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Safety and efficacy of everolimus-eluting stents compared with first-generation drug-eluting stents in patients undergoing primary percutaneous coronary intervention

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ABSTRACT

Objective: To assess the safety and efficacy everolimus-eluting stents (EES) compared with first-generation drug-eluting stents (DES) in patients with acute myocardial infarction (MI) undergoing primary percutaneous coronary intervention (PCI).
Background: EES have been associated with improved clinical outcomes compared to paclitaxel-eluting stents (PES) and with similar outcomes compared to sirolimus-eluting stents (SES).
Methods: A total of 520 patients who presented with ST-elevation myocardial infarction (STEMI) from 2003 to 2013, who underwent primary PCI with DES, were retrospectively analyzed. Of these, 247 received SES, 136 PES, and 137 EES. Patients were followed up to 2 years for major adverse cardiac events (MACE). Univariate and multivariate models detected correlates to outcome.
Results: EES implantation, compared with PES and SES, resulted in comparable rates of MACE (8.8% vs. 16.2%, $p = 0.06$ and 8.8% vs. 12.6%, respectively, $p = 0.26$), stent thrombosis, MI, and target lesion revascularization. Patients who received EES had lower rates of all-cause mortality (3.7% vs. 12.6% vs. 9.4%, $p = 0.03$) at 1-year follow up. However, in the univariate and multivariate analyses, stent type was not independently associated with the primary outcome or with all-cause mortality. Diabetes mellitus and number of stents implanted were independently associated with the primary outcome.
Conclusion: While EES seem to be associated with better outcome when compared to PES, the main correlates of STEMI patients are the presence of diabetes and number of stents implanted, and not the type of stent used for intervention.

1. Introduction

Primary percutaneous coronary intervention (PCI) in patients presenting with ST-segment elevation myocardial infarction (STEMI) leads to significantly improved clinical outcomes compared with thrombolytic therapy [1]. Meta-analyses of randomized trials showed similar safety and superior efficacy of 1st-generation drug-eluting stents (DES) over bare metal stents in primary PCI for STEMI, driven primarily by lower rates of target lesion revascularization (TLR) [2]. Long-term studies have suggested that both 1st-generation DES achieve similar clinical outcomes [3]. The XIENCE V everolimus-eluting stent (EES) (Abbott Vascular, Santa Clara, CA) was approved in the United States in 2008 after the Everolimus-Eluting Coronary Stent System in the Treatment of Patients with de novo Coronary Artery Lesions (SPIRIT) randomized trial series [4–7] demonstrated its safety and efficacy compared with 1st-generation DES. Two prospective, randomized clinical trials have compared the XIENCE V stent with 1st-generation DES in primary PCI for patients presenting with acute myocardial infarction (MI) in a selected population. Xience V stent vs. Cypher stent in primary PCI for Acute Myocardial Infarction (XAMI) [8] and the European Comparison of the Everolimus-eluting XIENCE V stent with the paclitaxel eluting TAXUS Liberté stent in all-comers: a randomized open label trial (COMPARE) trials [9] evaluated EES vs. sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES), respectively. The present study assessed the long-term safety and efficacy of EES compared with the 1st-generation DES in patients who presented with STEMI.

2. Methods

From 2003 to 2012, 520 patients underwent primary PCI for new ST-segment elevation in 2 contiguous leads or a new left bundle branch block, cardiogenic shock (defined as systolic blood pressure <90 mm Hg for at least 30 minutes or cardiac index $<2.2\ L\ min^{-1}\ m^{-2}$, and increased filling pressures), or significant ventricular arrhythmia with either PES, SES, or EES. This study complied with the principles of the

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Table 1
Baseline characteristics.

Variable	EES (n = 137)	PES (n = 136)	SES (n = 247)	Overall (n = 520)	p Value
Age (years)	60 ± 11.4	61 ± 12.3	61 ± 12.7	61 ± 12.2	0.45
Men	91 (66%)	94 (69%)	156 (63%)	341 (65%)	0.55
European American	79 (57%)	80 (59%)	176 (71%)	335 (64%)	<0.01
African American	49 (36%)	42 (31%)	53 (21%)	144 (28%)	<0.01
Hispanic	3 (2.2%)	2 (1.5%)	3 (1.2%)	8 (1.5%)	0.89
Diabetes mellitus	43 (32%)	49 (36%)	62 (25%)	154 (30%)	0.08
Chronic renal failure	16 (12%)	18 (13%)	34 (14%)	68 (13%)	0.82
Systemic hypertension*	104 (76%)	104 (77%)	198 (81%)	406 (79%)	0.42
Hypercholesterolemia**	100 (73%)	110 (81%)	204 (84%)	414 (81%)	0.02
Heart failure	18 (13%)	10 (8%)	18 (8%)	46 (9%)	0.16
Peripheral vascular disease	13 (9.5%)	13 (10%)	24 (10%)	50 (10%)	0.99
Current smoker	50 (36%)	58 (42%)	96 (39%)	204 (40%)	0.57
Family history of coronary disease	42 (31%)	55 (43%)	110 (48%)	207 (42%)	<0.01
Previous myocardial infarction	27 (20%)	11 (8%)	39 (16%)	77 (15%)	0.02
Previous coronary intervention	29(21%)	18 (14%)	38 (16%)	85 (17%)	0.27
Previous coronary artery bypass graft	10 (7%)	18 (13%)	25 (10%)	53 (10%)	0.27
Cardiogenic shock	6 (4.4%)	24 (18%)	41 (17%)	71 (14%)	<0.01

* History of systemic hypertension diagnosed and/or treated with medication or currently being treated with diet and/or medication by a physician.
** Includes patients with a previously documented diagnosis of hypercholesterolemia. The patient may be treated with diet or medication. A new diagnosis can be made during this hospitalization with an elevated total cholesterol >160 mg/dl. Does not include elevated triglycerides.

Declaration of Helsinki regarding investigation in humans and was approved by our institutional review board.

All patients underwent primary PCI by standard techniques according to clinical guidelines current at the time of procedure. The choice of stent type, interventional strategy, and use of adjunctive devices and pharmacotherapy were at the discretion of the operator. All patients received aspirin 325 mg before the procedure. A clopidogrel loading dose of 300–600 mg or prasugrel 60 mg was co-administered. Aspirin was continued indefinitely and clopidogrel 75 mg/day was continued for ≥12 months after PCI. During the procedure, patients were anticoagulated with bivalirudin or unfractionated heparin. The use of glycoprotein IIb/IIIa inhibitors was left to the discretion of the operator.

The primary end point was major adverse cardiovascular events (MACE) at 1 year, defined as the composite of all-cause death, MI, and TLR. All-cause death was defined as death from any cardiac or noncardiac cause. Q-wave MI was defined as evidence of new pathological Q waves in >2 contiguous leads on the electrocardiogram. MI was defined as a total creatinine kinase increase of >2× the upper limit of normal and/or creatinine kinase (MB fraction) >20 ng/ml, along with symptoms and/or electrocardiographic changes suggestive of myocardial ischemia. TLR was defined as ischemia-driven percutaneous or surgical repeat intervention in the stent or within 5 mm proximal or distal to the stent. Stent thrombosis (ST) was defined according to the Academic Research Consortium definitions as definite or probable ST. Systemic hypertension was defined as a blood pressure >140/90 mm Hg or the use of antihypertensive therapy. Hypercholesterolemia was defined as fasting cholesterol of >250 mg/dl or the use of lipid-lowering therapy. Congestive heart failure was defined as evidence of fluid retention from cardiac causes before admission. Angiographic success was defined as postprocedural stenosis <30% and Thrombolysis In Myocardial Infarction flow grade 3.

Statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC). Continuous variables are expressed as mean ± SD for normally distributed variables. Categorical variables are expressed as percentages. Analyses of the differences among the 3 groups were performed using analysis of variance for continuous variables and chi-square test or Fisher exact test for categorical variables. Cox proportional hazard analysis was performed to detect predictors of 1-year MACE. Variables were selected on the basis of overall clinical relevance. Variables included in the model were blood transfusion, bivalirudin use, hypercholesterolemia, systemic hypertension, diabetes mellitus, type C lesion, type B1/2 lesion, stent type (EES, paclitaxel-eluting stent, or sirolimus-eluting stent), total stent length per lesion, number of stents implanted, and left anterior descending artery stent implantation.

After univariate analysis, variables with a p value of <0.1 were incorporated into the multivariate analysis. The results are presented

Table 2
Procedural and lesion characteristics.

Variable	EES (n = 180)	PES (n = 190)	SES (n = 372)	Overall (n = 742)	p Value
Procedural characteristics					
Number of stents implanted	1.5 ± 0.76	1.4 ± 0.7	1.5 ± 0.7	1.5 ± 0.7	0.27
Angiographic success	179 (99%)	190 (100%)	366 (99%)	735 (99%)	0.44
Maximum stent diameter (mm)	2.9 ± 0.3	3 ± 0.2	3.1 ± 2	3 ± 1.4	0.51
Total stent length (mm)	19 ± 5.2	21.2 ± 5.3	20.8 ± 6.1	20.4 ± 5.7	<0.01
Glycoprotein IIb/IIIa	21 (15%)	31 (23%)	71 (29%)	123 (24%)	0.01
Bivalirudin	113 (82%)	64 (47%)	96 (39%)	273 (52%)	<0.01
Blood transfusion	8 (6%)	18 (13%)	15 (6%)	41 (8%)	0.03
Lesion characteristics					
Left main	4 (2.2%)	3 (1.6%)	1 (0.3%)	8 (1.1%)	0.04
Left anterior descending	63 (35%)	67 (35%)	164 (44%)	294 (39%)	0.04
Left circumflex	38 (21%)	29 (15%)	60 (16%)	127 (17%)	0.25
Right coronary	73 (40%)	82 (43%)	137 (37%)	292 (39%)	0.32
Saphenous vein graft	2 (1.1%)	8 (4.2%)	10 (2.7%)	20 (2.7%)	0.18
Type A lesion	12 (7%)	11 (6%)	17 (5%)	40 (5.5%)	0.59
Type B1 or B2 lesion	69 (38%)	119 (63%)	254 (69%)	442 (60%)	<0.01
Type C lesion	99 (55%)	57 (30.5%)	95 (26%)	251 (34%)	<0.01