

ORIGINAL ARTICLE

Outcomes of drug-eluting stents compared to bare-metal stents in ST-segment elevation acute myocardial infarction

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KEYWORDS

Stents;
Myocardial infarction;
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Abstract

Introduction: Primary percutaneous coronary intervention (PPCI) has become the treatment of choice in patients with ST-segment elevation myocardial infarction (STEMI). Drug-eluting stents (DES) reduce restenosis compared to bare-metal stents (BMS) but there is conflicting data concerning their use in the setting of STEMI. We aimed to evaluate the influence of the type of stent on the outcomes of PPCI.

Methods: This was a single-center longitudinal study including 213 consecutive patients (76% men, mean age 60 ± 12 years) with STEMI undergoing PPCI between 2003 and 2007, divided into two groups: BMS (43.7%) and DES (56.3%). We assessed clinical and demographic features as well as angiographic and electrocardiographic signs of myocardial reperfusion. The composite outcome of death, myocardial infarction (MI) or target-lesion revascularization (TLR) was evaluated.

Results: At a median follow-up of 26 months there were no differences in the composite outcome of death/MI/TLR (BMS 18.3% vs DES 15.8%) or in the incidence of stent thrombosis. Angiographic results of the procedure were also similar. Independent predictors of the composite outcome were age (HR=1.06, 95% CI [1.02-1.11], left anterior descending artery as infarct-related vessel (HR=2.69, 95% CI [1.17-6.19]) and use of glycoprotein IIb/IIIa inhibitors (HR=0.33, 95% CI [0.13-0.83]).

Conclusions: There was no benefit in angiographic outcomes or major cardiac events after treatment with drug-eluting stents compared to bare-metal stents in this group of patients with STEMI.

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PALAVRAS-CHAVE

Stents;
 Enfarte do miocárdio;
 Intervenção coronária
 percutânea;
 Doença coronária/
 terapêutica

Comparação entre *stents* revestidos e não revestidos por fármaco no enfarte agudo do miocárdio com supradesnivelamento de ST

Resumo

Introdução: A angioplastia primária (ICPP) é o tratamento de eleição para enfarte agudo do miocárdio com elevação de ST (EAM ST). Os *stents* farmacológicos (DES) permitem reduzir a taxa de restenose coronária, sendo controverso o seu uso no contexto de EAM ST. O objectivo deste estudo foi avaliar os resultados clínicos da ICPP em função do tipo de *stent* usado (não revestido *versus* DES).

População e métodos: Estudo longitudinal de centro único, incluindo 213 doentes consecutivos, idade média 60 ± 12 anos, 76% homens, submetidos a ICPP no contexto de EAM ST, entre 2003 e Novembro 2007. Foram considerados 2 grupos: *stent* não revestidos (BMS) (43,7%) e DES (56,3%). Analisaram-se as características clínicas e demográficas dos 2 grupos, comparando-se também variáveis angiográficas, de perfusão miocárdica, grau de resolução de segmento ST pós-ICPP e pico de troponina. Determinou-se no seguimento a incidência do evento combinado: morte, enfarte do miocárdio (EAM) ou revascularização de lesão alvo (TLR).

Resultados: No seguimento mediano de 26 meses não se encontraram diferenças no evento combinado Morte/EAM/TLR (BMS 18,3% *versus* 15,8%) nem na trombose de *stent*. Os resultados angiográficos foram também semelhantes. Os preditores independentes de morte/EAM/TLR foram a frequência cardíaca (HR = 1.06 95% IC [1.02-1.11], descendente anterior como vaso *culprit* (HR = 2.69 95% IC [1.17-6.19]) e utilização de inibidores da glicoproteína IIb/IIIa (HR = 0.33 95% IC [0.13-0.83]).

Conclusão: O tipo de *stent* utilizado não parece ter influência na ocorrência de eventos cardíacos em doentes submetidos a angioplastia primária, no contexto de EAM ST.

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Introduction

The use of stents in primary and rescue percutaneous coronary intervention (PCI) is superior to balloon angioplasty, with lower rates of repeat revascularization and lower mortality^{1,2}. Drug-eluting stents (DES) have been shown to be safe and more effective than bare-metal stents (BMS) in reducing restenosis and the frequency of repeat interventions in patients undergoing elective PCI^{3,4}. However, there are conflicting results regarding the efficacy of DES as compared to BMS in the setting of primary PCI for ST-elevation acute myocardial infarction (STEMI). In particular, late stent thrombosis due to delayed endothelialization and malapposition after DES implantation raises safety concerns, since there are studies suggesting that DES are associated with an increased rate of this event compared to BMS^{5,6}.

The aim of this study was to compare the clinical outcomes of patients presenting with STEMI treated with DES or BMS as part of primary PCI.

Methods**Study design and data collection**

This was a single-center, longitudinal, observational study which included 213 patients treated with primary PCI for STEMI between January 2003 and November 2007. Of these, 93 were treated only with BMS and 120 were treated only with DES. All data were collected prospectively by the study investigators. Procedural data, including adjunctive

pharmacology, device utilization, reference vessel diameter, pre- and post-procedural TIMI flow, lesion length and lesion characteristics were assessed by the operating interventional cardiologist.

All the angiography films were reviewed to assess the following variables: pre- and post-procedural TIMI frame count, thrombus grade and myocardial blush grade at the end of the procedure.

The electrocardiograms on admission and after the procedure were also reviewed to evaluate the degree of ST-segment resolution. Peak troponin I and CK-MB were recorded.

Patients were prospectively followed for the occurrence of major adverse cardiac events (defined as a composite of all-cause death, non-fatal myocardial infarction [MI] or target lesion revascularization [TLR]).

Post-discharge clinical follow-up was conducted by telephone interview. All data were entered into a centralized database (CardioBase®).

Definitions

Reinfarction was defined as a clinical event with any new elevation of troponin I or creatine kinase-MB above the upper reference limit and included both ST- and non ST-elevation myocardial infarction. Target vessel and target lesion revascularization were defined as any revascularization procedure of the target vessel or target lesion (from 5 mm distally to the stent up to 5 mm proximally to the stent), respectively. Stent thrombosis was classified as

Table 1 Baseline characteristics according to type of stent.

	Total	BMS	DES	p
<i>n</i>	213	93 (43.7%)	120 (56.3%)	
Mean age±SD (years)	60±12	62.2±12.3	58.3±11.8	0.014
Male	161 (75.6%)	67 (72%)	94 (78.3%)	0.289
Cardiovascular risk factors				
Hypertension	118 (55.4%)	53 (57%)	65 (54.2%)	0.681
Diabetes	37 (17.5%)	14 (15.2%)	23 (19.2%)	0.453
Smoking	122 (57.3%)	49 (52.7%)	73 (60.8%)	0.233
Hyperlipidemia	107 (50.2%)	43 (46.2%)	64 (53.3%)	0.304
Body mass index (median and interquartile range)	26.2 (24-29)	26 (24-29)	26.4 (24.3-29)	0.319
Normal LVEF (<i>n</i> =200)	167 (83.5%)	72 (80%)	95 (86.4%)	0.228
Previous history				
PCI	39 (18.3%)	18 (19.4%)	21 (17.5%)	0.728
CABG	8 (3.8%)	2 (2.2%)	6 (5%)	0.278
MI	39 (18.3%)	16 (17.2%)	23 (19.2%)	0.713
Killip-Kimball 1 on admission	171 (80.3%)	71 (76.3%)	100 (83.3%)	0.204
Heart rate on admission	75.6±17.4	75.5±18.8	75.7±16.3	0.925
Systolic arterial pressure (median and interquartile range)	132.5 (115-159)	135 (118.5-156)	130 (110-160)	0.468
CKD on hemodialysis	4 (1.9%)	3 (3.2%)	1 (0.8%)	0.202

MI: myocardial infarction; CABG: coronary artery bypass graft; CKD: chronic kidney disease; LVEF: left ventricular ejection fraction; PCI: percutaneous coronary intervention.

definite if a thrombus was angiographically or echographically documented within the stent, as probable in the case of unexplained death within one month of the index procedure, or as possible in the case of unexplained death within one year of the index procedure. Stent thrombosis was classified as acute if it occurred within 24 hours of the index procedure, subacute if it occurred between 1 and 30 days, and late if it occurred after 30 days.

Study outcomes

The primary objective of the study was the composite outcome of all-cause death, non-fatal MI or TLR. Secondary outcomes were target vessel revascularization (TVR), stent thrombosis, final TIMI flow, final TIMI frame count, myocardial blush grade and degree of ST-segment resolution.

Statistical analysis

Baseline and outcome variables were compared using the Student's unpaired t-test or the Mann-Whitney test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables. The normality assumption for continuous variables was assessed by the Kolmogorov-Smirnov test. Event-free survival was computed using Kaplan-Meier estimates and compared between groups with the log-rank test. The predictors of the primary objective of the study were found by multivariate analysis with a Cox proportional hazard regression model. All p values were 2-sided, and a p value of less than 0.05 was considered statistically significant. All analyses were conducted with SPSS version 17 statistical analysis software (SPSS Inc, Chicago, Illinois).

Results

Baseline clinical, angiographic and procedural variables

The study population were 75.6% male, 17.5% diabetic and with a mean age of 60±12 years. Patients treated with DES were younger. All the other baseline demographics were similar between the groups (Table 1).

DES patients more often had the left anterior descending artery as the infarct-related vessel (45.8% vs 32.3%, $p=0.045$) and complete revascularization (60% vs 41%, $p=0.006$). There were fewer coronary lesions in DES patients (2.21 ± 1.33 vs 2.60 ± 1.47 , $p=0.036$) but on average more vessels were stented in this group (1.24 ± 0.48 vs 1.10 ± 0.30 , $p=0.017$). The median implanted stent diameter was larger in the BMS group (3.30 mm vs 3.00 mm, $p<0.001$) (Table 2).

Angiographic, electrocardiographic and laboratory results

No significant differences were found in the following variables: final TIMI flow grade=3 (80.6% in BMS vs 84.2% in DES, $p=0.501$), corrected final TIMI frame count ≤ 21 (62% in BMS vs 56% in DES, $p=0.088$), myocardial blush grade=3 (43.5% in BMS vs 50% in DES, $p=0.432$), degree of ST-segment elevation resolution $\geq 70\%$ (45.2% in BMS vs 45% in DES, $p=0.981$), peak troponin I (median and interquartile range: 74; 34-123 $\mu\text{g/l}$ in BMS vs 72; 22-125 $\mu\text{g/l}$ in DES, $p=0.422$) (Table 3).

Table 2 Procedure characteristics according to type of stent.

	Total (n=213)	BMS (n=93)	DES (n=120)	p
Pain-to-balloon time, median (h:m) and interquartile range	4:30 (3:10-7:56)	4:20 (3:04-7:24)	4:44 (3:16-8:09)	0.439
Infarction-related vessel =LAD	85 (40%)	30 (32.3%)	55 (45.8%)	0.045
TIMI flow pre-procedure =0	129 (60.6%)	60 (64.5%)	69 (57.5%)	0.299
Number of diseased vessels	1.83±0.82	1.94±0.84	1.75±0.80	0.103
Number of treated vessels	1.18±0.42	1.10±0.30	1.24±0.48	0.017
Complete revascularization	113 (53.1%)	40 (43%)	73 (60.8%)	0.010
Number of lesions	2.38±1.40	2.60±1.47	2.21±1.33	0.036
Number of stents implanted	1.15±0.46	1.17±0.46	1.14±0.46	0.689
Median stent diameter (mm) and interquartile range	3.00 (2.75-3.50)	3.30 (3.00-3.50)	3.00 (2.75-3.50)	<0.001
Median total stent length (mm) and interquartile range	23 (18-28)	19 (16-24)	23 (18-28)	0.133
Use of GP IIb/IIIa inhibitors	151 (71.2%)	62 (66.7%)	89 (74.8%)	0.195

LAD: left anterior descending artery; GP IIb/IIIa: glycoprotein IIb/IIIa.

Table 3 Angiographic, electrocardiographic and laboratory results according to type of stent.

	Total (n=213)	BMS (n=93)	DES (n=120)	p
Median troponin I peak ($\mu\text{g/l}$) and interquartile range	73 (28-123)	74 (34-123)	72 (22-125)	0.422
Corrected final TIMI frame count ≤ 21	167 (78.4%)	78 (83.9%)	89 (74.2%)	0.088
Final TIMI flow =3	176 (82.6%)	75 (80.6%)	101 (84.2%)	0.501
Myocardial blush grade =3 (n=145)	68 (46.9%)	30 (43.5%)	38 (50%)	0.432
ST-segment resolution $\geq 70\%$	96 (45.1%)	42 (45.2%)	54 (45%)	0.981

Outcomes of DES compared with BMS

At 30 days, the primary outcome of death/reinfarction/TLR occurred in 12 patients (5.6%), with no differences between the two groups (5.4% in BMS vs 5.8% in DES, $p=0.886$). At one year the primary outcome was similar (14% in BMS vs 9.2% in DES, $p=0.271$). The occurrence of TLR was not statistically different (5.4% in BMS vs 2.5% in DES, $p=0.273$) (Table 4).

Patients treated with DES had a longer median follow-up (29.5 vs 17.3 months, $p=0.004$). In the entire follow-up period there were no differences in the primary outcome (18.3% in BMS vs 15.8% in DES, $p=0.637$). There were also no differences between the two groups when these variables were analyzed individually (Table 4).

Kaplan-Meier estimates of survival free from death, MI or TLR are shown in Fig. 1; there was no significant difference between the groups during follow-up (75.9% in BMS vs 79% in DES, $p=0.355$ by the log rank test).

There were six cases (2.8%) of stent thrombosis, of which three occurred in the DES group (2.5%) and three in the BMS group (3.2%) (Table 5).

Predictors of primary outcome

The independent predictors of the composite outcome (death/MI/TLR) in the overall population were: age (hazard ratio=1.06, 95% confidence interval [CI] 1.02-1.11), LAD as infarct-related vessel (hazard ratio=2.69, 95% CI 1.17-6.19) and use of glycoprotein IIb/IIIa inhibitors (hazard ratio=0.33, 95% CI 0.13-0.83) (Fig. 2).

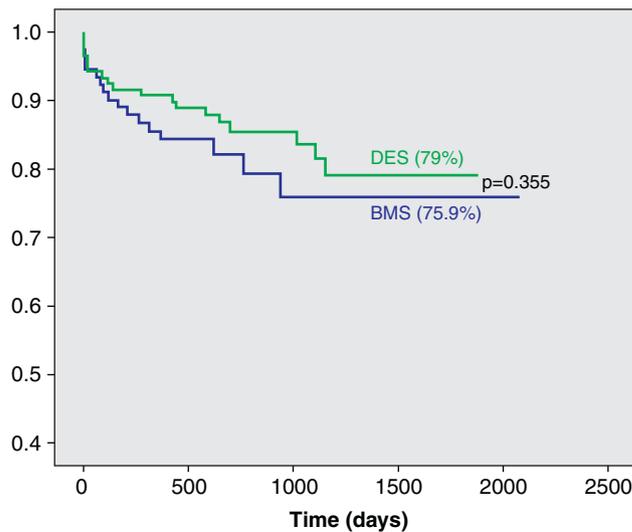


Figure 1 Kaplan-Meier estimates of survival free from death, MI or TLR. There was no statistically significant difference between the DES and BMS groups. BMS: bare-metal stent; DES: drug-eluting stent.

Discussion

The data from this registry show that DES are safe in the setting of STEMI, although it demonstrates no benefit in efficacy, since there was no significant difference in the incidence of the primary outcome of death, MI or TLR at one year and during the entire follow-up.

Table 4 Clinical outcomes according to type of stent.

	Total (n=213)	BMS (n=93)	DES (n=120)	p
Median follow-up (months) and interquartile range	26.2 (15.5-38.4)	17.3 (12.8-36.1)	29.5 (18.3-39.1)	0.004
Death	20 (9.4%)	8 (8.6%)	12 (10%)	0.729
Death at 30 days	8 (3.8%)	4 (4.3%)	4 (3.3%)	0.713
Death at 1 year	13 (6.1%)	6 (6.5%)	7 (5.8%)	0.852
Reinfarction	18 (8.5%)	9 (9.7%)	9 (7.5%)	0.571
Reinfarction at 30 days	6 (2.8%)	1 (1.1%)	5 (4.2%)	0.176
Reinfarction at 1 year	14 (6.6%)	6 (6.5%)	8 (6.7%)	0.950
TLR	11 (5.2%)	5 (5.4%)	6 (5%)	0.902
TLR at 30 days	3 (1.4%)	1 (1.1%)	2 (1.7%)	0.716
TLR at 1 year	8 (3.8%)	5 (5.4%)	3 (2.5%)	0.273
Death, reinfarction or TLR	36 (17%)	17 (18.3%)	19 (15.8%)	0.637
Death, reinfarction or TLR at 30 days	12 (5.6%)	5 (5.4%)	7 (5.8%)	0.886
Death, reinfarction or TLR at 1 year	24 (11.3%)	13 (14%)	11 (9.2%)	0.271
Stent thrombosis	6 (2.8%)	3 (3.2%)	3 (2.5%)	0.731

TLR: target lesion revascularization.

Table 5 Characteristics of patients with stent thrombosis.

Patient	Gender	Age	Type of stent	Days to stent thrombosis	Acute, subacute or late	Probable, possible or definite	Direct cause of death
#1	Female	61	DES	0	Acute	Probable	Yes
#2	Male	52	DES	0	Acute	Definite	No
#3	Male	50	DES	3	Subacute	Definite	No
#4	Male	60	BMS	3	Subacute	Definite	No
#5	Male	75	BMS	210	Late	Definite	No
#6	Male	74	BMS	94	Late	Possible	Yes

BMS: bare-metal stent; DES: drug-eluting stent.

The incidence of stent thrombosis and the angiographic and electrocardiographic variables that were assessed showed that the procedure results were similar regardless of type of stent. Although the groups were well matched in most clinical and angiographic characteristics, patients

in the DES group tended to be younger and had a greater incidence of the LAD as the infarct-related vessel.

Results from registries and randomized trials have shown conflicting results. The main proven benefit of DES over BMS is a reduction in restenosis, which may be outweighed by

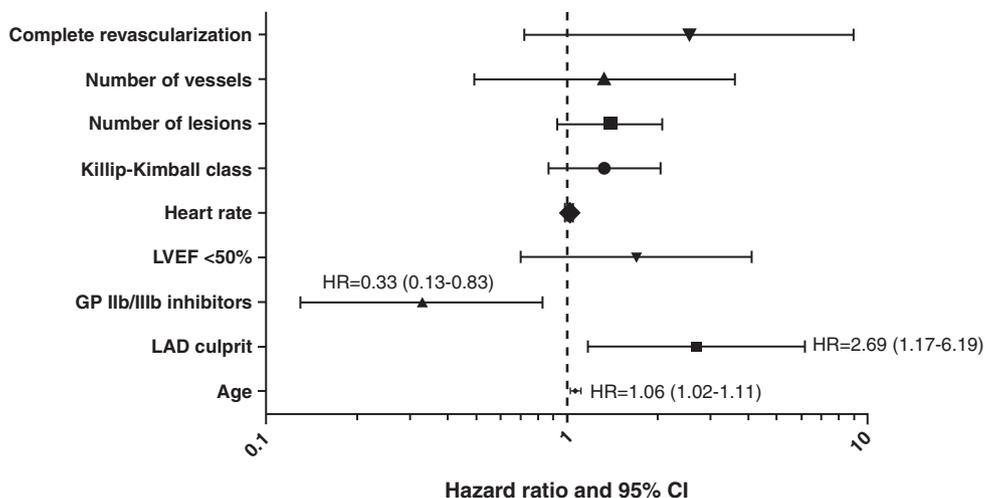


Figure 2 Independent predictors of the primary outcome. All the predictors by univariate analysis are shown and were included in the model, but only age, LAD as the infarct-related vessel and use of GP IIb/IIIa inhibitors remained as predictors by multivariate analysis. GP: glycoprotein; LAD: left anterior descending artery; LVEF: left ventricular ejection fraction.

the need for prolonged dual antiplatelet therapy and the potentially higher risk of very late stent thrombosis. Recent robust data from the HORIZONS-AMI trial demonstrate that in patients with STEMI undergoing primary angioplasty, implantation of paclitaxel-eluting stents, compared with bare-metal stents, significantly reduced angiographic evidence of restenosis and ischemia-driven repeat revascularization procedures, with no differences in death, stent thrombosis, reinfarction or stroke⁷. However, the PASSION trial, which compared 619 patients treated with paclitaxel-eluting stents or BMS in the setting of STEMI, found no significant difference in death, reinfarction, stent thrombosis or TLR at one year⁸, which is in line with the results of our study. Trials that randomized patients to sirolimus-eluting stents or BMS, such as STRATEGY, TYPHOON and SESAMI, have different results from our registry, showing a lower rate of repeat revascularization procedures, but no difference in other clinical outcomes^{9–11}. It should be emphasized, however, that these studies on sirolimus-eluting stents all had angiographic follow-up, which may have biased the operator to intervene in the BMS group.

Late stent thrombosis is a matter of concern when DES are used in patients with STEMI, since there are published data indicating that late healing and re-endothelialization may be impaired when DES are implanted at the site of a ruptured plaque, and this may lead to late stent thrombosis¹². In fact, incomplete expansion and undersizing may occur more often in the setting of STEMI because of the presence of coronary thrombus. This may be more frequently associated with DES, where there is little tissue in-growth, compared with BMS, where more extensive tissue in-growth occurs and may prevent malapposition. The MISSION intervention study showed that acquired stent malapposition at 9 months was more common with DES than with BMS (25% vs 5%, $p < 0.001$)¹³. Our study found no difference in stent thrombosis between DES and BMS, which is similar to the results from several randomized trials, as shown by De Luca et al. in a recent meta-analysis of randomized trials on the efficacy and safety of DES in STEMI (1.6% in DES vs 2.2% in BMS, $p = \text{NS}$, at 12-month follow-up)¹⁴. The incidence of this event in our registry is higher than in this meta-analysis but is similar to the results of HORIZONS-AMI and TYPHOON^{7,10}. In our study most stent thromboses occurred within the first days after STEMI, which suggests that they were related to the procedure rather than the type of stent. The only two cases of late stent thrombosis were observed in the BMS group, which is surprising given the concern regarding this event and the use of DES.

A parallel finding of our study concerns the protective effect of glycoprotein IIb/IIIa inhibitors on the occurrence of death, MI and TLR in this population. Randomized trials have shown conflicting results regarding the use of glycoprotein IIb/IIIa inhibitors in this setting. A previous meta-analysis showed significant benefits in mortality and reinfarction¹⁵, but more recent large randomized trials with the adjunctive administration of clopidogrel (BRAVE-3 and HORIZONS trials) failed to demonstrate the same results^{16,17}. One striking feature is the proportion of patients (over 70%) undergoing this therapy, in contrast to the data in the Portuguese Registry of Acute Coronary Syndromes, in which only 20% of patients with STEMI were treated with glycoprotein IIb/IIIa inhibitors¹⁸.

Our study has the limitations of a single-center registry and as such the outcomes may be influenced by confounders. For instance the larger stent diameter in the BMS group may mean that these patients had a lower risk of restenosis than the patients in the DES group, which would underestimate the benefit of DES use. Moreover, the results are based on a relatively small patient cohort and may lack power. Nevertheless the study provides outcomes of a cohort of patients with STEMI treated with BMS or DES and in addition to having a long follow-up, it takes into account important reperfusion variables such as TIMI frame count, myocardial blush grade and ECG ST-segment elevation resolution.

Conclusions

This study found no differences in major adverse cardiovascular events or angiographic outcomes after treatment with DES or BMS in this group of patients with STEMI, which validates the safety of coated stents but shows no improvement in efficacy.

Concomitant administration of glycoprotein IIb/IIIa inhibitors still confers protection in this setting.

Conflicts of interest

The authors declare they have no conflicts of interest.

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