and platelet glycoprotein IIb/IIIa–targeted microbubbles to achieve epicardial and microvascular reperfusion in a porcine model of acute coronary thrombosis. In conjunction with lytic therapy, target microbubbles resulted in significantly greater rates of arterial recanalization and microvascular recovery. Cavitational activity created by application of ultrasound in the presence of microbubbles has potential to be used with proven reperfusion therapies in ST-elevation myocardial infarction to enhance cardio-protection and warrants further investigation.9

Therapy—Other

A Pilot Study of Rapid Cooling by Cold Saline and Endovascular Cooling Before Reperfusion in Patients With ST-Elevation Myocardial Infarction

Summary: The use of endovascular hypothermia in awake patients with acute myocardial infarction has previously been evaluated in the clinical trials ICE-IT and COOL-MI. The trials failed to show a benefit of hypothermia in reducing infarct size. A major problem was that the induction of hypothermia was too slow, and only a minority of patients reached target temperature before reperfusion (percutaneous coronary intervention). In this pilot study, a combination of an infusion of cold saline with an endovascular cooling catheter was evaluated in awake patients with acute myocardial infarction. All patients reached a core body temperature of <35°C without any significant delay in reperfusion therapy, and no increase in heart failure or pulmonary congestion was observed as the result of the hypothermia therapy. Furthermore, a significant reduction in infarct size and Troponin-T levels was observed. Although these promising results must be verified in a larger trial, hypothermia may be a promising candidate for adjunct therapy to revascularization in patients with acute myocardial infarction.

Conclusions: The protocol demonstrates the ability to reach a core body temperature of <35°C before reperfusion in all patients without delaying primary percutaneous coronary intervention and that combination hypothermia as an adjunct therapy in acute myocardial infarction may reduce infarct size at 3 days as measured by MRI.

Editor’s Comment: Hypothermia has been shown to improve survival and neurological outcomes in patients with cardiac arrest and improve outcomes during cardiac surgery. Experimental studies have shown that it can reduce infarct size, but 2 randomized trials have failed to show benefit. It has been suggested that this may be due to inadequate cooling before primary percutaneous coronary intervention. This pilot study demonstrated that rapid cooling can reduce measures of infarct size by MR and troponin release. The findings are encouraging and support a larger, more definitive study.10

Erythropoietin in Patients With Acute ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention: A Randomized, Double-Blind Trial

Summary: Experimental studies have demonstrated a protective role of erythropoietin during ischemia and reperfusion in the heart, with a reduction in infarct size and apoptosis. This randomized, double-blind, clinical trial investigated the effect of short-term erythropoietin in patients with acute myocardial infarction. One hundred thirty-eight patients received either erythropoietin or placebo intravenously during percutaneous coronary intervention, as well as 24 and 48 hours later. The primary end point, left ventricular ejection fraction after 6 months, measured by MRI, showed no differences between groups. Left ventricular ejection fraction, end-systolic end-diastolic volumes, and infarct size were also similar. Moreover, the cumulative 6-month rates of death, recurrent myocardial infarction, stroke, or target-vessel revascularization in the 2 groups were not different. The present clinical study could not confirm any benefit of short-term erythropoietin treatment for patients with acute myocardial infarction.

Conclusions: In patients with acute ST-elevation myocardial infarction treated with primary percutaneous coronary intervention, erythropoietin treatment did not improve left ventricular ejection fraction or reduce infarct size but may increase clinical adverse events.
Effect of Supersaturated Oxygen Delivery on Infarct Size After Percutaneous Coronary Intervention in Acute Myocardial Infarction

Summary: Primary percutaneous coronary intervention (PCI) in patients with acute ST-segment elevation myocardial infarction has become widely accepted as the preferred reperfusion modality because of its high success rate in restoring patency of the occluded infarct artery, with resultant low rates of death, reinfarction, recurrent ischemia, and stroke. Nonetheless, myocardial salvage is often suboptimal in many patients after primary PCI, in part because of late presentation and also because of microcirculatory dysfunction and reperfusion injury. The intracoronary delivery of supersaturated oxygen with a PaO2 of 760–1000 mm Hg into the coronary artery supplying the myocardial infarct zone for 90 minutes after successful primary PCI has been shown in preclinical models to markedly enhance myocardial recovery. In the randomized AMIROT-I and AMIROT-II trials, this therapy was compared with primary PCI without intracoronary infusion in a total of 406 patients with anterior ST-segment elevation myocardial infarction reperfused by successful PCI within 6 hours of symptom onset. Compared with control, supersaturated oxygen (SSO2) resulted in a significantly smaller infarct size at 14 days as measured by Tc-99m sestamibi single-photon emission-computed tomography imaging, with noninferior rates of major adverse cardiovascular events at 30 days. The benefit in terms of infarct size reduction was particularly profound in patients with the largest infarctions (baseline left ventricular ejection fraction <40%), in whom an incremental 10% salvage of the left ventricular myocardium was noted. As such, supersaturated oxygen represents the first adjunctive therapy demonstrated in a pivotal trial to reduce infarct size when used in concert with a mechanical reperfusion strategy in ST-segment elevation myocardial infarction.

Conclusions: Among patients with anterior ST-segment elevation myocardial infarction undergoing PCI within 6 hours of symptom onset, infusion of SSO2 into the left anterior descending artery infarct territory results in a significant reduction in infarct size with noninferior rates of major adverse cardiovascular events at 30 days. The Editors

Paclitaxel-Eluting Stents Compared With Bare Metal Stents in Diabetic Patients With Acute Myocardial Infarction: The Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) Trial

Summary: Diabetes mellitus is associated with an increased risk of adverse outcomes after primary percutaneous intervention (PCI) in patients with ST-segment elevation myocardial infarction. In particular, the rates of angiographic and clinical restenosis as well as mortality are higher in patients with diabetes. The Editors

Effects of Hydration in Contrast-Induced Acute Kidney Injury After Primary Angioplasty: A Randomized, Controlled Trial

Summary: In patients with ST-segment elevation myocardial infarction (STEMI), the incidence of contrast-induced acute kidney injury (CI-AKI) is significantly reduced by intravenous volume expansion with preprocedural and postprocedural infusion of sodium bicarbonate. The findings suggest that routine procedure for patients with STEMI, candidates to primary PCI, should include standard pharmacological treatment associated with early hydration protocol, dosed according to patient weight and baseline ejection fraction, and started in the emergency room whenever feasible.

Conclusions: Adequate intravenous volume expansion may prevent CI-AKI in patients undergoing primary PCI. A regimen of preprocedure and postprocedure hydration therapy with sodium bicarbonate appears to be more efficacious than postprocedure hydration only with isotonic saline.

Editor’s Comment: Iatrogenic CI-AKI is associated with significant cardiovascular morbidity and mortality. At present, the only proven strategy to limit CI-AKI is adequate intravascular volume expansion; data to support the routine use of sodium bicarbonate are still controversial. Patients with STEMI are at particularly high risk for CI-AKI, owing to the lack of adequate prehydration, their clinical comorbidities, and compromised left ventricular function. This study confirms that the rate of CI-AKI remains unacceptably high (20.6%) in STEMI patients and found that a total hydration volume of more than 960 mL was necessary to decrease the rate of CI-AKI. Although both early (weight-based bolus over 1 hour followed by 12 hours of intravenous fluids after the procedure) and late (12 hours of intravenous fluids after the procedure) hydration regimens were studied, no firm conclusion can be made about the superiority of either strategy, given that different intravenous fluids (sodium bicarbonate in dextrose and water versus isotonic saline) were infused for each treatment group, respectively. Thus, although the timing and type of intravenous fluid to prevent CI-AKI remain to be determined, this study provides a benchmark for the volume of intravenous fluids that should be given for intracoronary expansion in STEMI patients undergoing primary PCI.

Editor’s Comment: Although therapies of coronary reperfusion have substantially improved the outcomes of patients with ST-elevation myocardial infarction, not all patients survive, and many are left with impaired left ventricular function. Recognizing the nonhematopoietic effects of erythropoietin and in particular the potential protective activity for cardiomyocytes and endothelial cells after reperfusion, the investigators of this report found no benefit from epoetin-β in reducing infarct size or left ventricular ejection fraction. The negative findings of this trial should not lessen enthusiasm for further studies to reduce reperfusion injury in ST-elevation myocardial infarction.11

Summary: Primary percutaneous coronary intervention (PCI) in patients with acute ST-segment elevation myocardial infarction has become widely accepted as the preferred reperfusion modality because of its high success rate in restoring patency of the occluded infarct artery, with resultant low rates of death, reinfarction, recurrent ischemia, and stroke. Nonetheless, myocardial salvage is often suboptimal in many patients after primary PCI, in part because of late presentation and also because of microcirculatory dysfunction and reperfusion injury. The intracoronary delivery of supersaturated oxygen with a PaO2 of 760–1000 mm Hg into the coronary artery supplying the myocardial infarct zone for 90 minutes after successful primary PCI has been shown in preclinical models to markedly enhance myocardial recovery. In the randomized AMIROT-I and AMIROT-II trials, this therapy was compared with primary PCI without intracoronary infusion in a total of 406 patients with anterior ST-segment elevation myocardial infarction reperfused by successful PCI within 6 hours of symptom onset. Compared with control, supersaturated oxygen (SSO2) resulted in a significantly smaller infarct size at 14 days as measured by Tc-99m sestamibi single-photon emission-computed tomography imaging, with noninferior rates of major adverse cardiovascular events at 30 days. The benefit in terms of infarct size reduction was particularly profound in patients with the largest infarctions (baseline left ventricular ejection fraction <40%), in whom an incremental 10% salvage of the left ventricular myocardium was noted. As such, supersaturated oxygen represents the first adjunctive therapy demonstrated in a pivotal trial to reduce infarct size when used in concert with a mechanical reperfusion strategy in ST-segment elevation myocardial infarction.

Conclusions: Among patients with anterior ST-segment elevation myocardial infarction undergoing PCI within 6 hours of symptom onset, infusion of SSO2 into the left anterior descending artery infarct territory results in a significant reduction in infarct size with noninferior rates of major adverse cardiovascular events at 30 days. The Editors

Editor’s Comment: Reperfusion injury limits the potential benefits of restoring coronary blood flow in patients with ST-segment elevation myocardial infarction. This small, randomized trial indicates that SSO2 delivered directly into an infarct-related artery at the time of primary PCI can significantly reduce infarct size. Although operationally challenging, this treatment holds promise. We hope the investigators and sponsor will be successful in demonstrating clinical benefits of this adjunct to PCI.12

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lesion revascularization and angiographic restenosis at 1 year, with comparable safety outcomes, including stent thrombosis. These results suggest that PES can safely be used to reduce restenosis in high-risk diabetic patients presenting with STEMI.

**Editor's Comment:** Drug-eluting stents used in primary PCI have been shown to decrease the rate of repeat procedures without increasing stent thrombosis or recurrent infarction as compared with BMS. Despite these advantageous outcomes, there has been some uncertainty as to whether or not this benefit is equally applicable to patients with diabetes mellitus. This concern has arisen from the fact that patients with diabetes are known to have an increased risk of restenosis after BMS procedures and to respond differently to sirolimus-eluting stents and PES than nondiabetic individuals. This study adds information about the safety and efficacy of PES in diabetic patients undergoing primary PCI, using a robust data set: diabetic patients treated with a PES had a lower rate of ischemia-driven target lesion revascularization at 1 year without an increase in stent thrombosis. Interestingly, insulin-requiring diabetics had the greatest decrease in adverse cardiovascular events, with higher but nonsignificant rates of stent thrombosis. Thus, this study uses a robust data set to add to other subgroup analyses of diabetic patients by confirming the safety and efficacy of PES in primary PCI in this subgroup.14

**Outcomes**

**Concurrent Microvascular and Infarct Remodeling After Successful Reperfusion of ST-Elevation Acute Myocardial Infarction**

**Summary:** This study provides a new insight into the relationship between microvascular improvement and infarct healing among patients who were treated with primary percutaneous coronary intervention for ST-elevation acute myocardial infarction. The authors enrolled 35 patients with first ST-elevation acute myocardial infarction and measured microvascular function and infarct size at the second day and at 5 months. Microvascular function at the early phase was associated with long-term infarct size even after controlling for confounding factors such as baseline patient characteristics, pain-to-balloon time, and early-phase infarct size. Moreover, microvascular function at the early phase is the single most important determinant of relative decrease in infarct size. On the basis of these findings, further studies evaluating therapeutic approaches for protecting microvascular integrity at the acute phase of ST-elevation acute myocardial infarction that might improve infarct healing and functional recovery are warranted.

**Conclusions:** Improvement in microvascular function in the infarcted territory is associated with reduction in infarct size after reperfused ST-elevation acute myocardial infarction. This link suggests that further investigations are warranted to determine whether therapeutic protection of microvascular integrity results in augmentation of infarct healing.

**Editor’s Comment:** Microvascular damage during ST-elevation acute myocardial infarction has been shown to result in greater infarct size, worse myocardial function, and poorer long-term outcome. To understand the temporal relationships between reperfusion and microvascular function, this study measured coronary flow reserve, index of microvascular resistance by a pressure wire, and infarct size by SPECT imaging. The study confirmed that there was a strong relationship and suggests that microvascular flow should be targeted as a means of reducing infarct size.15

**Mehran Contrast-Induced Nephropathy Risk Score Predicts Short- and Long-Term Clinical Outcomes in Patients With ST-Elevation Myocardial Infarction**

**Summary:** Several ST-elevation myocardial infarction (STEMI) risk scores have been developed to facilitate the decision-making process and predict adverse clinical outcomes in patients treated with fibrinolytics or percutaneous coronary intervention (PCI). In a similar way, different scores have been developed to predict the risk of contrast-induced nephropathy (CIN) in elective or primary PCI setting. Nevertheless, scores validated in both contexts have not been evaluated yet. The present study reports the results of a study done on 891 STEMI patients to validate the Mehran Risk Score (MRS) in a primary PCI setting for short- and long-term clinical outcomes prediction. The results of the present study demonstrated a 10-fold increase in mortality according to the severity of MRS groups. A similar increasing gradient effect was seen across MRS groups for rehospitalizations for angina or congestive heart failure and for major adverse cardiac and cerebrovascular events. Even in a STEMI setting, a positive trend in CIN incidence was seen among strata. Thus, MRS could be applied in the setting of primary PCI to define the best clinical strategy to reduce CIN risk and major adverse cardiac and cerebrovascular events, both in the short- and long-term periods.

**Conclusions:** The MRS may be applied in the primary angioplasty setting population and is able to predict CIN and to stratify patients for poor clinical outcomes both in the short- and long-term follow-up.

**A Model for Predicting Mortality in Acute ST-Segment Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention: Results From the Assessment of Pexelizumab in Acute Myocardial Infarction Trial**

**Summary:** Models to predict mortality using variables available before procedure are needed for risk stratification in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI). The authors used the Cox proportional hazards model to determine baseline independent predictors of 90-day mortality among 5745 patients with STEMI undergoing primary PCI in the Assessment of Pexelizumab in Acute Myocardial Infarction Trial. At 90 days, 271 (4.7%) of the 5745 patients died. Baseline variables independently associated with 90-day mortality included age (hazard ratio [HR], 2.07/10-year increment; 95% confidence interval [CI], 1.84–2.33), Killip class (class 3 or 4: HR, 4.08; 95% CI, 2.84–5.84), heart rate >70 beats per minute (HR, 1.45/10 beats per minute; 95% CI, 1.32–1.60), systolic blood pressure (HR, 0.86/10 mm Hg; 95% CI, 0.82–0.90), creatinine >90 μmol/L (HR, 1.10/10-μmol/L increment; 95% CI, 1.06–1.13), sum of ST-segment deviations (HR, 1.26/mm; 95% CI, 1.12–1.41), and anterior STEMI location (HR, 1.44; 95% CI, 1.09–1.89) (C index, 0.82). The study provides a clinically practical method to assess intermediate-term prognosis of patients with STEMI undergoing primary PCI using baseline clinical and ECG variables that may be helpful in guiding clinical care and for risk adjustment for observational analyses.

**Conclusions:** The study provides a practical method to assess intermediate-term prognosis of patients with STEMI undergoing primary PCI, using baseline clinical and ECG variables. This model identifies key factors affecting prognosis and enables quantitative risk stratification that may be helpful in guiding clinical care and for risk adjustment for observational analyses.
Long-Term Prognosis in an ST-Segment Elevation Myocardial Infarction Population Treated With Routine Primary Percutaneous Coronary Intervention: From Clinical Trial to Real-Life Experience

Summary: Primary percutaneous coronary intervention (pPCI) is the recommended treatment for ST-segment elevation myocardial infarction. The short-term benefit of pPCI compared with fibrinolysis has been demonstrated in a number of trials, the largest of which was the Danish multicenter, randomized study on thrombolytic therapy versus acute coronary angioplasty in acute myocardial infarction (DANAMI)-2 trial. However, our knowledge of long-term prognosis—especially in real-life ST-segment elevation myocardial infarction—populations—is very limited. Furthermore, it is questionable whether patients treated during off hours experience similar outcomes compared with patients treated during office hours. This article demonstrates that ST-segment elevation myocardial infarction patients treated with pPCI have similar baseline variables and exhibited similar good long-term prognosis similar to that in ST-segment elevation myocardial infarction patients in the landmark DANAMI-2 trial. Furthermore, the results suggest that patients treated with routine pPCI during off hours do not experience poorer long-term outcomes compared with patients treated during office hours. This indicates that routine pPCI—performed within an effective organizational structure—can be applied successfully in a real-life population around the clock, even when most patients are transported to the angioplasty center from noninvasive centers.

Conclusions: This study shows that ST-segment elevation myocardial infarction patients treated with contemporary routine pPCI achieve a similar long-term prognosis as patients in the landmark randomized pPCI trial (DANAMI-2). Furthermore, the long-term prognosis was the same regardless of whether the pPCI was performed during off hours or office hours. Thus, pPCI including transportation of patients from noninvasive centers can be applied successfully in a real-life population.

Editor’s Comment: A common criticism of randomized trials is that findings may not be applicable to routine clinical practice. DANAMI-2 provided critical evidence supporting the superiority of primary PCI for patients with STEMI in comparison to fibrinolytic therapy even when patients required intrahospital transfer to have access to PCI. This report validates the findings of DANAMI-2 outside the rigor of a clinical trial, in the “real-world” setting of routine clinical practice.

Long-Term Mortality of Patients Undergoing Cardiac Catheterization for ST-Elevation and Non–ST-Elevation Myocardial Infarction

Summary: In this study of outcomes over a median follow-up period of 4 years among a contemporary cohort of patients undergoing cardiac catheterization for ST-elevation myocardial infarction (STEMI; n=1974) and non-STEMI (NSTEMI; n=2413) at an academic medical center, we compared mortality rates over restricted time intervals and the differential impact of early revascularization on mortality stratified by ST-elevation status. The long-term mortality rates of 29% and 45% for STEMI and NSTEMI, respectively, remain very similar to historical mortality rates among patients with Q-wave and non-Q-wave MI in the era before reperfusion and early invasive therapy, indicating a critical need to develop more efficacious treatment strategies for both types of MI. The adjusted mortality risk was greater for STEMI during the first 2 months (hazard ratio for STEMI versus NSTEMI, 1.85; 95% confidence interval, 1.45–2.38) but greater for NSTEMI after 2 months (hazard ratio for STEMI versus NSTEMI, 0.68; 95% confidence interval, 0.59–0.83). Compared with late or no revascularization, early revascularization was associated with a lower adjusted risk of long-term mortality for both STEMI (hazard ratio, 0.73; 95% confidence interval, 0.58–0.90) and NSTEMI (hazard ratio, 0.76; 95% confidence interval, 0.65–0.89) (P for interaction=0.22). These data suggest that the relative mortality among patients managed invasively for STEMI and NSTEMI is time dependent, with NSTEMI imparting a delayed but substantial enhancement of mortality risk; moreover, early revascularization may improve very late survival to a similar extent for both infarct types. In clinical investigations of early revascularization among patients with NSTEMI, extended follow-up may therefore be necessary to demonstrate treatment benefit.

Conclusions: Among a contemporary cohort of acute MI patients with significant coronary disease during cardiac catheterization, STEMI was associated with a higher risk of short-term mortality, but NSTEMI was associated with a higher risk of long-term mortality. Early revascularization was associated with a similar improvement in long-term outcomes for both STEMI and NSTEMI. These data suggest that in clinical investigations of early revascularization among patients with NSTEMI, extended follow-up may be necessary to demonstrate treatment benefit.

Editor’s Comment: Historically, studies evaluating long-term outcomes after MI have categorized patients according to the presence of Q waves or other ECG changes. In current practice, the definition of MI has evolved to one based on biomarkers and evidence of ischemia, including symptoms and/or ECG changes, and there has been an increase in the utilization of early revascularization procedures. This study utilizes this new definition to provide a contemporary view of changes in the incidence of NSTEMI and STEMI as well as outcomes. The study also documents that NSTEMI patients continue to have more high-risk clinical and angiographic factors and left main and multivessel disease and are less likely to undergo early revascularization procedures than are STEMI patients. Although mortality rates were higher in NSTEMI compared with STEMI patients, those patients who did undergo early revascularization had improved late survival. These observations suggest that to continue to improve late survival in NSTEMI patients, early revascularization in combination aggressive advanced medical therapies should be considered.

Use of Evidence-Based Therapies in Short-Term Outcomes of ST-Segment Elevation Myocardial Infarction and Non–ST-Segment Elevation Myocardial Infarction in Patients With Chronic Kidney Disease: A Report From the National Cardiovascular Data Acute Coronary Treatment and Intervention Outcomes Network Registry

Summary: Chronic kidney disease (CKD) is a risk factor for myocardial infarction (MI) and death. The authors sought to characterize the association between CKD severity and short-term outcomes and the use of in-hospital evidence-based therapies among patients with ST-segment elevation MI (STEMI) and non–ST-segment elevation MI (NSTEMI) using the Acute Coronary Treatment and Intervention Outcomes Network registry, a nationwide sample of STEMI and NSTEMI patients admitted to hospitals in the United States. Overall, 30.5% and 42.9% of patients with STEMI and NSTEMI, respectively, had CKD. Regardless of MI type, patients with progressively more severe CKD had higher rates of death. In addition, patients with
progressively more severe CKD were less likely to receive immediate evidence-based therapies including aspirin, β-blockers, or clopidogrel, were less likely to undergo any reperfusion (STEMI) or revascularization (NSTEMI), and had higher rates of bleeding. We conclude that a large proportion of patients presenting with STEMI or NSTEMI have CKD and have increased in-hospital mortality rates. These patients receive fewer evidence-based therapies. Additional research to define optimal post-MI care in patients with CKD is warranted.

Conclusions: Reports over the past decade have highlighted the importance of CKD among patients with MI. Data from this contemporary cohort suggest that patients with CKD still receive fewer evidence-based therapies and have substantially higher mortality rates.

Editor’s Comment: CKD is known to increase the risk of death and major adverse cardiovascular outcomes after an acute coronary syndrome. The reasons for the poorer outcomes are multifactorial. Using a large nationally representative registry of STEMI and NSTEMI patients, investigators demonstrated a higher prevalence of stage 3–5 CKD than previously recognized in this population. The study documented lower use of revascularization procedures and cardioprotective medication, higher rates of medication dosing errors and bleeding, and progressively higher mortality in more advanced stages of CKD. Although some omissions of care may be appropriate and related to lack of proven therapies or end-of-life directives in this population, the study suggests that there is a great opportunity to improve care in acute coronary syndrome patients with CKD.20

Declining Severity of Myocardial Infarction From 1987 to 2002: The Atherosclerosis Risk in Communities (ARIC) Study

Summary: Death rates for coronary heart disease have been declining in the United States. From a public health standpoint, it is important to identify factors that are contributing to this decline. The authors investigated whether a reduction in severity of myocardial infarction (MI) may contribute to lower death rates. They tracked residents 35–74 years of age in the community surveillance component of the Atherosclerosis Risk in Communities (ARIC) Study who were hospitalized with acute incident MI and looked at severity indicators abstracted from hospital charts. Included in these were ECG, biomarker, and hemodynamic indicators. With few exceptions, the MI severity indicators suggested a significant decline in the severity of MI during the period of 1987–2002. This reduction in severity may have contributed, along with other factors, to the decline in death rates. There may be several reasons for a decline in severity of incident MI; the findings from the present study suggest that 1 factor may be better primary prevention and support ongoing research to determine how preventive care may further reduce coronary heart disease death.

Conclusions: Evidence from ARIC community surveillance suggests that the severity of acute MI has declined among community residents hospitalized for incident MI. This reduction in severity may have contributed, along with other factors, to the decline in death rates for coronary heart disease.

Editor’s Comment: Coronary heart disease mortality rates have been decreasing over the past several decades. To understand the potential mechanisms for the decline in death rates, this study used an observational community surveillance registry to analyze indexes of severity in patients hospitalized for MI. During the time period examined, the use of thrombolytic therapy declined and percutaneous coronary intervention increased. After adjusting for year of MI, several indexes of MI severity remained associated with 28-day case fatality, suggesting that the clinical risk profile of patients in the acute setting of MI is improving. The findings were not race or sex specific. The findings could not be attributed to changes in prehospital delay, which remained constant. These changes likely reflect a combination of improvements in primary prevention and acute hospital care.21

Comparison of Primary Percutaneous Coronary Intervention and Fibrinolytic Therapy in ST-Segment-Elevation Myocardial Infarction: Bayesian Hierarchical Meta-Analyses of Randomized Controlled Trials and Observational Studies

Summary: The American Heart Association Mission Lifeline recently recommended major reorganizations in the structures and processes involved in reperfusion therapy for acute myocardial infarction with ST-segment elevation. In view of the major investments required for these reorganizations, systematic reviews of randomized controlled trials (RCTs) and observational studies to compare primary percutaneous coronary intervention (PCI) and fibrinolytic therapy in diverse patient populations and clinical contexts are particularly timely. Meta-analyses of both RCTs and observational studies are consistent in showing short-term reductions in mortality and reinfection with primary PCI, attesting to the superiority of this reperfusion strategy. The smaller reductions in short-term mortality and reinfection with primary PCI reported in observational studies compared with RCTs may relate to confounding and selection bias, as well as less optimal application of primary PCI in the real world. The inconclusive evidence in observational studies for differences between the 2 reperfusion strategies in long-term mortality and reinfection may be due to optimal long-term medical therapy and coronary intervention in the patients who received fibrinolytic therapy that may have attenuated the early benefits associated with primary PCI. The potential benefits of prehospital fibrinolysis could not be ascertained in this systematic review and may be better evaluated in large RCTs and observational studies.

Conclusions: Compared with fibrinolytic therapy, primary PCI was associated with short-term reductions in mortality, reinfarction, and stroke in ST-segment elevation myocardial infarction. Primary PCI was associated with long-term reductions in mortality and reinfection in RCTs, but there was no conclusive evidence for a long-term benefit in mortality and reinfection in observational studies.

Editor’s Comment: Primary PCI has consistently been shown to be superior to fibrinolytic therapy in RCTs. Whether these findings are generalizable to all comers with ST-elevation myocardial infarction treated outside of clinical trials is less clear. This study used meta-analysis methodology to evaluate both RCTs and observational studies comparing primary PCI and fibrinolytic therapy. Although differences in the magnitude of benefit were found according to study type, primary PCI was associated with reductions in mortality, reinfection, and stroke during short-term follow-up. Long-term reductions in mortality and reinfection with primary PCI was only observed in RCTs. Overall, the study findings support the use of primary PCI over fibrinolysis when available.22

Ticagrelor Versus Clopidogrel in Patients With ST-Elevation Acute Coronary Syndromes Intended for Reperfusion With Primary Percutaneous Coronary Intervention: A Platelet Inhibition and Patient Outcomes (PLATO) Trial Subgroup Analysis

Summary: Ticagrelor, a reversible oral P2Y12-receptor antagonist, provides faster, greater, and more consistent platelet inhibition than clopidogrel. We compared ticagrelor with clopidogrel within the subset of 7544 patients with ST-segment elevation (STE) acute myocardial infarction and planned percutaneous coronary intervention from the Platelet Inhibition and Patient Outcomes (PLATO) randomized, double-blind trial. Patients were allocated to ticagrelor 180-mg loading dose followed by 90 mg twice daily or to clopidogrel 300-mg loading dose (with provision for 300 mg clopidogrel at...
percutaneous coronary intervention) followed by 75 mg daily for 6–12 months plus aspirin. The reduction of the primary end point (myocardial infarction, stroke, or cardiovascular death) with ticagrelor versus clopidogrel (10.8% versus 9.4%; hazard ratio [HR], 0.87; 95% confidence interval, 0.75–1.01; P = 0.07) was consistent with the overall PLATO results. There was no interaction between presentation with STE/left bundle-branch block and randomized treatment (interaction P = 0.29). Ticagrelor also reduced several secondary end points, including myocardial infarction alone (HR, 0.80; P = 0.03), total mortality (HR, 0.82; P = 0.05), and definite stent thrombosis (HR, 0.66; P = 0.03). The risk of stroke was higher with ticagrelor than with clopidogrel (1.7% versus 1.0%; HR, 1.63; 95% confidence interval, 1.07–2.48; P = 0.02). Ticagrelor did not increase the risk of major bleeding (HR, 0.98; P = 0.76) compared with clopidogrel (possibly because of the reversibility of the agent). Dyspnea was more frequent with ticagrelor than with clopidogrel but rarely required drug discontinuation (0.5% versus 0.1%; P = 0.0004). Given the mortality reduction without increased risk of major bleeding, ticagrelor is an attractive alternative to clopidogrel for patients with STE myocardial infarction and planned percutaneous coronary intervention.

Conclusions: In patients with STE–acute coronary syndromes (ACS) and planned primary percutaneous coronary intervention, the effects of ticagrelor were consistent with those observed in the overall PLATO trial.

Editor’s Comment: Dual antiplatelet therapy with aspirin and a P2Y12 receptor antagonist is standard of care in patients with ACS or undergoing percutaneous coronary intervention. Since percutaneous coronary intervention potentiates the thrombogenic milieu that occurs with plaque rupture, rapid and potent platelet inhibition is of paramount importance in the treatment of STE-ACS with intended coronary stenting. The PLATO trial demonstrated that ticagrelor, compared with clopidogrel, reduced the risk of vascular death, myocardial infarction, or stroke at 1 year without increasing the overall risk of major bleeding in a broad population of ACS patients. The current study analyzed the subgroup of patients at highest risk for ischemic and bleeding complications, the STE-ACS cohort, and demonstrated similar overall efficacy with a 13% reduction in the primary efficacy end point. Major bleeding was not increased; however, the risk of stroke was higher in STE-ACS patients receiving ticagrelor. These findings, along with data from trials of other potent oral platelet inhibitors, suggest that the majority of ACS patients benefit more from potent platelet inhibition than can be achieved with clopidogrel but that caution should be exercised in certain individuals such as those at high risk of stroke.23

Intracoronary Versus Intravenous Administration of Abciximab in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention With Thrombus Aspiration: The Comparison of Intracoronary Versus Intravenous Abciximab Administration During Emergency Reperfusion of ST-Segment Elevation Myocardial Infarction (CICERO) Trial

Summary: Administration of the glycoprotein IIb/IIIa inhibitor abciximab is an effective adjunctive antiplatelet strategy during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Experimental studies have reported that higher local concentrations of abciximab exert additional effects, including disaggregation of newly formed thrombus, and can be achieved by intracoronary administration. Recently, small-scale studies have suggested beneficial clinical effects of intracoronary over intravenous administration. In the present Comparison of Intracoronary versus Intravenous Abciximab Administration During Emergency Reperfusion of ST-Segment Elevation Myocardial Infarction (CICERO) trial, 534 ST-segment elevation myocardial infarction patients were randomized within 12 hours of symptom onset to either an intracoronary or an intravenous bolus of abciximab during primary percutaneous coronary intervention with thrombus aspiration. Patients were pretreated with aspirin, heparin, and high-dose clopidogrel. Intracoronary administration of abciximab compared with intravenous administration did not improve the rate of successful myocardial reperfusion as assessed by ST-segment resolution. In contrast, intracoronary administration was associated with a significantly higher rate of successful myocardial reperfusion as assessed by myocardial blush grade and a smaller enzymatic infarct size. In addition, bleeding complications occurred at similar frequencies between both treatment groups. Although intracoronary administration did not improve the primary end point of ST-segment resolution, the beneficial effects on secondary end points may translate into improved clinical outcome. Larger randomized, multicenter trials are required to investigate whether intracoronary administration of abciximab reduces major adverse cardiac events.

Conclusions: In ST-segment elevation myocardial infarction patients undergoing primary percutaneous coronary intervention with thrombus aspiration, intracoronary administration of abciximab compared with intravenous administration does not improve myocardial reperfusion as assessed by ST-segment resolution. However, intracoronary administration is associated with improved myocardial reperfusion as assessed by myocardial blush grade and a smaller enzymatic infarct size.

Editor’s Comment: Clinical and angiographic benefit resulting from the adjunctive administration of intracoronary abciximab to patients presenting with ST-segment elevation myocardial infarction treated with aspiration thrombectomy has not been conclusively determined. This 534-patient, randomized trial comparing an intracoronary with an intravenous abciximab strategy reports improved myocardial blush scores and greater ECG ST-segment resolution in the population receiving intracoronary drug administration suggesting improved microcirculation. Smaller infarct size determined by serial measurements of cardiac biomarkers is also found in the intracoronary abciximab treatment group. Although this study is not powered to provide conclusive data regarding important clinical safety or efficacy end points, the laboratory and angiographic findings are encouraging, suggesting that this intracoronary abciximab treatment strategy not infrequently used in clinical practice might have some merit in combination with aspiration thrombectomy.24

Triple Versus Dual Antiplatelet Therapy in Patients With Acute ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

Summary: Drug-eluting stent implantation in acute myocardial infarction is associated with an increased risk for acute and subacute in-stent thrombosis. Increased platelet activity also has been observed in acute myocardial infarction. Therefore, more aggressive antiplatelet therapy rather than conventional dual antiplatelet therapy may offer extra benefits for acute myocardial infarction patients undergoing primary percutaneous coronary intervention with drug-eluting stents. This article retrospectively evaluates the safety and efficacy of triple antiplatelet therapy (aspirin plus clopidogrel plus cilostazol; n = 1634) and dual antiplatelet therapy (aspirin plus clopidogrel; n = 2569) in 4203 ST-segment elevation myocardial infarction patients who underwent primary percutaneous coronary intervention with drug-eluting stents. Selection of patients for treatment with triple antiplatelet therapy was left to the physician’s discretion. Compared with dual antiplatelet therapy, triple antiplatelet therapy had a similar incidence of major bleeding events but a significantly lower incidence of in-hospital mortality. After adjustment for known confounders, triple antiplatelet therapy had significantly lower incidences of cardiac death (adjusted odds ratio, 0.52; 95% confidence interval, 0.32–0.84; P = 0.007), total death (adjusted odds ratio, 0.60; 95% confidence interval, 0.41–0.89; P = 0.010), and
total major adverse cardiac events (adjusted odds ratio, 0.74; 95% confidence interval, 0.58–0.95; \( P = 0.019 \)) at 8 months than dual antiplatelet therapy. In this large, real-world clinical study in patients with ST-segment elevation myocardial infarction who underwent primary percutaneous coronary intervention with drug-eluting stents, triple antiplatelet therapy not only had a good safety profile but also improved midterm clinical outcomes. Randomized trials are needed to compare the safety and efficacy of the triple and dual antiplatelet therapies in these patients.

**Conclusions:** Triple antiplatelet therapy appears to be superior to dual antiplatelet therapy in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention with drug-eluting stents. These results may provide the rationale for the use of triple antiplatelet therapy in these patients.

**Editor’s Comment:** Pharmacodynamic studies have shown that patients presenting with acute coronary syndrome who are treated with aspirin and clopidogrel demonstrate increased platelet inhibition with the addition of cilastozol. Possible clinical benefit resulting from this triple antiplatelet strategy remains to be proven. Reporting on data obtained from 4203 patients undergoing primary percutaneous coronary intervention with drug-eluting stents who were entered into the Korean Acute Myocardial Infarction Registry, the investigators compare clinical outcomes in patients treated with >6 months of dual antiplatelet therapy (aspirin and clopidogrel) with patients receiving triple antiplatelet therapy involving additional pharmacological treatment with cilastozol for a minimum of 1 month. This nonrandomized, observational study reports that the population treated with the triple antiplatelet therapy strategy had lower inhospital mortality and significantly lower incidences of cardiac death, total death, and major adverse cardiac events at 8 months. No increased bleeding risk was detected in the population receiving early triple antiplatelet therapy. This report supports the concept that early robust antiplatelet therapy in high risk-patients may provide short- and longer-term clinical benefit and suggests that the addition of cilastozol to currently used dual antiplatelet treatment strategies offers possible benefit when treating high-risk patients presenting with ST-segment elevation myocardial infarction for percutaneous coronary intervention with drug-eluting stents. A prospective, randomized, clinical trial will be required to more conclusively address this question.

**Abciximab in Patients With Acute ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention After Clopidogrel Loading: A Randomized, Double-Blind Trial**

**Summary:** Several previous randomized trials have shown that the glycoprotein IIb/IIIa receptor inhibitor abciximab can improve outcomes after primary percutaneous coronary interventions (PCI) in patients with acute ST-segment elevation myocardial infarction. A high loading dose of clopidogrel is increasingly being used before primary PCI. The role of abciximab has not been investigated in patients undergoing primary PCI if given after clopidogrel loading. The aim of the Bavarian Reperfusion Alternatives Evaluation-3 (BRAVE-3) trial was to assess whether upstream administration of abciximab reduces infarct size in patients with ST-segment elevation myocardial infarction undergoing primary PCI after treatment with 600 mg clopidogrel. Left ventricular infarct size was measured by single-photon emission computed tomography with technetium-99m sestamibi performed before discharge. Of the 800 patients enrolled in this multicenter, double-blind, placebo-controlled, randomized trial, 401 patients were assigned to receive abciximab plus a reduced dose of heparin and 399 patients to receive placebo plus a full dose of heparin. Full restoration of flow in the infarct-related artery was achieved in comparable proportions of patients in both groups. Administration of abciximab was not associated with a reduction in infarct size. In addition, this drug did not reduce the combined incidence of all-cause death, recurrent myocardial infarction, stroke, and urgent revascularization of the infarct-related artery over 30 days after randomization. Therefore, abciximab administration might not be needed in patients with ST-segment elevation myocardial infarction undergoing primary PCI after loading with 600 mg clopidogrel.

**Conclusions:** Upstream administration of abciximab is not associated with a reduction in infarct size in patients presenting with acute myocardial infarction within 24 hours of symptom onset and receiving 600 mg clopidogrel.

**Editor’s Comment:** Benefit resulting from the upstream use of abciximab in patients undergoing PCI has been extensively investigated with mixed results. This group of investigators has previously reported no reduction in ischemic events in a low-intermediate patient population undergoing elective PCI that was pretreated with aspirin and 600 mg clopidogrel and received upstream abciximab. However, they subsequently found that pretreatment with clopidogrel 600 mg did not prevent abciximab from showing a positive anti-ischemic effect in patients presenting with acute coronary syndromes. This article reports the findings of an 800-patient, prospective, randomized trial designed to assess whether the upstream (emergency room or cardiac intensive care unit) administration of abciximab results in infarct size reduction in patients presenting within 24 hours of ST-elevation myocardial infarction after loading with 600 mg of clopidogrel before primary PCI. This adjunctive abciximab strategy resulted in no significant reduction in infarct size, with no significant beneficial effect on 30-day clinical outcomes (death, acute or subacute stent thrombosis, and the cumulative end point of death, recurrent myocardial infarction, urgent infarct vessel revascularization, and stroke). These findings do not support using an upstream abciximab treatment strategy in ST-elevation myocardial infarction patients presenting for primary PCI treated with aspirin and 600 mg of clopidogrel to reduce infarct size. A larger clinical trial would be necessary to determine whether this lack of benefit regarding infarct size reduction reflects a lack of clinical benefit.

**Impact of a Statewide ST-Segment Elevation Myocardial Infarction Regionalization Program on Treatment Times for Women, Minorities, and the Elderly**

**Summary:** Prior studies have demonstrated differences in time to reperfusion for ST-elevation myocardial infarction (STEMI) in women, minorities, and the elderly, relative to their counterparts. Regionalization has been shown to improve overall STEMI treatment times. Whether women, the elderly, and minorities are equally likely to benefit from STEMI regionalization compared with middle-aged, white male patients has not been studied. A statewide STEMI regionalization program was associated with comparable improvement in treatment times for women, blacks, and elderly patients compared with middle-aged, white male patients. There remain important opportunities to further reduce STEMI reperfusion times, particularly among the elderly.

**Conclusions:** A statewide STEMI regionalization program was associated with comparable improvement in treatment times for female, black, and elderly patients compared with middle-aged, white male patients. Nevertheless, there remain opportunities to further narrow treatment differences, particularly among the elderly.

**Editor’s Comment:** Does the improvement in overall STEMI treatment time attributed to the development and implementation of statewide STEMI regionalization programs benefit historically underserved populations including women, the elderly, and minorities equally when compared with their white, middle aged, male counterparts? This study analyzes data from before (July 2007 to September 2005) and after (January 2007 to March 2007) the 2006 implementation of Reperfusion of Acute Myocardial Infarction in North Carolina Emergency Department statewide RACE program. They determine that statewide regionalization of STEMI care is
Outcomes Among Patients With ST-Segment Elevation Myocardial Infarction Presenting to Interventional Hospitals With and Without On-Site Cardiac Surgery

Summary: In this analysis of data from the National Registry of Myocardial Infarction, ST-segment elevation myocardial infarction (STEMI) patients presenting to hospitals without back-up cardiac surgery had higher in-hospital mortality and were less likely to receive acute reperfusion therapy when compared with those who presented to hospitals with back-up cardiac surgery, even in a propensity-matched analysis matching for patient characteristics. However, when this propensity-matched analysis was further adjusted for differences in the use of reperfusion therapy, medications within 24 hours, and other hospital characteristics, the difference in mortality was attenuated, suggesting that the difference in outcomes between hospitals with and without cardiac surgery is driven by factors other than the presence of on-site surgery.

Conclusions: STEMI patients presenting to No-OHS hospitals have substantially higher mortality, are less likely to receive guideline-recommended medications within 24 hours, and are less likely to undergo acute reperfusion therapy, although this difference was of borderline significance after adjusting for hospital and treatment variables. There was no difference in mortality among patients undergoing primary percutaneous coronary intervention (PCI).

Editor's Comment: Current data strongly support primary PCI (when available) as the preferable treatment strategy for patients presenting with STEMI. Primary PCI is currently being performed with increasing frequency in hospitals that do not have on-site back-up cardiac surgery. This study analyzes data involving 186 267 STEMI patients treated at 456 hospitals enrolled in the National Registry of Myocardial Infarction from April 2004 to December 2006, comparing outcomes in patients treated at hospitals with and without on-site cardiac surgery. Adjusting for clinical differences in the 2 populations, the investigators found that STEMI patients presenting to hospitals without back-up cardiac surgery had higher in-hospital mortality and were less likely to receive acute reperfusion therapy compared with patients presenting to hospitals with cardiac surgery programs. However, when this analysis was further adjusted for differences in the use of reperfusion therapy and adherence to guideline recommendations regarding medications received within 24 hours, the difference in hospital mortality was attenuated, suggesting that the differences in outcomes were related to factors other than the presence of on-site cardiac surgery. These data suggest that efforts of increase adherence to guideline-recommended protocols at non–cardiac surgery hospitals performing primary PCI may be beneficial.

References


Most Important Papers in ST-Elevation Myocardial Infarction
The Editors

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