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REVIEW

Pre-Therapy With Statins in Percutaneous Coronary Interventions

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List of Abbreviations:
ACS = acute coronary syndrome
CABG = coronary artery bypass graft surgery
CAD = coronary artery disease
CK-MB = creatine kinase- myocardial band
CPK = creatine kinase
CRP = C-reactive protein
CTFC= corrected TIMI frame count
cTnI = cardiac troponin I
cTnT = cardiac troponin T
MACE = major adverse cardiac event
MI = myocardial infarction
NSTE = non-ST elevation
PCI = percutaneous coronary intervention
RCT = randomized controlled trial
STEMI= ST-elevation myocardial infarction
TFG= TIMI flow grade
TIMI= thrombolysis in myocardial infarction
TMPG= TIMI myocardial perfusion grade
TVR = target vessel revascularization
ULN = upper limit of normal
WHO = World Heart Organization

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ABSTRACT

Statins present a number of beneficial effects on endothelial function and atherosclerotic plaque, modulating oxidative stress and inflammation. The benefits of long-term statin treatment in the entire spectrum of atherosclerotic vascular disease can largely be explained by its cholesterol-lowering effects and the associated reduction of the progression of atherosclerosis. The short-term benefits of statin use are most likely due to their non-lipid, pleiotropic effects. Myocardial injury during percutaneous coronary intervention (PCI) occurs in 10-40% of cases and is often characterized by a slight increase in the markers of myocardial necrosis, sometimes without symptoms, electrocardiographic changes or impairment of cardiac function. Periprocedural myocardial infarction is associated with a worse outcome on long-term follow-up. Several randomized trials have suggested a beneficial effect of pre-treatment with statins in the outcome of the procedure. Myocardial protection by statin pre-therapy in PCI has been studied in several trials published over the last decade. The mechanisms underlying the beneficial pleiotropic effects of statins may be an anti-inflammatory action reducing myocardial injury necrosis due to microembolization, an improvement in endothelial function on microcirculation, and direct myocardial protection. This article reviews the major randomized trials which have studied the use of statins as pre-treatment in PCI and explores future perspectives.

INTRODUCTION

The increasing burden of vascular disease risk factors has led to an increase in the incidence of coronary artery disease (CAD). According to the World Health Organization (WHO), an estimated 7.2 million people died from CAD in 2004, representing 12% of all global deaths and making CAD a leading cause of morbidity and mortality in the developed,[1] as well as in developing countries. Improvements in the medical and surgical care of patients suffering from heart disease have led to a large number of people surviving an acute coronary event. Compared with individuals without CAD, those with previous CAD have a greater absolute risk of recurrent coronary events and hence, derive greater absolute benefits from conventional therapies, such as lipid lowering and blood pressure control. It is well established that patients with dyslipidemias are at an increased risk of developing atherosclerosis and subsequent CAD. The availability of the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors ("statins") has revolutionized the treatment of lipid abnormalities.

Conflict of interest: None declared

Not surprisingly, the decade of the 1990s has been termed the "statin decennial" in the history of CAD prevention.[2]

THE ROLE OF STATINS IN CORONARY ARTERY DISEASE

In patients without cardiovascular disease, a meta-analysis of 7 landmark studies (WOSCOPS, AFCAPS/ TexCAPS, PROSPER, ALLHAT-LLT, ASCOT-LLA, HPS, CARDS) published in 2006, showed that statin therapy decreases the incidence of major coronary and cerebrovascular events and revascularizations but not CAD or overall mortality.[3] On the other hand, in subjects with known cardiovascular disease, statin therapy has proved to be not only beneficial but also cost effective. Several studies have shown that statins improve coronary and cerebrovascular disease outcomes and reduce mortality, in patients with established cardiovascular disease (i.e., secondary prevention).[4-7]

The secondary preventive benefits of atorvastatin are confirmed in various clinical settings, including established CAD. Statin therapy was associated with a 20–42% reduction in long-term mortality.[8] The IDEAL (Incremental Decrease in End Points Through Aggressive Lipid Lowering)[9] and TNT (Treating to New Targets)[10,11] trials demonstrated the preventive efficacy of atorvastatin in patients with stable CAD.

The benefits of long-term statin treatment can largely be explained by its cholesterol-lowering effects (especially the reduction of low-density lipoprotein-LDL cholesterol) and the associated retardation of the progression of atherosclerosis.[12,13] Mechanisms related to the stability of the atherosclerotic plaque may be important in determining clinical outcomes in the early post- acute coronary syndrome (ACS) period. The short-term benefits of statins are most likely due to their non-lipid, pleiotropic effects. Many in vitro as well as in vivo studies have demonstrated that statins acutely decrease the inflammatory response, improve endothelial function, reduce adhesion molecules expression and adhesiveness of leukocyte to vascular endothelium, increase plaque stability, decrease platelet aggregation and thrombus formation, decrease apoptosis, increase stem cell availability and function and have direct protective effects on myocardial cells.[8,14-16] A considerable number of studies published in early-mid 2000s confirmed the beneficial pleiotropic effects of statins on several clinical settings including patients undergoing non-cardiac vascular surgery,[17] coronary artery bypass graft surgery (CABG)[18] as well as patients with ACS. Especially in ACS patients, several studies showed that not only it might be advantageous to start a statin early after hospital admission but also that intensive statin therapy using higher dose of either simvastatin (A-to-Z[19]) or atorvastatin (MIRACL,[20] PROVE-IT TIMI-22[21]) leads to significantly reduced clinical outcomes after 4 months (A-to-Z, MIRACL) with the benefit starting at 30 days (PROVE-IT TIMI-22). Moreover, PCI-PROVE IT,[22] a substudy of PROVE-IT TIMI-22, published in 2009, showed that intensive atorvastatin therapy in patients undergoing PCI, results in significant reduction in target vessel revascularization (TVR) compared to standard statin therapy, an outcome irrelevant to on-treatment LDL-cholesterol when multivariate logistic regression analysis was performed.

THE USE OF STATINS PRIOR TO PERCUTANEOUS CORONARY INTERVENTION (PCI)

Over the last 20 years there is an increasing number of percutaneous coronary intervention (PCI) procedures performed for either stable CAD or ACS. An increase in cardiac enzyme levels is observed in 5-30% of patients undergoing PCI.[23] A considerable number of cases fulfill the criteria (CK-MB>3 x upper limit of normal-ULN) for post-PCI myocardial infarction (MI) (type 4a) according to the latest guidelines,[24] indicating a varying extent of peri-procedural myocardial necrosis. Troponin and CK-MB elevation is not uncommon after PCI as a result of iatrogenic controlled plaque rapture and the subsequent release of many vasoactive substances to the circulation leading to vasoconstriction, endothelial dysfunction, myocardial ischemia and necrosis.[14] Moreover, a considerable number of PCIs are complicated with vessel dissection, compromise of side branches, thrombus formation, distal embolization, or the no-reflow phenomenon.[25] Due to the fact that measurement of cardiac biomarkers after PCI is quite simple, peri-procedural MI has been established as the most suitable quality indicator for PCI care.[26] Since the early '90s, many researchers have examined the impact and the clinical significance of cardiac biomarker elevation after PCI. Although some early studies, using low cutoff concentrations of cardiac enzymes after PCI, had not shown significant correlation with an increased incidence of composite adverse events,[27,28] the majority of the studies conducted over the last 10 years indicate that while minimal increases in troponin after PCI may be benign, a significant rise in CK-MB, especially >5×ULN, appears linked to increased cardiac morbidity and mortality.[29-35] Therefore, a variety of interventions were proposed and tested in order to prevent periprocedural MI, including use of ticlopidine,[36] GpIIb/IIa inhibitors,[37-40] beta blockers,[41] high-dose of clopidogrel[42] and statins. Among them, pre-treatment with statins is the strategy that is most frequently followed.

RANDOMIZED TRIALS (TABLE 1)

In the beginning of the previous decade, two studies showed a decrease in infarct size following an acute statin load given before ischemia[43] or before reperfusion,[44] followed by several other observational studies that demonstrated a significant benefit of statin pre-therapy on peri-procedural elevation of cardiomarkers.[45-48] The first randomized trial scheduled to evaluate the effects of statins before PCI on preventing myocardial damage was the ARMYDA (Atorvastatin for Reduction of Myocardial Damage During Angioplasty)

TABLE 1. Randomized trials of Statin-Loading Before PCI

Study	Year	N	Trial	Clinical status	Previous Statin use	Statin used	Dose	Initiation of therapy before PCI	End point	P value
STATIN-STEMI[59]	2010	171	RCT	STEMI	No	Atorvastatin	80 mg vs 10 mg	Emergency Department	30-day MACE CTFC Myocardial Blush Grade ST-elevation resolution	NS 0.01 0.02 0.01
Yun et al[56]	2009	445	Open label	NSTE-ACS	No	Rosuvastatin	40 mg	7-25h	Peri-procedural MI 30-day MACE	<0.05 0.002
NAPLES II[52]	2009	668	RCT	Stable Angina (53%)	No	Atorvastatin	80 mg	<24h	Peri-procedural MI In hospital MACE	<0.05 0.029
ARMYDA-RECAPTURE[53]	2009	393	RCT	Stable Angina	Yes	Atorvastatin	80 mg	80 mg 12 h and 40 mg before PCI	30-day MACE Peri-procedural MI	0.037 <0.05
Veselka et al.[54]	2009	200	RCT	Stable Angina	No	Atorvastatin	80 mg	48 h	Peri-procedural MI	NS
Jia et al.[55]	2009	228	RCT	NSTE-ACS	No	Simvastatin	80 mg vs. 20 mg	Seven days	Peri-procedural MI TFG CTFC TMPG	0.003 <0.05 <0.001 0.001
ARMYDA-ACS[51]	2007	171	RCT	NSTE-ACS	No	Atorvastatin	80/40 mg	80 mg 12 h and 40 mg before PCI	30-day MACE Peri-procedural MI	0.01 <0.05
Chyrchel et al.[50]	2006	140	Open Label	NSTE-ACS	No	Atorvastatin	80 mg	3 days	Long-term: MI Death+MI Death+MI+PCI	 0.03 0.013 0.006
ARMYDA[49]	2004	153	RCT	Stable Angina	No	Atorvastatin	40 mg	7 days	Peri-procedural MI 30-day MACE	<0.05 0.025
Briguori et al.[23]	2004	451	Open Label	Elective PCI	No	All	80 mg	≥3 days (84% >2weeks)	Peri-procedural MI	0.012

ACS = acute coronary syndrome; MACE = major adverse cardiac event; PCI = percutaneous coronary intervention; RCT = randomized controlled trial; STEMI = ST-elevation Myocardial Infarction; CTFC = corrected TIMI frame count; TFG = TIMI flow grade; TMPG = TIMI myocardial perfusion grade

trial.[49] The investigators randomized 153 stable angina patients to atorvastatin 40 mg/day for seven days before PCI or to placebo. All patients had a positive stress test and were statin-naive, although 40% of them were hypercholesterolemic. The primary end-point of the trial was the incidence of MI, defined as post-PCI increase of CK-MB >2 x the upper limit of normal. Investigators found that treatment with atorvastatin 40 mg was significantly associated with reductions in CK-MB (5% vs 18%, p=0.025). In addition, post-PCI peak values of CK-MB (2.9 ng/ml vs 7.5 ng/ml, p=0.007), troponin I (0.09 ng/ml vs 0.47 ng/ml, p=0.0008) and myoglobin (58 ng/ml vs 81 ng/ml, p=0.0002) were significantly lower in the statin-treated patients than in those who received placebo.

In the same year, Briguori et al[23] randomized 451 statin-naive patients to different types and doses of statins, 17±8 days prior to elective PCI in order to examine the impact of statin administration on periprocedural myocardial infarction. The results were similar with the ARMYDA trial. CK-MB

elevation >5 times ULN occurred in 8% of the patients in the statin group and in 15.6% in the control group (p=0.012; odds ratio- OR=0.47; 95% confidence intervals-CI=0.26–0.86), while CK-MB elevation >3 times ULN was not significant. Moreover, cardiac troponin I elevation >5 times ULN occurred in 23.5% of the patients in the statin group and in 32% in the control group (p=0.043; OR=0.65; 95% CI 0.42–0.98). The authors concluded that pre-procedural statin therapy reduces the incidence of large non-Q-wave myocardial infarction after PCI.

In a Polish study by Chyrchel et al,[50] 140 consecutive patients presenting with non-ST elevation ACS (NSTE-ACS), increased C-reactive protein (CRP) levels and no history of statin use, were randomized either to receive 80 mg of atorvastatin for 3 days prior to intervention or placebo. The incidence of primary endpoint of major adverse cardiac events (MACE) (death, MI, repeat PCI) during long-term follow-up was significantly lower in patients pretreated with a high loading dose of atorvastatin (2.32% vs 14.8%, p=0.013).

The subsequent ARMYDA-ACS study[51] was the first to include patients presenting with NSTE-ACS. In this study, 171 statin-naive patients were randomized either to a short-term pre-treatment strategy of high dose atorvastatin (80 mg) given 12 hours pre-PCI followed by atorvastatin 40 mg immediately prior to the procedure, or to placebo. Statin use reduced 30-day incidence of the composite endpoint of death, MI, and target vessel revascularization-TVR at 30 days by 88% compared to placebo (17% vs 5%, p=0.01). The benefit on major cardiac events was largely driven by a significant reduction in periprocedural MIs defined as a CK-MB level >2×ULN for patients with normal preprocedural CK-MB or a two-fold increase for patients with elevated baseline levels of CK-MB (7% vs 27%, p=0.001). Given the results, the investigators supported the short-term pretreatment with high dose atorvastatin (80+40 mg) in patients with NSTE-ACS planned for early invasive strategy.

During 2009, more prospective randomized trials providing new evidence on the effect of high-dose acute administration of statins prior to PCI were published. The Naples II trial[52] assessed whether a single high loading dose (80 mg) of atorvastatin may reduce the rate of periprocedural MI among a group of 1385 statin-naive patients undergoing elective PCI. The patients were randomized to receive either 80 mg atorvastatin or usual care without additional atorvastatin the day before the procedure (no placebo control was present in the study). There were 668 patients who underwent PCI and stenting in de novo lesions of native coronary artery included in the analysis. At 30 days, treatment with atorvastatin significantly reduced the risk of periprocedural MI as defined by elevations of CK-MB and cardiac troponin I. The primary end point of the study, a CK-MB level 3×ULN alone or with chest pain or ST-T abnormalities, was reached by 9.5% of patients in the active treatment group compared to 15.8% of patients in the control group (p=0.014). A similar effect was also observed with troponin I levels (26.6% vs 39.1%, p<0.001). A post-hoc analysis suggested that the cardioprotective effect of atorvastatin was more pronounced in the subgroup of patients with baseline high levels of CRP. Finally, there was a significant reduction in all in-hospital events including death, MI and repeated revascularization (10% vs 15.7%, p=0.029).

While the previous ARMYDA trials enrolled statin-naive patients, in ARMYDA-RECAPTURE trial[53] researchers randomized a group of patients pretreated with statins, presenting with stable angina and NSTE-ACS to either atorvastatin "reload" or to placebo. The "reload" patients received 80 mg of atorvastatin 12 hours prior to PCI, followed by an additional 40 mg approximately 2 hours before the procedure. All patients were treated with atorvastatin 40 mg after PCI. Of the 457 patients who were randomized, 383 who underwent PCI were analyzed: At 30 days, the rate of major adverse cardiac events, a composite of cardiac death, MI and target vessel revascularization, was significantly lower among patients reloaded with atorvastatin prior to PCI (3.4% vs 9.4%, p=0.045). This benefit was primarily driven by a 2.4-fold reduction in the incidence of periprocedural MI (3.7% vs 8.9%, p=0.056), defined as elevation of CK-MB and troponin I >3×ULN. Logistic regression analysis also revealed a significant benefit on 30-day MACE especially in patients presenting with ACS (3.3% vs 14.8%, p=0.015) as compared to a non-significant difference in patients with stable angina (4% vs 4.9%, p=0.98).

A Czech study by Veselka et al[54] examined once more the effect of high-dose atorvastatin two-day pretreatment in 200 statin-naive patients presenting for elective PCI due to stable angina. This specific study did not find a statistically significant difference between the two groups concerning periprocedural MI, whether CK-MB (10% vs 12%, p=0.70) or troponin I (17% vs 16%, p=0.54) was used as an indicator.

The first randomized control trial not to use atorvastatin was published by Jia et al.[55] The authors investigated the role of an intensive simvastatin regimen (80 mg vs 20 mg) seven days before a programmed PCI after an ACS. A total of 228 patients were randomized and a variety of variables were assessed before and after stent deployment. The authors concluded that intensive simvastatin treatment reduced CK-MB-related periprocedural MI (15.9% vs 27.8%, p=0.003) as well as improved myocardial blood perfusion as measured by Thrombolysis in Myocardial Infarction (TIMI) flow grade (TFG) (p<0.05), corrected TIMI frame count (CTFC) (p<0.001) and TIMI myocardial perfusion grade (TMPG) (0.001) of the intervened vessel.

Yun et al[56] examined whether a single high-dose rosuvastatin loading is beneficial on the outcome of patients with ACS who undergo PCI. A total of 445 patients presenting with NSTE-ACS and planned to early invasive strategy were randomized to receive either a 40 mg rosuvastatin loading 16±5 hours (range 7–25 hours) before PCI or placebo. The

primary end point was the occurrence of periprocedural MI, defined as a post-procedural increase of CK-MB >2×ULN in patients with normal baseline enzyme levels. In patients with elevated baseline levels of CK-MB, MI was defined as a subsequent increase of more than 2-fold in CK-MB from baseline value and an additional increase in second sample. Myocardial infarction by CK-MB elevation was detected after PCI in 11.4% of patients in the control group and in 5.8% of those in the rosuvastatin group (p=0.035). Moreover, after rosuvastatin 40 mg loading, high sensitivity-CRP (hsCRP) levels were less elevated than in patients without rosuvastatin loading (p<0.001).

The same authors just published the results from the12-month follow-up of the above patients[57] that show a reduced incidence of MACE (20.5% vs. 9.8%, p=0.005) and death and non-fatal MI (p=0.021) indicating a beneficial long-term effect of statin pretreatment.

In a meta-analysis[58] including 2804 patients from 10 randomized control trials (four studies included ACS patients and the remaining six studies included patients scheduled for elective PCI), the authors concluded that statins administered before PCI significantly reduce post-procedural MI (7.5% vs. 13.3%, p<0.0001) while repeat revascularization was non-significantly reduced.

In 2010, STATIN STEMI trial[59] was published being the first one to examine the effect of statin preloading in a primary PCI setting after a ST-elevation MI (STEMI). A total of 171 patients presenting with STEMI were randomized to receive either 80 mg atorvastatin or 10 mg atorvastatin before PCI, while all patients continued with a 10-mg regimen after PCI. Although high-dose (80 mg) atorvastatin treatment before primary PCI was associated with a 46% reduction in the primary composite endpoint of 30-day MACE, including death, non-fatal MI and target vessel revascularization, compared with low-dose atorvastatin, this result did not reach statistical significance. The authors attributed this finding to the fact that the study was not nearly powered enough to assess this end-point, because of the small number of events occurring in both groups. Nevertheless, the same study showed significantly improved immediate coronary flow after primary PCI as measured by CTFC (p=0.01), myocardial blush grade (p=0.02) and ST-elevation resolution at 90 min after PCI (p=0.01), indicating better microvascular myocardial perfusion.

PERSPECTIVE

According to the studies presented above, there is a general consensus that statin use before the initiation of PCI is associated with decreased incidence of peri-procedural myonecrosis compared with placebo. Periprocedural CK-MB elevation is independently associated with an increased risk of mortality and other early adverse outcomes in patients with NSTE-ACS, but a definite cause and effect relationship is not well established.[60] Most of the randomized controlled trials showed that statin-naive patients undergoing either elective PCI for chronic stable angina or semi-urgent PCI for ACS, enjoy a significant reduction in peri-procedural MI as well as in major adverse cardiac events (MACE) following oral atorvastatin loading regimens.

Following several non-randomized clinical trials indicating that prior statin use improves outcomes in patients undergoing PCI,[61,62] the ARMYDA-RECAPTURE trial moved forward indicating that a short-term pre-treatment with high-dose atorvastatin load before PCI improves outcomes in patients already receiving chronic statin therapy. An interesting point in this study was that the reduction in periprocedural MIs was observed among patients with ACS whereas no benefit was seen among patients with stable angina. The investigators of Naples-II study suggest that among clinically stable patients undergoing elective PCI, the benefit of acute atorvastatin loading is present in patients with elevated CRP levels and not in patients with normal CRP. Similarly, in the recent study conducted by Yun et al[53] the hsCRP peak after PCI was significantly lower in the rosuvastatin loading group than in the control group. Additionally, the findings derived by previous trials, such as the PROVE-IT TIMI-22 trial, also imply that the anti-inflammatory role of atorvastatin is probably responsible for the early benefit observed within 30 days of an ACS in patients enrolled in comparison to 4 months seen in MIRACL and A-to-Z trials.

From all the above we conclude that survival benefit with statin pretreatment is dependent on the periprocedural inflammatory status and the periprocedural myocardial injury observed is well correlated with subsequent vascular inflammation.[20] Thus, the overall beneficial effect of statins in cardiovascular disease can be explained not only by their lipid-lowering potential but also by their pleiotropic effects, i.e. non-lipid-related mechanisms that may potentially improve outcome after a PCI.[63]

Anti-inflammatory effects of chronic treatment with atorvastatin have been already documented in a randomized controlled trial in patients with rheumatoid arthritis.[64] Statins may also be protective against the development of rheumatoid arthritis in patients with hyperlipidemia,[65] while simvastatin has antiatherosclerotic activity beyond its plasma cholesterol–lowering activity owing to anti-inflammatory effects similar to indomethacin.[66] Early fluvastatin administration decreases dose-dependently the serum concentrations of hs-CRP and tumor necrosis factor (TNF-α) of patients with ACS indicating a strong anti-inflammatory effect beyond the lipid lowering[67] and high dose atorvastatin (80 mg) initiated at the time of coronary artery stent implantation reduces the acute inflammatory response measured by CRP, and six-month clinical events. In patients with NSTE-ACS, the anti-inflammatory activity of statins in CRP and interleukin 6 (IL-6) concentrations may occur as early as a few hours after the first administration before the levels of circulating lipids are significantly affected.[68]

As we have already mentioned, a systemic inflammatory response takes place during PCI as a result of iatrogenic plaque rupture. Coronary angioplasty is followed by a transient increase in adhesion molecule levels due to local endothelial activation/damage,[69] a point that was studied in the ARMYDA-CAMs subanalysis.[70] This study demonstrated that procedural protection in the atorvastatin arm was paralleled by reduction of PCI-induced endothelial activation, as expressed by significant attenuation in the increase of intercellular cell adhesion molecule-1 and E-selectin levels at 24 hours after intervention. Surprisingly, while the cardioprotective effect of statins in animals is lost after chronic treatment, it can be restored when an acute high dose atorvastatin is delivered immediately before ischemia/reperfusion.[71] This finding is in agreement with the results of the ARMYDA-recapture study. This can be explained by the fact that ACS patients have increased plaque inflammatory cell density and a greater local production of inflammatory cytokines, a situation demanding acute suppression afforded by atorvastatin reload.

Other cardioprotective mechanisms include atorvastatin-induced early increase of endothelial progenitor cell differentiation and subsequent augmentation of circulating endothelial progenitors cells with attendant cardioprotective effects,[72,73] inhibition of isoprenoids, which serve as lipid attachments for intracellular signaling molecules,[74] inhibition of plasminogen activator inhibitor I (PAI-I),[73] a rapid increase in nitric oxide bioavailability[75,76] or an activation of specific intracellular pathways such as the PI3-K family.[77]

CONCLUSIONS

Thrombosis and inflammation are intrinsically linked in the pathogenesis of periprocedural myonecrosis in the setting of PCI. Especially in ACS patients, this concept may support the utilization of high dose, intensive statin load taking advantage of their acute pleiotropic effects. All patients should be treated with a high dose of a potent statin as outpatients, which should be continued until the performance of PCI or as soon as possible on arrival at the hospital. In patients previously on statin therapy, it is not unreasonable to consider upstream use of high-dose potent statins by reloading at least 12 hours prior to PCI. Statin naive patients may obtain a significant benefit by atorvastatin loading even 12 and 2 hours prior to the planned PCI, otherwise it would be prudent to postpone elective PCI unless the appropriate preparation has been made along with aspirin and clopidogrel use.

Current data from four ACS trials and at least four elective PCI trials support the notion that use of 80 mg atorvastatin is both beneficial and safe. More randomized control trials are needed to determine the type, dose and appropriate scheme of statin preloading as well as the safety and outcomes of higher anti-inflammatory statin doses. Moreover, there is a need to assess the efficacy of preprocedural statin loading in various clinical settings poorly described as STEMI and emergency/primary PCI.

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