Study Question: Although there is an excellent outcome conferred by primary angioplasty in patients with STEMI, the prognostic role of early recanalization in these patients has yet to be investigated. The aim of the study was to evaluate the impact of preprocedural Thrombolysis In Myocardial Infarction (TIMI) flow on 1-year mortality in patients with ST-segment elevation myocardial infarction (STEMI) treated by primary angioplasty.
Methods: The study population was composed of 1791 patients with acute myocardial infarction treated by primary angioplasty at one institution from 1994 to 2001. All angiographic, clinical and follow-up data were prospectively collected. According to the TIMI risk score, patients were stratified in low- and high-risk groups.
Results: Preprocedural TIMI flow was related to postprocedural TIMI flow grade 3 ($p=0.002$), myocardial blush grade 2–3 ($p<0.001$), enzymatic infarct size ($p<0.001$), predischarge ejection fraction ($p<0.001$) and 1-year mortality ($p<0.05$). Multivariate analysis showed that preprocedural TIMI flow grade 3 was an independent predictor of 1-year survival in high-risk patients ($p<0.05$).
Conclusions: This study shows that preprocedural TIMI flow grade 3 is an independent predictor of 1-year survival in high-risk patients with acute myocardial infarction treated by primary angioplasty.
Perspective: The primary finding of the present study is that preprocedural TIMI flow grade 3 is an independent predictor of 1-year survival in high-risk patients with STEMI undergoing mechanical reperfusion. The results suggest that all efforts should be made to obtain optimal restoration of antegrade flow as early as possible in patients with STEMI. DM

Atorvastatin Does Not Affect the Antiplatelet Potency of Clopidogrel When it Is Administered Concomitantly for 5 Weeks in Patients With Acute Coronary Syndromes

Mitsios JV, Papathanasiou AI, Rodis FI, Elisaf M, Goudevenos JA, Tselepis AD. Circulation 2004;109:1335–8.

Study Question: Prior *ex vivo* studies have suggested that the antiplatelet effect of clopidogrel may be attenuated by short-term coadministration of lipophilic statins. The authors investigated whether the coadministration of atorvastatin for 5 weeks in patients with acute coronary syndromes (ACSs) could affect the antiplatelet potency of clopidogrel.
Methods: The study was an open-labeled prospective trial. 45 hypercholesterolemic patients with the first episode of an ACS were included in the study. Patients were randomized to receive daily either 10 mg of atorvastatin ($n=21$) or 40 mg of pravastatin ($n=24$). 30 patients who underwent percutaneous coronary intervention (PCI) received a loading dose of 375 mg of clopidogrel, followed by 75 mg/d for at least 3 months. In the remaining 15 patients who refused to undergo PCI, clopidogrel therapy was not administered. 8 normolipidemic patients with the first episode of an ACS were also included and received only clopidogrel. The serum levels of soluble CD40L and the adenosine 5′-diphosphate– or thrombin receptor activating peptide-14–induced platelet aggregation, as well as P-selectin and CD40L surface expression, were studied at baseline (within 30 minutes after admission) and 5 weeks later.
Results: Neither atorvastatin nor pravastatin significantly influenced the clopidogrel- induced inhibition of platelet activation, nor did clopidogrel influence the therapeutic efficacy of atorvastatin. Coadministration of clopidogrel with either atorvastatin or pravastatin inhibited ADP-induced platelet activation to the same extent as that observed for clopidogrel alone.
Conclusions: The authors concluded that atorvastatin does not affect the antiplatelet potency of clopidogrel when coadministered for 5 weeks in ACS patients.
Perspective: The current study demonstrated that the therapeutic efficacy of clopidogrel in patients with ACS is not significantly influenced by the concomitant administration of atorvastatin for 5 weeks. Moreover, clopidogrel did not affect the therapeutic efficacy of atorvastatin. The results are consistent with data from observational clinical studies suggesting that the proposed CYP3A4 clopidogrel-statin interaction is likely an *ex vivo* phenomenon and not likely to be clinically relevant. DM

Limited Early Antiplatelet Effect of 300 mg Clopidogrel in Patients With Aspirin Therapy Undergoing Percutaneous Coronary Interventions

Lepäntalo A, Virtanen KS, Heikkilä J, Wartiovaara U, Lassila R. Eur Heart J 2004;25:476–83.

Study Question: The study aim was to evaluate the efficacy and variability of the platelet inhibition exerted by 300 mg clopidogrel for the purpose of acute percutaneous coronary interventions (PCIs) using platelet function tests.
Methods: The study was a prospective cohort study. In patients undergoing elective PCI, clopidogrel was added to ongoing acetylsalicylic acid (aspirin) (100 mg/day) at 2.5 hours prior to procedure. Blood samples were collected before administration of clopidogrel and immediately before the intervention from 50 patients. Platelet functions were assessed with traditional aggregation and PFA-100.
Results: At baseline, 14 (28%) patients were poor responders to aspirin according to PFA, and 9 patients (18%) continued to show arachidonic acid-induced aggregation. After clopidogrel, ADP-triggered aggregation was only modestly inhibited in 40% of the patients. 8% of the study population had no measurable antiplatelet effect. The patients with modest response to clopidogrel had higher levels of c-peptide (1.5 nmol/L) than the ones responding well (0.9 nmol/L, $p<0.05$).
Conclusions: The authors concluded that neither ongoing aspirin treatment nor added clopidogrel reached an expected extent of platelet inhibition in all patients. Aspirin-treated patients undergoing PCI have highly variable levels