

# A Randomized, Placebo-Controlled Trial of Enoxaparin After High-Risk Coronary Stenting: The ATLAST Trial

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<b>OBJECTIVES</b>	We performed a multicenter, double-blind placebo-controlled trial to examine the efficacy and safety of enoxaparin in patients at high risk for stent thrombosis (ST).
<b>BACKGROUND METHODS</b>	The optimal antithrombotic regimen for such patients is unknown. We randomized 1,102 patients with clinical, angiographic or ultrasonographic features associated with an increased risk of ST to receive either twice-daily injections of weight-adjusted enoxaparin or placebo for 14 days after stenting. All patients received aspirin and ticlopidine. The primary end point was a 30-day composite end point of death, myocardial infarction (MI) or urgent revascularization.
<b>RESULTS</b>	The target enrollment for the study was 2,000 patients. However, the trial was terminated prematurely at 1,102 patients after interim analysis revealed an unexpectedly low event rate. The primary outcome occurred in 1.8% enoxaparin-treated patients versus 2.7% treated with placebo (odds ratio [OR] 0.66; 95% confidence interval [CI] 0.29 to 1.5, $p = 0.30$ ); for death or MI the rates were 0.9% vs. 2.2%, respectively (OR 0.41, 95% CI 0.14 to 1.2, $p = 0.13$ ); and for MI, 0.4% vs. 1.6%, respectively (OR 0.22, 95% CI 0.05 to 0.99, $p = 0.04$ ). The groups had comparable rates of major bleeding (3.3% for enoxaparin, 1.6% for placebo, $p = 0.08$ ), but minor nuisance bleeding was increased with enoxaparin (25% vs. 5.1%, $p < 0.001$ ).
<b>CONCLUSIONS</b>	The clinical outcomes of patients at increased risk of ST are more favorable than previously reported, rendering routine oral antiplatelet therapy adequate for most. However, given its relative safety and potential to reduce the risk of subsequent infarction, a 14-day course of enoxaparin may be considered for carefully selected patients. (J Am Coll Cardiol 2001;38: 1608–13i) © 2001 by the American College of Cardiology

Platelet-fibrin thrombus is central to the pathophysiology of stent thrombosis (ST) (1–8). After successful elective coronary stenting, dual oral antiplatelet therapy (aspirin and a thienopyridine) reduces the risk of ST (1,4,8). However, when stents are urgently implanted for abrupt vessel closure, or when stent deployment is suboptimal, the risks of thrombotic complications such as ST increase at least twofold, to between 3% and 10% (1,2). Although intravenous platelet glycoprotein IIb/IIIa inhibitors reduce periprocedural thrombotic events after both elective and unplanned coronary stenting (9,10), the optimal outpatient antithrombotic regimen for patients at increased risk for ST following hospital discharge has not been established.

Low-molecular-weight heparins (LMWHs) have superior bioavailability, enhanced anti-Xa effects, longer plasma half-lives, lower rates of thrombocytopenia, greater resis-

tance to inactivation by platelets and potentially greater antiplatelet effects than unfractionated heparin (UFH) (11–15). The predictable dose-response of LMWHs obviates laboratory monitoring, facilitating outpatient administration. The LMWH enoxaparin sodium has been shown to be clinically superior to UFH for treatment of acute coronary syndromes (ACS) (16–18). In a pilot study, a 14-day course of enoxaparin combined with ticlopidine and aspirin reduced thrombotic and bleeding risks after coronary stenting compared with the Food and Drug Administration (FDA)-approved post-stent regimen of warfarin, UFH, dextran, dipyridamole and aspirin (19). We performed this study to determine whether the addition of a 14-day course of enoxaparin to oral antiplatelet therapy (aspirin and ticlopidine) would safely reduce postprocedural major thrombotic events in patients at increased risk of ST.

## METHODS

**Study population.** Each site's ethics committee approved the protocol. Patient enrollment occurred between December 1996 and August 1998 in 47 centers across the Netherlands, France, the U.S. and Canada. The study population

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#### Abbreviations and Acronyms

ACS	= acute coronary syndromes
CABG	= coronary artery bypass surgery
CEC	= Clinical Events Committee
CK	= creatine kinase
DSMB	= Data and Safety Monitoring Board
FDA	= Food and Drug Administration
LMWH	= low-molecular-weight heparin
MI	= myocardial infarction
PCI	= percutaneous coronary intervention
SC	= Steering Committee
ST	= stent thrombosis
TIMI	= Thrombolysis In Myocardial Infarction
UFH	= unfractionated heparin

consisted of patients with coronary disease who had received any FDA-approved stent and were considered to be at increased risk of ST because of unplanned urgent stenting, a high likelihood of intracoronary thrombus or suboptimal stent results (1,2).

Patients were eligible if they had any of the following: acute MI <48 h before stenting, abrupt closure with Thrombolysis In Myocardial Infarction (TIMI) grade 0 or 1 flow (20), threatened abrupt closure (TIMI grade 2 flow or angina with significant residual dissection in a target vessel <3.0 mm) before stenting, ejection fraction <35% by ventriculography, total occlusion of target vessel <7 days before stenting, stenting of a degenerated saphenous vein graft <4 mm in diameter with diffuse distal vessel disease, placement of a 2.5-mm diameter stent in a vessel  $\leq$ 2.5 mm, placement of  $\geq$ 1 stents in a true bifurcation lesion, or any of the following by angiography or ultrasound: intracoronary thrombus (discrete intraluminal filling defect occupying  $\geq$ 50% of the target-vessel diameter outlined by intravenous contrast in  $\geq$ 2 orthogonal views), diffuse distal disease (>40% stenosis  $\geq$ 10 mm beyond the distal stent margin), persistent filling defect within the stent, persistent dissection at the stent margin, or suboptimal stent deployment based on residual angiographic stenosis >20% or incomplete stent apposition by ultrasound (failure to achieve a stent cross-sectional area >80% of the smallest proximal or distal reference segment).

Patients were excluded for contraindication to anticoagulation; uncontrolled hypertension (blood pressure  $\geq$ 180/110 mm Hg despite treatment); hemoglobin <9 mg/dl; platelet count <100,000/mm<sup>3</sup>; glycoprotein IIb/IIIa inhibitor or dipyridamole therapy within <72 h; thrombolysis <6 h; planned coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) within 30 days of index stenting; indications for anticoagulation (such as atrial fibrillation); groin hematoma at sheath site >5 cm after stenting; allergy or intolerance to aspirin, ticlopidine, heparin or any LMWH; prior heparin-associated thrombocytopenia; pork allergy; unwillingness or inability to give or receive subcutaneous injections; or serious noncardiac illness.

**Study protocol.** Written informed consent was obtained before or immediately after stenting. Once vascular access was achieved, UFH was given intravenously; the dose was at the discretion of the interventional cardiologist. All patients were treated with open-label, oral aspirin and ticlopidine. Aspirin (325 mg) was given daily, starting on or before the day of stenting and continuing for  $\geq$ 6 months. Ticlopidine (250 mg) was given twice daily for 14 days, beginning  $\leq$ 72 h before stenting. "Loading" doses of aspirin (650 mg) and ticlopidine (500 mg) were recommended for patients not already taking either drug. Stents were implanted in the standard manner according to local practice. To ensure compliance with angiographic and intravascular ultrasound-specified inclusion criteria, the first three angiograms (and randomly selected procedural angiograms thereafter) and all intravascular ultrasound tapes were forwarded to a central core angiographic laboratory (George Washington University Medical Center, Washington, DC) for review. Vascular access sheaths were removed  $\geq$ 4 h after procedural UFH, and compression applied for  $\geq$ 20 min. FDA-approved vascular closure devices were permitted. An activated clotting time <200 s was required before study drug initiation.

At vascular sheath removal, patients were randomized to receive twice daily (every 12 h) subcutaneous injections of either enoxaparin (Lovenox, Aventis Pharma, ) (40 mg in 0.4 ml for patients <65 kg, 60 mg in 0.6 ml for patients >65 kg) or matching placebo (0.4 ml for patients <65 kg, 0.6 ml for patients >65 kg) for 14 days. The first injection was given  $\geq$ 2 h after sheath removal and 4 to 10 h after the last dose of UFH.

**Study committees.** A Clinical Events Committee (CEC), whose members were blinded to treatment allocation, independently adjudicated all efficacy and safety end points. A Data and Safety Monitoring Board (DSMB) reviewed the trial's progress in terms of safety, efficacy and compliance. Neither DSMB nor CEC members participated in the trial or were affiliated in any way with the study sponsor. The DSMB made recommendations to a Steering Committee (SC), whose responsibility was to oversee administrative and scientific progress, and to amend or terminate the study.

**Evaluation of efficacy and safety end points.** The primary end point was a composite of all-cause mortality, nonfatal MI (or reinfarction, for patients with MI at enrollment) or urgent revascularization at 30 days. Urgent revascularization was defined as an urgent need for repeat PCI or CABG. Nonfatal MI required either an increase in creatine kinase (CK) or CK-MB (CK-MB taking precedence over CK when available) to  $\geq$ 3 times the upper limit of normal before discharge, with levels  $\geq$ 50% above the preceding trough when applicable, or new Q waves  $\geq$ 0.04 s in  $\geq$ 2 contiguous electrocardiographic leads. Myocardial enzymes (CK or CK-MB) were assessed at 8 and 16 h after the procedure and every 8 h thereafter until a return to normal, or hospital discharge. A 12-lead electrocardiogram was obtained within 2 h after the stent procedure and then daily until discharge. All myocardial enzyme elevations were

**Table 1.** Baseline Characteristics

Characteristics	Placebo (n = 549)	Enoxaparin (n = 553)
Age (yrs)	61 ± 0.5	59 ± 0.5
Male gender	73%	78%
Race		
Caucasian	91%	90%
Black	8%	8%
Other	1%	1%
Hypertension	58%	57%
Hyperlipidemia	53%	54%
Diabetes	28%	24%
Current smoking	32%	33%
Prior infarction	32%	30%
Prior congestive heart failure	9%	8%
Renal disease	3%	3%
Prior bypass surgery	18%	19%
Prior angioplasty	27%	27%
Ejection fraction (%)	51 ± 0.7	51 ± 0.7
Clinical presentation*		
Myocardial infarction	43%	47%
Unstable angina	50%	50%
Stable angina	17%	15%

p < 0.05 for all comparisons, placebo vs. enoxaparin. \*Not mutually exclusive.

reviewed by two CEC physicians, who made the final determination of MI after complete review of biomarker data, clinical information from the case report form and additional data from the medical record. Only MIs that were deemed to have occurred after study-drug initiation (post-PCI) were counted in the primary efficacy analysis. Secondary end points included the incidence of the composite end point at 14 days, and of death or MI at 14 and 30 days.

Safety end points included all adverse events, major and minor bleeding and thrombocytopenia (platelet count <100,000/mm<sup>3</sup>). Major bleeding included retroperitoneal, intraocular or intracranial hemorrhage (by magnetic resonance imaging or computerized tomography), or other clinically overt bleeding associated with death, transfusion of ≥1 U of packed red cells or whole blood, a ≥3-g/dl decrease in hemoglobin, hemodynamic compromise or need for surgical intervention. Clinically significant bleeding not fulfilling the criteria for major bleeding was considered minor.

**Sample-size determination and interim analyses.** Based on published reports (1,2,19), the expected incidence of the primary end point with placebo was 6.5%. Assuming a 5% Type I error rate, 1,000 patients per group were required to have ≥90% power to detect a 50% relative risk reduction with enoxaparin. To reassess sample size, a blinded evaluation of the overall primary end point was planned after enrollment of 500 patients, and a blinded efficacy analysis after ~1,000 patients. Early termination rules for overwhelming efficacy were established, using Peto's stopping rules to maintain an overall p = 0.05 at trial completion (21).

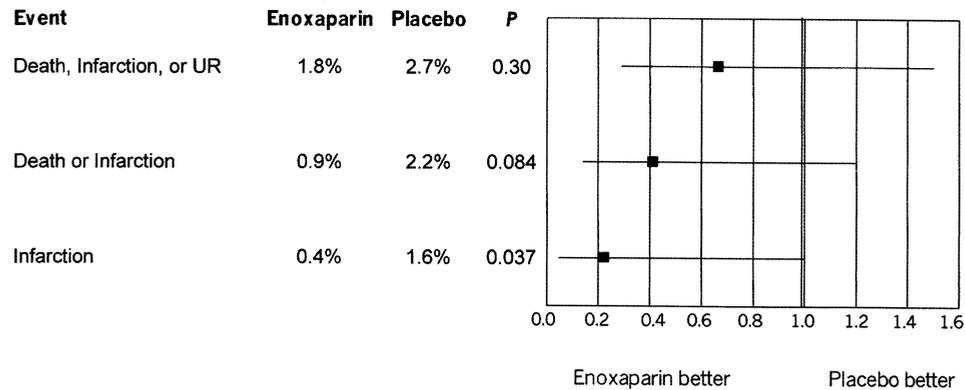
**Table 2.** Procedural and Angiographic Characteristics

Characteristics	Placebo (n = 549)	Enoxaparin (n = 553)
Risk factors for stent thrombosis*		
Infarction <48 h	27%	31%
Distal disease beyond stent	24%	21%
Intracoronary thrombus	17%	17%
Total vessel occlusion	14%	13%
Ejection fraction <35%	10%	11%
Persistent dissection at margin	8%	10%
Abrupt closure	7%	5%
Threatened closure	8%	8%
Other	20%	19%
Patients with 1/2/3/≥4 risk factors	67/25/7/1	66/27/6/1
Stent design*		
Palmaz-Schatz	44%	47%
ACS Multi-Link	19%	19%
Gianturco-Roubin II	14%	12%
Gianturco-Roubin I	5%	5%
Medtronic Wiktor	2%	3%
Other	23%	21%
Patients with 1/2/≥3 stents deployed	65/26/9	65/25/10
Stent diameter (mm)	3.23 ± 0.02	3.22 ± 0.02
Stent length (mm)	18.4 ± 0.3	18.1 ± 0.2
Additional interventions		
Rotational atherectomy	4%	3%
Laser	0%	0.2%
Other	2%	2%
Maximum activated clotting time (s)	319 ± 3.9	318 ± 3.8
Angiographic characteristics		
Preprocedural TIMI flow grade 0/1/2/3	20/8/17/54	18/8/20/53
Preprocedural stenosis (%)	92 ± 0.4	92 ± 0.3
Postprocedural TIMI flow grade 0/1/2/3	0/0/3/97	0.2/0.2/1.3/98
Postprocedural stenosis (%)	3.7 ± 0.3	3.7 ± 0.3

p > 0.05 for all comparisons, placebo vs. enoxaparin. \*Not mutually exclusive. ACS = acute coronary syndromes; TIMI = Thrombolysis In Myocardial Infarction.

**Statistical analysis.** Continuous variables were described as means ± SE and compared between groups by one-way analysis of variance with treatment effect. Categorical variables were described as percentages and compared with chi-square statistics, or Fisher exact test for rare events. The primary and secondary efficacy analyses were performed on the treated population. All tests were two-sided with a 5% level of significance (α = 0.05).

**Interim analysis.** Interim analysis after 500 patients revealed a lower than expected incidence of the primary end point (3.5%). Therefore, the SC and DSMB agreed to include a futility rule to allow premature study termination if efficacy expectations were unlikely to be met. The DSMB met on August 7, 1998, and reviewed the blinded data of 825 patients who had completed 30-day event adjudication. The overall event rate remained only 2.6%. Although no important safety issues surfaced, futility analysis suggested that, given the low event rate, the planned sample size of 2,000 would provide insufficient power to address the primary hypothesis. With the Gould method (22), a sample size of ≥3,590 patients would have been required to



**Figure 1.** Odds ratios and 95% confidence intervals for the risk of primary and secondary 30-day clinical events with enoxaparin versus placebo. UR = urgent revascularization.

maintain adequate statistical power ( $1-\beta \geq 0.80$ ). In view of this and other challenges facing enrollment (including the increasingly widespread use of glycoprotein IIb/IIIa inhibitors in high-risk stenting), the SC and sponsor later agreed to terminate the trial; 1,102 patients (553 enoxaparin, 549 placebo) had been enrolled at that point. The following represent the final CEC-adjudicated results on these patients.

**RESULTS**

**Clinical and procedural characteristics.** The groups shared similar baseline characteristics (Table 1). Most patients had only one or two risk factors for ST, the most common being recent MI, diffuse distal disease or intracoronary thrombus (Table 2). Most stents were of Palmaz-Schatz, ACS Multi-Link or Gianturco-Roubin (Cook) design. About one third received  $\geq 1$  stent. Mean stent diameter and length were similar between groups. Adjunctive interventions, such as rotational atherectomy, laser ablation or other techniques, were used infrequently. TIMI flow grades and lesion severity were comparable between groups before and after stenting.

The median intravascular sheath size was 8.0 Fr. The median time from sheath removal to first dose of study drug was similar between the enoxaparin and placebo groups (3.3 vs. 3.5 h, respectively,  $p = ns$ ), as was the median time from the last dose of procedural UFH to first dose of study drug (8.0 vs. 8.3 h, respectively,  $p = ns$ ).

**Clinical outcomes.** The overall incidence of the CEC-adjudicated primary end point in the final cohort of 1,102 patients was low (2.3%). Fewer enoxaparin-treated patients experienced the primary end point compared with placebo (1.8% vs. 2.7%, respectively, Fig. 1); however, this difference was not statistically significant. Although statistical comparisons were not performed between subgroups, risk appeared to be influenced by the type and number of risk factors, and perhaps also by stent design (Table 3). Enoxaparin was associated with significantly fewer MIs at both 14 and 30 days (78% relative risk reduction at 30 days), and

a 59% reduction in death or MI that approached statistical significance at 30 days (Table 4, Fig. 1). Urgent revascularization was infrequent in both groups (Table 4).

Serious and nonserious adverse events also occurred infrequently in both groups (Table 5). Bleeding was more common with enoxaparin, but the vast majority was minor (oozing or ecchymosis at vascular access or subcutaneous injection sites). Major bleeding was not significantly increased with enoxaparin. Thrombocytopenia and gastrointestinal or genitourinary bleeding were rare. There was one

**Table 3.** Primary End Point by Risk Factors and Stent Design

Variable	Primary End Point*
<b>Risk factors†</b>	
Infarction <48 h	8/318 (2.5%)
Distal disease beyond stent	8/247 (3.2%)
Intracoronary thrombus	3/186 (1.6%)
Total occlusion	3/149 (2.0%)
Ejection fraction <35%	7/119 (5.9%)
Persistent dissection at margin	3/98 (3.1%)
Threatened closure	5/86 (5.8%)
Abrupt closure	2/65 (3.1%)
Degenerated vein graft <4 mm	1/52 (1.9%)
Target vessel $\leq 2.5$ mm	1/43 (2.3%)
Bifurcation lesion	1/43 (2.3%)
Persistent filling defect	0/39 (0.0%)
Residual stenosis >20%	0/31 (0.0%)
Other	0/5 (0.0%)
<b>No. of risk factors</b>	
1	9/730 (1.2%)
$\geq 2$	16/372 (4.3%)
<b>Stent design</b>	
Palmaz-Schatz	14/503 (2.8%)
ACS Multi-Link	0/211 (0.0%)
Gianturco-Roubin II	5/142 (3.5%)
Gianturco-Roubin I	4/52 (7.7%)
Medtronic Wiktor	0/27 (0.0%)
Other	4/249 (1.6%)

\*Death, nonfatal myocardial infarction, or urgent revascularization. †Not mutually exclusive.

ACS = acute coronary syndrome.

**Table 4.** Other Secondary Clinical Outcomes

Event	Placebo (n = 549)	Enoxaparin (n = 553)	p Value
14 days			
Death, infarction or urgent revascularization	2.2%	1.1%	0.15
Death or infarction	1.8%	0.5%	0.049
Death	0.5%	0.4%	0.69
Infarction	1.3%	0.2%	0.038
Urgent revascularization	1.3%	0.7%	0.38
30 days			
Death	0.5%	0.5%	1.0
Urgent revascularization	1.8%	1.1%	0.33

intracranial hemorrhage in the enoxaparin group. Although most patients tolerated the study drugs well, enoxaparin was more often discontinued early (24% vs. 13%,  $p < 0.001$ ).

**DISCUSSION**

ATLAST is the largest study to prospectively evaluate the efficacy and safety of LMWH for the prevention of ST in high-risk patients. The most pertinent finding was the low rate of adverse cardiac events (2.3%), substantially lower than has been reported in such patients. A 14-day course of enoxaparin, begun 4 to 10 h after procedural heparin, did not significantly reduce this low overall event rate, but was generally well tolerated, safe and associated with a reduced risk of MI.

Oral antiplatelet therapy effectively reduces ST to  $\leq 1.6\%$  in planned, successful stent procedures (4,8). However, clinical and angiographic characteristics that indicate thrombus, residual dissection, or suboptimal stent deployment (such as those forming the inclusion criteria for ATLAST), increase the risk of thrombotic events, particularly ST, to between 3% and 10% (1-8,19). Intravenous

glycoprotein IIb/IIIa inhibitors improve outcome in both high-risk and elective PCI, primarily through a reduction in periprocedural MI (10,23,24). However, these agents have not been shown to convincingly reduce the risk of ST, and prolonged IIb/IIIa blockade by oral agents only increases thrombotic events (25-27). Therefore, the optimal postdischarge antithrombotic regimen for patients at increased risk of ST has remained unclear.

Enoxaparin's clinical superiority over UFH has been shown in patients with acute coronary syndromes (16-18). Extended LMWH therapy (three months) also reduces the short-term risk of thrombotic events, although benefits are not sustained at six months (28). Before ATLAST, the benefit of adding a LMWH to oral antiplatelet therapy in patients at risk of ST had undergone limited investigation. Registry data suggest that the combination of ticlopidine, aspirin and one month of LMWH effectively limits ST to  $< 2\%$  in patients undergoing elective or bailout stenting (29). The only prospective randomized assessment of LMWH's efficacy after coronary stenting was a small trial (ENTICES,  $n = 122$ ), which compared the combination of aspirin, ticlopidine and enoxaparin with the original FDA-recommended post-stent regimen (UFH, warfarin, aspirin, dipyridamole and dextran) (19). The enoxaparin, ticlopidine and aspirin combination significantly reduced stent thrombosis (0% vs. 7%), major ischemic events (5% vs. 21%) and major bleeding or vascular complications (5% vs. 16%). The ATLAST trial provides a more contemporary assessment of the incremental benefits of adding LMWH to an oral antiplatelet regimen for ST prophylaxis.

The most striking observation in ATLAST was the low 30-day event rate (2.3%) in a presumably high-risk cohort. Although the relatively small number of events precluded multivariable regression techniques to define independent outcome predictors, some interesting trends suggest that the type and number of risk factors, and stent design, may affect risk. Despite this, even patients with  $\geq 2$  risk factors had a relatively low event rate (4.3%). By comparison, placebo-treated patients in prior studies of intravenous glycoprotein IIb/IIIa inhibitors have had 30-day composite event rates of 10% to 15% (9,23,30-32). The higher event rates recorded in these studies may be explained in part by the timing of drug administration and end point evaluation. In the IIb/IIIa inhibitor trials, study drug was initiated before vessel injury, and most of the therapeutic benefit reflected prevention of periprocedural MI. In ATLAST, because the study drug was initiated *after* PCI, periprocedural CK-MB elevations were not counted; only MIs believed to occur after administration of study drug (i.e., those predominantly related to ST) were included. Furthermore, patient selection may have also influenced event rates. With the FDA approving abciximab in 1997, some ATLAST investigators felt compelled to use abciximab in the highest risk stent patients, thereby selectively enrolling lower risk patients. Finally, the traditional clinical and angiographic high-risk features forming the basis for inclusion into ATLAST

**Table 5.** 30-Day Safety Endpoints

Event	Placebo (n = 549)	Enoxaparin (n = 553)	p Value
Any adverse event	9.4%	9.2%	0.97
Serious adverse event	7.3%	5.8%	0.31
Any bleeding	6.7%	28%	$< 0.001$
Major	1.6%	3.3%	0.08
Minor	5.1%	25%	$< 0.001$
Bleeding sites			
Skin injection hematoma $\geq 5$ cm	1.5%	13.9%	$< 0.001$
Vascular sheath hematoma $\geq 5$ cm	1.8%	7.8%	$< 0.001$
Other bruising	0.7%	4.2%	$< 0.001$
Intracranial	0.0%	0.2%	0.96
Gastrointestinal	2.0%	1.1%	0.33
Genitourinary	0.2%	0.4%	0.96
Epistaxis	0.2%	0.4%	0.96
Other	1.1%	4.4%	$< 0.001$
Thrombocytopenia	0.4%	0%	0.48
Premature drug discontinuation	13%	24%	$< 0.001$

(recent MI, diffuse disease beyond the stent, threatened abrupt vessel closure and so on) may be no longer be predictive of ST in an era of newer stent designs and deployment techniques.

Because of the low event rate and premature termination of the study, the lack of a statistically significant reduction in the primary end point with enoxaparin could be due to beta error. The observation that enoxaparin reduced the risk of subsequent MI does suggest some degree of efficacy, the clinical significance of which is limited in this setting because of the overall low risk. Enoxaparin was generally safe and well tolerated in this study. However, similar to other studies (16,33), more frequent minor bleeding at vascular access and drug-injection sites did occur with enoxaparin, leading to more frequent drug discontinuation than with placebo. Despite this, enoxaparin rarely caused major bleeding. This suggests that LMWH can be safely initiated soon after PCI (within 4 to 10 h), once adequate vascular access site hemostasis has been achieved.

ATLAST extends our knowledge of the risks and optimal therapy for patients traditionally deemed to be at increased risk of ST. Clinical outcomes in this setting are more favorable than previously reported, rendering a post-stent oral antiplatelet regimen adequate for most patients. However, given its relative safety and potential to reduce the subsequent risk of MI due to ST, a 14-day course of enoxaparin might be justified for carefully selected high-risk patients. The safety and efficacy of enoxaparin, alone and in combination with glycoprotein IIb/IIIa inhibitors, to prevent thrombotic complications during PCI is currently under investigation.

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