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Randomized Comparison of Everolimus-Eluting Stents and Sirolimus-Eluting Stents in Patients With ST Elevation Myocardial Infarction

RACES-MI Trial

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ABSTRACT

OBJECTIVES The aim of the current study was to compare everolimus-eluting stents (EES) with sirolimus-eluting stents (SES) in patients undergoing primary angioplasty.

BACKGROUND Drug-eluting stents may offer benefits in terms of repeat revascularization. However, as shown for first-generation drug-eluting stents, they may be counterbalanced by a potential higher risk of stent thrombosis, especially among patients with ST-segment elevation myocardial infarction (STEMI). No data have been reported so far on the long-term benefits and safety of the new generation of drug-eluting stents in STEMI.

METHODS Consecutive STEMI patients admitted within 12 h of symptom onset and undergoing primary angioplasty and stent implantation at a tertiary center with 24-h primary percutaneous coronary intervention capability were randomly assigned to SES or EES. The primary endpoint was a major adverse cardiac event at 3-year follow-up. The secondary endpoints were death, reinfarction, definite or probable stent thrombosis, and target vessel revascularization at 3-year follow-up. No patient was lost to follow-up.

RESULTS From April 2007 to May 2009, 500 patients with STEMI were randomized to EES (n = 250) or SES (n = 250). No difference was observed in terms of baseline demographic and clinical characteristics between the groups. No difference was observed between the groups in terms of number of implanted stents per patient or total stent length. However, a larger reference diameter was observed with SES (3.35 ± 0.51 mm vs. 3.25 ± 0.51 mm, p = 0.001), whereas patients randomized to EES more often received glycoprotein IIb/IIIa inhibitors (54.4% vs. 42.4%, p = 0.006). Follow-up data were available in all patients (1,095 ± 159 days). No significant difference was observed between EES and SES in major adverse cardiac events (16% vs. 20.8%, adjusted hazard ratio [HR]: 0.75 [95% confidence interval (CI): 0.5 to 1.13], p = 0.17), cardiac death (4.4% vs. 5.6%, adjusted HR: 0.77 [95% CI: 0.35 to 1.71], p = 0.53), recurrent MI (6.4% vs. 10%, adjusted HR: 0.62 [95% CI: 0.33 to 1.16], p = 0.13), and target vessel revascularization (4.8% vs. 4.8%, adjusted HR: 1.00 [95% CI: 0.45 to 2.32], p = 0.99). However, EES was associated with a significant reduction in stent thrombosis (1.6% vs. 5.2%, adjusted HR: 0.3 [95% CI: 0.1 to 0.92], p = 0.035).

CONCLUSIONS This study shows that among STEMI patients undergoing primary angioplasty, EES has similar efficacy as SES, but is associated with a significant reduction in stent thrombosis. (Randomized Comparison of Everolimus Eluting Stents and Sirolimus Eluting Stent in Patients With ST Elevation Myocardial Infarction [RACES-MI]; NCT01684982) (J Am Coll Cardiol Intv 2014;7:849–56) © 2014 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

BMS = bare-metal stent(s)

CI = confidence interval

DES = drug-eluting stent(s)

EES = everolimus-eluting stent(s)

HR = hazard ratio

MACE = major adverse cardiac events

PCI = percutaneous coronary intervention

SES = sirolimus-eluting stent(s)

ST = stent thrombosis

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

TVR = target vessel revascularization

Several randomized trials have clearly shown the adjunctive benefits in terms of mortality from primary percutaneous coronary intervention (PCI) as compared with thrombolysis as reperfusion strategy in the treatment of patients with ST-segment elevation myocardial infarction (STEMI) (1,2). Even though stent implantation, compared with balloon angioplasty, has reduced the occurrence of restenosis in selected STEMI patients (3,4), the outcome of bare-metal stents (BMS) seem to be worse in unselected patients with a rate of target vessel revascularization (TVR) up to 20% (5,6). Several randomized trials have shown that drug-eluting stents (DES), compared with BMS, are associated with a significant reduction in restenosis and TVR in STEMI patients (7–17). However, concerns have emerged on the higher risk of stent thrombosis (ST) with first-generation DES (18). The new-generation DES with more biocompatible polymers may potentially provide benefits in both TVR and ST in the setting of STEMI (19). Therefore, the aim of the RACES-MI (Randomized Comparison of Everolimus Eluting Stents and Sirolimus Eluting Stent in Patients With ST Elevation Myocardial Infarction) trial was to compare everolimus-eluting stents (EES) with sirolimus-eluting stents (SES) in patients undergoing primary angioplasty for STEMI at short- and long-term follow-up.

METHODS

The RACES-MI trial is a prospective, single-center, randomized trial evaluating the benefits of EES versus SES implantation in patients undergoing primary angioplasty for acute STEMI. Individuals eligible for enrollment were consecutive patients presenting with STEMI who fulfilled all of the following inclusion criteria: 1) chest pain for more than 30 min; and 2) ST-segment elevation of ≥1 mm in ≥2 contiguous electrocardiograph leads or with presumably new left bundle branch block. Exclusion criteria included the following: 1) active internal bleeding or a history of bleeding diathesis within the previous 30 days; 2) contraindication to dual antiplatelet therapy for 12 months; 3) known allergy to sirolimus or everolimus; 4) a history of stroke within 30 days or any history of hemorrhagic stroke; 5) history, symptoms, or findings suggestive of aortic dissection; 6) pregnancy; 7) participation in other trials. No angiographic exclusion criteria were used.

The institutional review board of the Ospedale "S.G. Moscati" (Avellino, Italy) approved the protocol in 2007, and all patients gave written informed consent.

Open-label randomization was performed in the catheterization laboratory after initial angiography by the treating physician when eligibility criteria were met. A 1:1 computer-generated random sequence, without blocking or stratification, was used. Sealed envelopes indicated the treatment group to which the patients were assigned: SES or EES.

MEDICATIONS. All patients received a 70 U/kg intravenous bolus of unfractionated heparin, aspirin intravenously (500 mg), and clopidogrel (600-mg loading dose). Glycoprotein IIb/IIIa inhibitor administration, and the number and length of stents to be implanted were left to the operator's discretion. Postinterventional antiplatelet therapy for all patients consisted of aspirin (100 mg/day) indefinitely and clopidogrel (75 mg daily recommended for 12 months).

ANGIOPLASTY PROCEDURE. Stenting procedures were performed according to standard techniques. The number and length of stents to be implanted were

TABLE 1 Baseline Demographic and Clinical Characteristics of the 2 Groups of Patients

	SES (n = 250)	EES (n = 250)	p Value
Age, yrs	59 ± 12	59 ± 11	0.53
Male	62	67.6	0.19
Hypertension	41.2	42	0.86
Diabetes	27.2	25.6	
IDDM	9.6	10	0.69
NIDDM	17.6	15.6	
Smoking	34.4	33.6	0.85
Previous MI	12	14.4	0.43
Previous CABG	8	6.8	0.61
Previous PCI	12.4	9.6	0.32
Previous CVA	3.2	4	0.63
Family history of CAD	32.4	36	0.4
PAD	2.4	3.2	0.59
Chronic renal failure	8.4	10.4	0.45
Anemia	10.4	8.8	0.54
Heart rate at presentation, beats/min	65 ± 24	69 ± 24	0.25
Killip class >1	14.4	15.2	0.80
Anterior MI	45.2	42.4	0.53
Ejection fraction, %	47.4 ± 8.4	47.5 ± 8	0.9
Ischemia time, min	177 ± 148	182 ± 152	0.67
Door-to-balloon time, min	44 ± 17	46 ± 16	0.16

Values are mean ± SD or percentages.

CABG = coronary artery bypass graft; CAD = coronary artery disease; CVA = cerebrovascular accident; EES = everolimus-eluting stent(s); IDDM = insulin-dependent diabetes mellitus; MI = myocardial infarction; NIDDM = non-insulin-dependent diabetes mellitus; PAD = peripheral artery disease; PCI = percutaneous coronary intervention; SES = sirolimus-eluting stent(s).