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Atorvastatin Pretreatment Improves Outcomes in Patients With Acute Coronary Syndromes Undergoing Early Percutaneous Coronary Intervention

Results of the ARMYDA-ACS Randomized Trial

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Objectives This study sought to investigate potential protective effects of atorvastatin in patients with acute coronary syndromes (ACS) undergoing percutaneous coronary intervention (PCI).

Background Randomized studies have shown that pretreatment with atorvastatin may reduce periprocedural myocardial infarction in patients with stable angina during elective PCI; however, this therapy has not been tested in patients with ACS.

Methods A total of 171 patients with non–ST-segment elevation ACS were randomized to pretreatment with atorvastatin (80 mg 12 h before PCI, with a further 40-mg preprocedure dose [n = 86]) or placebo (n = 85). All patients were given a clopidogrel 600-mg loading dose. All patients received long-term atorvastatin treatment thereafter (40 mg/day). The main end point of the trial was a 30-day incidence of major adverse cardiac events (death, myocardial infarction, or unplanned revascularization).

Results The primary end point occurred in 5% of patients in the atorvastatin arm and in 17% of those in the placebo arm (p = 0.01); this difference was mostly driven by reduction of myocardial infarction incidence (5% vs. 15%; p = 0.04). Postprocedural elevation of creatine kinase-MB and troponin-I was also significantly lower in the atorvastatin group (7% vs. 27%, p = 0.001 and 41% vs. 58%, p = 0.039, respectively). At multivariable analysis, pretreatment with atorvastatin conferred an 88% risk reduction of 30-day major adverse cardiac events (odds ratio 0.12, 95% confidence interval 0.05 to 0.50; p = 0.004).

Conclusions The ARMYDA-ACS trial indicates that even short-term pretreatment with atorvastatin may improve outcomes in patients with ACS undergoing early invasive strategy. These findings may support routine use of high-dose statins before intervention in patients with ACS. (J Am Coll Cardiol 2007;49:1272–8) © 2007 by the American College of Cardiology Foundation

The ARMYDA (Atorvastatin for Reduction of MYocardial Damage During Angioplasty) trial (1) has shown that a 7-day pretreatment with atorvastatin is associated with an 81% risk reduction of periprocedural myocardial infarction in patients with stable angina undergoing elective percutaneous coronary intervention (PCI); attenuation of endothelial activation may explain this protective role at least in part (2). The efficacy of atorvastatin pretreatment in patients with acute coronary syndromes undergoing early PCI has not been investigated. Observational data (3) have suggested that patients with acute coronary syndromes who were already receiving statins at the time of intervention have a lower incidence of periprocedural myonecrosis and a better cardiac event-free survival at 6 months; however, patients were treated with different types of statins, variable doses, and unknown duration of previous treatment, and those findings have not been validated in a randomized trial.

Thus, the ARMYDA study group (1,2,4,5) has performed a randomized, placebo-controlled trial evaluating the effects of pretreatment with a specific statin load on 30-day clinical outcomes after PCI in patients with acute coronary syndromes.

Methods

Study population and design. The ARMYDA-ACS (Atorvastatin for Reduction of MYocardial Damage During

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Angioplasty-Acute Coronary Syndromes) trial is a multicenter, randomized, prospective, double-blind clinical trial performed in 3 Italian institutions (Campus Bio-Medico University of Rome, Vito Fazzi Hospital of Lecce, and University La Sapienza of Rome) (Fig. 1). Inclusion criteria were the presence of a non–ST-segment elevation acute coronary syndrome (unstable angina or non–ST-segment elevation acute myocardial infarction) sent to early (<48 h) coronary angiography. Exclusion criteria were a ST-segment elevation acute myocardial infarction; non–ST-segment elevation acute coronary syndrome with high-risk features warranting emergency coronary angiography (6); any increase in liver enzymes (aspartate amino transferases/alanine amino transferases); left ventricular ejection fraction <30%; renal failure with creatinine >3 mg/dl; history of liver or muscle disease; or previous or current treatment with statins. Between January 3, 2005, and December 21, 2006, a total of 771 patients fulfilling the inclusion criteria were initially evaluated; 451 patients were excluded because of previous or current treatment with statins, 41 for non–ST-segment elevation acute coronary syndrome requiring emergency invasive approach, 43 because of low ejection fraction, 30 because of contraindications to statin treatment (liver or muscle disease), and 15 because of renal failure. Eligible patients (n = 191) were randomized to receive placebo or atorvastatin (80-mg loading dose given a mean of 12 h before coronary angiography, with a further 40-mg dose approximately 2 h before the procedure). Patients were assigned to the study arm using an electronic spreadsheet indicating the group assignment by random numbers; randomization blocks were created and distributed to the 3 centers. After coronary angiography, 20 patients (10 in each randomization arm) who did not receive angioplasty were excluded from the study (8 were treated medically and 12 with bypass surgery); thus, 171 patients (86 randomized to atorvastatin and 85 to placebo) with significant coronary artery disease deemed responsible for the clinical instability and undergoing PCI immediately after diagnostic angiography were enrolled and represent the study population. Physicians performing the procedure and the follow-up assessment were not aware of the randomization assignment.

Abbreviations and Acronyms

CRP = C-reactive protein

MACE = major adverse cardiac event

PCI = percutaneous coronary intervention

All interventions were performed with a standard technique. According to protocol, patients were pretreated before intervention with aspirin (100 mg/day) and clopidogrel (600-mg loading dose at least 3 h before the

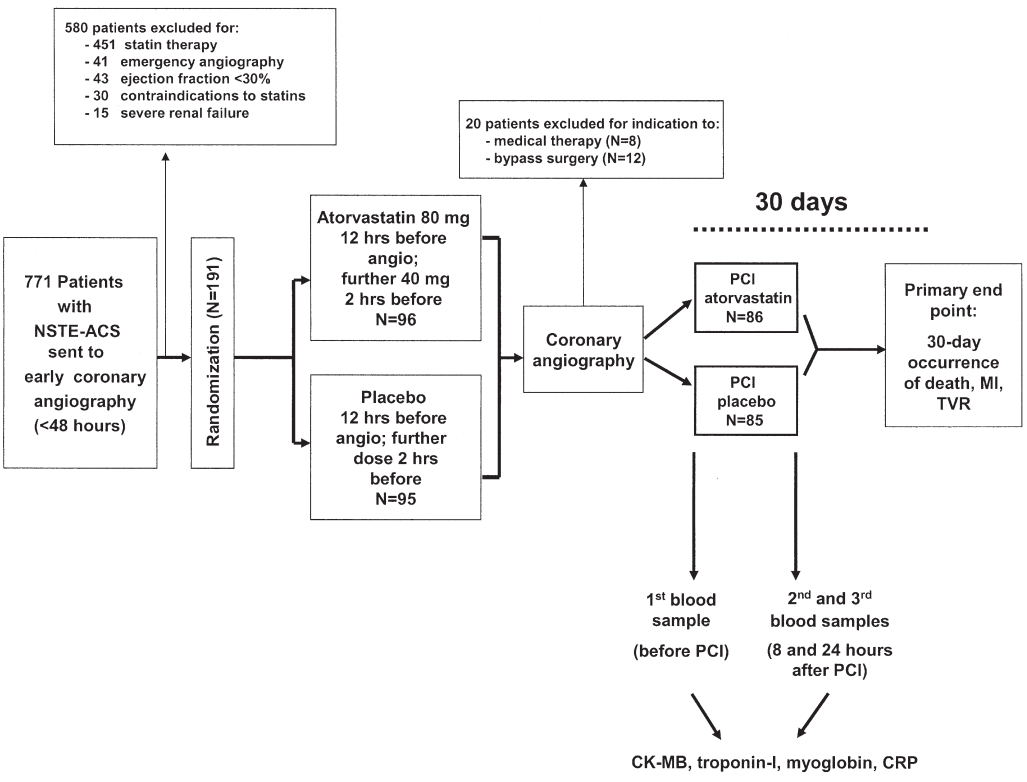

Figure 1 Study Design of the ARMYDA-ACS Trial

ARMYDA-ACS = Atorvastatin for Reduction of MYocardial Damage During Angioplasty—Acute Coronary Syndromes; CK-MB = creatine kinase-MB; CRP = C-reactive protein; MI = myocardial infarction; NSTE-ACS = non–ST-segment elevation acute coronary syndrome; PCI = percutaneous coronary intervention; TVR = target vessel revascularization.