Impact of *Bivalirudin* and *Paclitaxel*-Eluting Stents on Outcomes in Patients Undergoing Primary Percutaneous Coronary Intervention of the Left Anterior Descending Artery

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Patients with ST elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) of the left anterior descending artery (LAD) are at increased risk for cardiovascular events compared with patients undergoing non-LAD PCI. We assessed the impact of bivalirudin and paclitaxel-eluting stenting (PES) in patients with STEMI who underwent LAD PCI. In the HORIZONS-AMI trial, 1,445 patients had LAD PCI and 1,884 patients had non-LAD PCI. The 3-year composite rates of death, reinfarction, stroke, or ischemia-driven target vessel revascularization were significantly higher in patients who underwent LAD PCI compared with non-LAD PCI (24.0% vs 20.6%, hazard ratio [HR] 1.20, 95% confidence interval [CI] 1.04 to 1.39, p = 0.013), driven by a statistically significant increase in cardiac death (5.4% vs 2.7%, HR 2.00, 95% CI 1.40 to 2.86, p = 0.001). For patients who underwent LAD PCI, treatment with bivalirudin resulted in significantly lower rates of cardiac death (3.8% vs 6.8%, HR 0.55, 95% CI 0.34 to 0.89, p = 0.01), reinfarction (5.3% vs 9.5%, HR 0.55, 95% CI 0.37 to 0.83, p = 0.004), and major bleeding events (7.3% vs 11.8%, HR 0.60, 95% CI 0.43 to 0.86, p = 0.004) compared with unfractionated heparin plus glycoprotein IIb/IIIa inhibitor. Randomization to PES compared with bare-metal stenting resulted in a significant lower rate of target vessel revascularization (13.2% vs 19.8%, HR 0.64, 95% CI 0.47 to 0.86, p = 0.003) with no significant differences in stent thrombosis, reinfarction, or death. In conclusion, in patients with STEMI who underwent primary PCI of LAD, the use of bivalirudin was associated with a reduction in mortality and bleeding rates at 3 years. PES reduced revascularization rates in this population but did not have a significant impact on mortality. **(Am J Cardiol 2013;112:753−760)**

Primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy in patients with ST elevation myocardial infarction (STEMI).[1,2] Patients with acute anterior myocardial infarction undergoing primary PCI of the left anterior descending artery (LAD) experience worse outcomes including increased mortality, larger infarct size, left ventricular dysfunction, and impaired microvascular perfusion.[3−5] Those patients may benefit most from new treatments strategies regarding anticoagulation, antiplatelet therapy, and stent implantation. In the Harmonizing Outcomes with RevasculariZatiON and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial, patients with STEMI who underwent a primary PCI strategy did benefit from anticoagulation with bivalirudin and implantation of paclitaxel-eluting stents (PES). During long-term follow-up, the use of bivalirudin was associated with a significant reduction in bleeding events and cardiac mortality compared with administration of unfractionated heparin plus a glycoprotein IIb/IIIa inhibitor.[6] Moreover, patients who were randomized to PES implantation had significantly less target vessel revascularization (TVR) with no increase in the risk of stent thrombosis or mortality compared with bare-metal stent (BMS) implantation. Given the high risk of complications associated with primary PCI of LAD lesions, we sought to investigate the impact of bivalirudin and PES implantation on outcomes in this subgroup of the HORIZONS-AMI trial.

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See page 759 for disclosure information.

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Table 1
Baseline characteristics in patients who underwent left anterior descending (LAD) versus non-LAD percutaneous coronary intervention (PCI)

Variable	LAD (n = 1,445)	Non-LAD (n = 1,884)	p
Age (yrs)	61.0 (53.0, 70.7)	59.5 (52.1, 68.8)	0.004
Women	22.1% (320/1,445)	23.4% (441/1,884)	0.39
Diabetes mellitus	17.3% (250/1,443)	15.5% (292/1,884)	0.16
Hypertension	52.1% (752/1,443)	52.8% (995/1,884)	0.69
Hyperlipidemia	41.4% (597/1,443)	44.0% (829/1,884)	0.13
Smoking	57.6% (829/1,440)	69.7% (1,305/1,872)	<0.001
Body mass index (kg/m^2)	27.0 (24.4, 30.1)	27.2 (24.7, 30.3)	0.09
Renal insufficiency	2.7% (39/1,443)	2.9% (54/1,883)	0.77
Previous myocardial infarction	8.1% (117/1,443)	12.3% (232/1,884)	<0.001
Previous percutaneous intervention	9.0% (130/1,443)	11.6% (219/1,883)	0.015
Previous coronary artery bypass	1.3% (19/1,443)	3.5% (66/1,884)	<0.001
Killip class II–IV	12.9% (185/1,440)	5.5% (104/1,884)	<0.001
Symptom onset to balloon inflation (min)	221 (161, 340)	223 (160, 329)	0.83
Femoral access	93.6% (1,351/1,444)	93.8% (1,768/1,884)	0.74
Clopidogrel loading dose (mg)			
300	35.9% (519/1,445)	33.8% (636/1,884)	0.19
600	63.9% (924/1,445)	66.1% (1,246/1,884)	0.19
Randomization to bivalirudin	48.4% (699/1,445)	51.4% (968/1,884)	0.09
Preprocedural heparin	64.9% (937/1,443)	66.1% (1,245/1,884)	0.49
Glycoprotein IIb/IIIa inhibitor	57.3% (826/1,441)	55.3% (1,040/1,882)	0.24
Given with bivalirudin	12.6% (88/697)	13.4% (129/966)	0.66
Giant thrombus	3.4% (24/697)	3.6% (35/966)	0.84
Sustained no reflow	4.7% (33/697)	4.6% (44/966)	0.86
Left ventricular ejection fraction <40%	27.2% (333/1,225)	5.2% (83/1,600)	<0.001
2-Vessel coronary disease	33.5% (468/1,395)	35.9% (674/1,875)	0.15
3-Vessel coronary disease	20.4% (284/1,395)	22.4% (420/1,875)	0.16
Chronic total coronary occlusion	8.8% (121/1,381)	8.3% (154/1,867)	0.60
Number of stents implanted	1.5 ± 0.9	1.5 ± 0.8	0.59
Total stent length implanted (mm)	24 (16, 36)	24 (20, 36)	0.03
Any aspiration catheter	9.1% (131/1,432)	13.4% (250/1,864)	<0.001
Multiple vessels treated	6.9% (98/1,417)	1.9% (35/1,846)	<0.001
Number of vessels treated	1.1 ± 0.3	1.0 ± 0.1	<0.001
Any side branch lesion treated	9.3% (131/1,432)	3.9% (73/1,884)	<0.001
TIMI flow 0/1 before PCI	60.8%	69.0%	<0.001
TIMI flow 0/1 after PCI	2.1%	2.6%	0.34
TIMI flow 3 after PCI	90.8%	92.1%	0.17
Any CABG in-hospital	1.0% (14/1,445)	1.7% (32/1,884)	0.07

Data are presented as percentages (count/sample size), median (first, third quartiles), or mean ± SD.

CABG = coronary artery bypass grafting; TIMI = Thrombolysis In Myocardial Infarction.

Table 2
Three-year clinical outcomes in patients who underwent left anterior descending (LAD) and non-LAD percutaneous coronary intervention

Variable	LAD (n = 1,445)	Non-LAD (n = 1,884)	p
MACE*	24.0 (340)	20.6 (377)	0.013
Death or reinfarction	14.4 (205)	11.5 (210)	0.09
Death	8.3 (118)	5.3 (96)	0.001
Cardiac	5.4 (76)	2.7 (50)	0.001
Noncardiac	3.1 (42)	2.6 (46)	0.37
Reinfarction	7.4 (101)	7.2 (128)	0.74
Q-wave	3.1 (42)	4.1 (73)	0.15
Non–Q-wave	4.7 (63)	3.6 (63)	0.11
Stroke	1.6 (22)	1.6 (29)	0.99
Ischemic TVR†	14.8 (200)	13.2 (236)	0.19
Ischemic TLR	12.4 (167)	10.1 (180)	0.004
Ischemic TVR, non-TLR	4.4 (59)	5.4 (95)	0.24
Ischemic non-TVR	9.5 (129)	10.8 (193)	0.28
Stent thrombosis‡			
Definite	4.2 (56)	4.6 (80)	0.56
Definite/probable	4.8 (64)	5.3 (92)	0.51

Data are presented as percentages (counts).

MACE = major adverse cardiovascular events.

* Composite of death, reinfarction, stroke, or ischemic TVR.

† Ischemic TVR defined as any ischemia-driven repeat percutaneous intervention or bypass surgery of the target vessel. The target vessel consists of the target lesions plus any additional lesions in the main epicardial coronary artery or branches containing the target lesion.

‡ Academic Research Consortium definite or probable.

Methods

The design and primary outcomes of the HORIZONS-AMI trial have been previously reported.[6–9] Briefly, HORIZONS-AMI was a prospective multicenter trial in which patients with STEMI undergoing primary PCI were randomized in 2 phases to (1) bivalirudin alone plus provisional use of glycoprotein IIb/IIIa inhibitors versus unfractionated heparin plus routine glycoprotein IIb/IIIa inhibitors and (2) the paclitaxel-eluting TAXUS Express stent versus an otherwise identical bare-metal Express stent (both Boston Scientific, Natick, Massachusetts). Patients presenting ≤12 hours of symptom onset with STEMI were considered for enrollment. Clinical exclusion criteria included contraindications to study medication or conditions that increase the risk of hemorrhage. After pharmacologic randomization, emergent angiography was performed followed by assessment for eligibility in the stent-randomized phase of the trial (lesions with reference vessel diameter of 2.25 to 4.0 mm and length <100 mm were eligible). Left main lesions, bifurcation lesions requiring planned dual stenting, and those with excessive tortuosity or severe calcification were excluded. Complete end point definitions have been reported.[8] A blinded independent clinical events committee adjudicated all primary end point events using original source documents. Quantitative Coronary Angiography was performed at an independent core angiographic laboratory (Cardiovascular Research Foundation, New York, New York). Clinical follow-up was scheduled at 30 days, 6 months, 1, 2, and 3 years.