International Journal of Cardiology 168 (2013) 2632–2636

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Predictors and clinical implications of stent thrombosis in patients with ST-segment elevation myocardial infarction
Insights from the EXAMINATION trial

Salvatore Brugaletta [a], Manel Sabate [a,*], Victoria Martin-Yuste [d], Monica Masotti [a], Yoshitaka Shiratori [a], Luis Alvarez-Contreras [a], Angel Cequier [b], Andrés Iñiguez [c], Antonio Serra [d], Rosana Hernandez-Antolin [e], Vicente Mainar [f], Marco Valgimigli [g], Maurizio Tespili [h], Pieter den Heijer [i], Armando Bethencourt [j], Nicolás Vazquez [k], Josep Gomez-Lara [b], Bianca Backx [l], Patrick W. Serruys [m]

[a] University Hospital Clinic, IDIBAPS, Barcelona, Spain
[b] University Hospital of Bellvitge, Barcelona, Spain
[c] Hospital do Meixoeiro, Vigo, Spain
[d] University Hospital of Sant Pau, Barcelona, Spain
[e] University Hospital San Carlos, Madrid, Spain
[f] Hospital General of Alicante, Spain
[g] University Hospital Ferrara, Ferrara, Italy
[h] University Hospital Bolognini Seriate, Bergamo, Italy
[i] Amphia Ziekenhuis, Breda, The Netherlands
[j] Hospital Son Dureta, Palma de Mallorca, Spain
[k] Hospital Juan Canalejo, A Coruña, Spain
[l] Cardialysis, Rotterdam, The Netherlands.
[m] Erasmus Medical Center, Rotterdam, The Netherlands

ARTICLE INFO

Article history:
Received 2 December 2012
Received in revised form 7 February 2013
Accepted 17 March 2013
Available online 8 April 2013

Keywords:
Stent thrombosis
STEMI
Everolimus-eluting stent

ABSTRACT

Background: Few data are available about safety of second generation drug eluting stents in an all-comer ST elevation myocardial infarction (STEMI) population. We sought to investigate the predictors and clinical implications of 1-year stent thrombosis (ST) in patients with STEMI, included in the EXAMINATION trial.

Methods and results: The EXAMINATION trial is an all-comer prospective, randomized 1:1 controlled trial, testing everolimus-eluting stent (EES) vs. cobalt chromium bare metal stent (BMS) in STEMI patients. It included 1498 patients, randomized to EES (n = 751) or BMS (n = 747). At 1 year, definite/probable stent thrombosis, defined according to ARC criteria, occurred in 26 patients (1.73%), including 18 definite and 8 probable events. The incidence of ST was lower in patients treated with EES than in those treated with BMS (HR 0.16, 95% CI 0.03–0.29, p = 0.017). Patients with ST have higher 1-year rates of cardiac death (30.8% vs. 2.5%, p < 0.001), myocardial infarction (30.8% vs. 0.5%, p < 0.001) and target vessel revascularization (65.4% vs. 4.2%, p < 0.001) compared with those without. Independent predictors of 1-year definite/probable ST were BMS implantation at the index procedure (HR 3.41, 95% CI 1.35–8.60), ST segment resolution of at least 70% in the EKG post-PCI (HR 0.30, 95% CI 0.13–0.70) and Killip class on admission (HR 2.57, 95% CI 1.70–3.90).

Conclusions: ST had low frequency in the first year after implantation of EES/BMS in STEMI patients, but it is associated with adverse events. BMS implantation, lack of ST-segment resolution and high Killip class on admission were independent predictors of 1-year ST.

1. Introduction

Primary percutaneous coronary intervention (PCI) with stent implantation is the treatment of choice for most patients with ST-segment elevation myocardial infarction (STEMI) [1]. Compared with bare metal stents (BMS), first generation drug-eluting stents (DES) have been shown to reduce restenosis and target lesion revascularization in such patients [2,3]. However, safety concerns emerged regarding an increased risk of stent thrombosis (ST) with DES, especially in STEMI patients with a high thrombotic burden [4–7]. Endothelization and healing at the site of DES implantation in patients with STEMI may be indeed substantially delayed [8,9].

All these data, however, have been obtained from first-generation DES, such as sirolimus-eluting and paclitaxel-eluting stents [10,11].

* Corresponding author at: Cardiology Department, Thorax Institute, IDIBAPS, University of Barcelona, Hospital Clinic, c/Villarroel 170, 08036 Barcelona, Spain. Tel.: +34 932279305.
E-mail address: masabate@clinic.ub.es (M. Sabate).

0167-5273/$ – see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ijcard.2013.03.036

Subsequently, second generation DESs have been developed, using novel materials and designs, with improved biocompatible polymers and new antiproliferative drugs. These second generation DESs have shown better performance as compared to first generation DES and BMS with low rate of ST in on- and off-label lesions [12–16]. The COMPARE trial, in particular, showed the safety and efficacy of EES in unselected patients, including 25% of STEMI [13].

The EXAMINATION trial has recently tested the performance of the everolimus-eluting stent (EES) for the first time in an all comer STEMI population [17]. In particular it demonstrated equivalence in the composite endpoint of all-cause death, myocardial infarction and all revascularization as compared to BMS. In addition, despite not powered for this aim, it showed significantly low rates of ST of EES compared with BMS at 1 year follow-up [17].

Previous analyses, aimed to identify predictors of ST in patients with STEMI, who received first generation DES implantation, demonstrated the crucial role of antiplatelet and antithrombotic regimens [18]. We sought therefore to evaluate the clinical implications and the predictors of ST occurring within the first year after second generation DES implantation versus BMS in patients with STEMI included in the EXAMINATION trial.

2. Methods

The EXAMINATION trial design has been previously described in detail [19]. In brief, it was a prospective, randomized, multicenter trial that enrolled all-comer patients with STEMI. As per inclusion criteria the patient could fall into one of the following categories: STEMI < 12 h after the onset of symptoms (namely, primary PCI); rescue PCI after failed thrombolysis; PCI indicated early (<24 h) after effective thrombolysis; and, patients presenting late ("latecomers") with STEMI (>12 h to <48 h after the onset of symptoms). A total of 1504 patients at 12 centers in 3 countries were randomized (1:1) to EES (Xience™ V stent) vs. Cobalt–Chromium BMS (Multilink-Vision® stent). The primary endpoint of the study was the patient-oriented combined endpoint of all-cause death, any myocardial infarction or any revascularization at 1 year according to the Academic Research Consortium (ARC) [20]. The study was approved by the institutional review boards or ethics committee at each participating center and all patients signed an informed consent form.

2.1. Index procedure

At the index procedure, patients received appropriate anticoagulation and other antiplatelet therapies according to standard hospital practice. Either unfractionated heparin or bivalirudin might be used for procedural anticoagulation. The use of glycoprotein IIb/IIIa inhibitors was left to the discretion of the investigator. Aspirin (loading dose 250–500 mg) and clopidogrel (loading dose of at least 300 mg) had to be administered before PCI for those patients not on chronic antiplatelet treatment. Neither prasugrel nor ticagrelor was approved during the recruitment period. Clopidogrel was prescribed for at least one year (75 mg per day) and aspirin (100 mg) indefinitely. Manual thrombectomy followed by direct stenting was the recommended technique in this setting, although other devices could also be used if considered necessary. Operators were instructed to use only the assigned stent type at the index procedure. An EKG was by protocol collected within 30 min post-PCI for the evaluation of ST-segment resolution as compared to the EKG pre-PCI. All the data were analyzed by an independent CoreLab (Cardialysis BV, Rotterdam, The Netherlands).

2.2. Stent thrombosis

Stent thrombosis was classified according to the Academic Research Consortium definition as definite or probable [20]. Stent thrombosis occurring within 24 h was defined as acute; >24 h to 30 days was defined as subacute; and from >30 days to 1 year was defined as late. All adverse events, including stent thromboses, were adjudicated by an independent clinical events committee, blinded to stent assignment after review of original source documentation. Definitions of death (all-cause and cardiac), myocardial infarction (MI) and target vessel revascularization (TVR) have been already reported [17,19].

2.3. Statistical analysis

Categorical variables were expressed as number and percentage and were compared by chi-square analysis or Fisher exact test, as appropriate. Continuous variables were expressed as mean ± standard deviation or median and interquartile range and were compared by the Wilcoxon rank sum test. Cox proportional hazards analysis was used to identify the independent predictors of stent thrombosis via stepwise regression. In model 1 all the following covariates were considered: 1) clinical: age, diabetes mellitus, and Killip class on admission; 2) procedural variables: ST segment resolution > 70%, BMS implanted at the index procedure; peri-procedural use of IIb/IIIa, total stent length and maximum stent diameter. Due to the few number of ST, however, a maximum of 3 predictive variables were allowed into the final model (model 2) in order to avoid any overfitting. Various models were therefore developed and compared in order to select the best variables. The goodness-of-fit of all the models developed was compared according to the Akaike information criterion (AIC) in order to identify the best model, usually characterized by a low AIC [21].

A two-tailed p-value <0.05 was considered statistically significant. Statistical analyses were performed with SPSS statistical package, version 19.0 (SPSS Inc., Chicago IL, USA).

3. Results

3.1. Population

Six patients out of the 1504 initially recruited withdrew the consent after randomization. Therefore, the final study cohort comprised a total of 1498 patients, 751 of them allocated to the EES arm and 747 to the BMS arm. Among these patients, 26 definite or probable stent thromboses (1.73%, 18 definite and 8 probable stent thromboses) occurred within the 1-year follow-up. Acute stent thrombosis occurred in 9 patients (34.6%), sub-acute in 12 patients (46.1%) and late in the remaining 5 patients (19.3%). In particular, acute stent thromboses were 7 (77.8%) in the BMS arm vs. 2 (22.2%, p = 0.108) in the EES arm; subacute stent thromboses were 8 in the BMS arm (66.6%) vs. 3 (33.4%, p = 0.177) in the EES arm; late stent thromboses were 3 (60.0%) in the BMS arm vs. 2 (40.0%, p = 0.686) in the EES arm.

3.2. Predictors of stent thrombosis

Patients with stent thrombosis were older, with a worse Killip class and a lower ejection fraction at discharge than patients without stent thrombosis. No other differences with regards to clinical characteristics were found between the groups (Table 1).

Regarding procedural characteristics, patients who developed a stent thrombosis received more BMS than EES and had less ST-resolution > 70% in the EKG post-PCI as compared with patients who did not.

No differences were found in terms of anticoagulant and antiplatelet regimens during the index procedure or at the various time points of

Table 1
Baseline clinical characteristics.

Variable	Stent thrombosis (n = 26)	No stent thrombosis (n = 1472)	p-value
Age-yr	64.5 ± 11.0	61.4 ± 12.4	<0.001
Male sex, n (%)	22 (84.6)	1222 (83.0)	1.000
BMI	27.2 (3.8)	27.4 (3.9)	
Coronary risk factors, n (%):			
(Previous) smoker	16 (61.5)	538 (72.4)	0.387
Diabetes mellitus	5 (19.2)	253 (17.2)	0.793
Arterial hypertension	16 (61.5)	709 (48.2)	0.235
Hyperlipidemia	13 (50.0)	642 (43.6)	0.544
Family history	2 (7.7)	251 (17.1)	0.332
Cardiovascular history, n (%):			
Prior MI	3 (11.5)	77 (5.2)	0.158
Prior PCI	1 (3.8)	60 (4.1)	1.000
Prior CABG	1 (3.8)	9 (0.6)	0.161
Prior stroke	1 (3.8)	30 (2.0)	0.422
Clinical condition, n (%):			0.870
Primary PCI (<12 h)	22 (84.6)	1246 (84.7)	
Rescue PCI	2 (7.7)	96 (6.5)	
PCI post successful TBL	0 (0)	34 (2.3)	
Latecomer (>12 h < 48 h)	2 (7.7)	95 (6.5)	
Clinical status on admission, n (%):			<0.001
Killip I	17 (65.4)	1320 (90.0)	
Killip II	5 (19.2)	110 (7.5)	
Killip III	2 (7.7)	21 (1.4)	
Killip IV	2 (7.7)	16 (1.1)	
Multivessel disease, n (%)	5 (19.2)	183 (12.4)	0.362
Ejection fraction at discharge	45.0 ± 11.8	51.2 ± 10.4	0.013

BMI = body mass index; MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery by-pass graft. TBL = thrombolysis.

Table 2
Procedural characteristics.

Variable	Stent thrombosis (n = 26)	No stent thrombosis (n = 1472)	p-value
TIMI flow pre-PCI, n (%):			0.777
0	17 (68.0)	861 (58.8)	
1	2 (8.0)	113 (7.7)	
2	2 (8.0)	197 (13.5)	
3	4 (16)	293 (20.0)	
TIMI flow post-PCI, n (%):			0.319
0	0 (50 · 5)	26 (1.8)	
1	1 (3.8)	11 (0.7)	
2	1 (3.8)	58 (4.0)	
3	24 (92.3)	1372 (93.5)	
ST-resolution > 50%, n (%)	17 (70.8)	1106 (83.3)	0.162
ST-resolution > 70%, n (%)	8 (33.3)	844 (63.6)	0.004
Anticoagulation regimen, n (%):			
Unfractioned heparin	20 (76.9)	1169 (79.4)	0.756
Low molecular weight heparin	4 (15.4)	129 (8.8)	0.239
Bivalirudin	2 (7.7)	103 (7.0)	0.891
Antiplatelet regimen, n (%):			
Peri-PCI			
ASA	25 (96.2)	1363 (92.6)	0.492
Clopidogrel	25 (96.2)	1393 (94.6)	0.732
IIb/IIIa inhibitor	9 (34.6)	560 (38.0)	0.721
At discharge			
ASA	19 (100)	1446 (99.9)	0.909
Clopidogrel	19 (100)	1451 (99.9)	0.871
At 1 month			
ASA	17 (89.5)	1339 (93.0)	0.639
Clopidogrel	16 (88.9)	1346 (93.1)	0.360
At 6 months			
ASA	17 (89.5)	1300 (91.5)	0.674
Clopidogrel	16 (88.9)	1266 (91.3)	0.667
At 12 months			
ASA	16 (94.1)	1301 (92.8)	1.000
Clopidogrel	14 (93.3)	1250 (92.6)	1.000
Manual thrombectomy, n (%):	18 (69.2)	958 (65.1)	0.836
Everolimus-eluting stent, n (%)	7 (26.9)	744 (50.5)	0.018
Direct stenting, n (%)	18 (69.2)	867 (60.1)	0.421
Post-dilatation, n (%)	5 (19.2)	216 (14.7)	0.573
Overlapping stent, n (%)	9 (34.6)	395 (26.8)	1.000
Number of stents implanted at index procedure, mean ± SD	1.42 ± 0.58	1.38 ± 0.65	0.489
Max stent diameter (mm), mean ± SD	3.35 ± 0.41	3.20 ± 0.45	0.091
Total stent length, mean ± SD	28.31 ± 11.34	27.50 ± 14.05	0.317

PCI = percutaneous coronary interventions; ASA = aspirin; SD = standard deviation.

follow-up (Table 2). ASA (290 ± 154 vs. 291 ± 121 mg, p = 0.934) and clopidogrel loading doses (471 ± 167 vs. 479 ± 158 mg; p = 0.843) before the index procedure were also not different between patients with vs. without stent thrombosis. In particular either in the acute or in the subacute stent thrombosis, clopidogrel loading dose was not different. At the time of ST, all patients were taking regularly double antiplatelet therapy (Table 3).

Independent predictors of 1-year definite/probable ST were BMS implantation at the index procedure (HR 3.41, 95% CI 1.35–8.60), ST segment resolution of at least 70% in the EKG post-PCI (HR 0.30, 95% CI 0.13–0.70) and Killip class on admission (HR 2.57, 95% CI 1.70–3.90) (Table 4).

3.3. Clinical impact of stent thrombosis

Patients with stent thrombosis have higher 1-year rates of cardiac death (30.8% vs. 2.5%, p < 0.001), target-vessel related MI (30.8% vs. 0.5%, p < 0.001) and TVR (65.4% vs. 4.2%, p < 0.001) compared with those without (Fig. 1).

4. Discussion

Our analysis showed that 1) at 1-year follow-up incidence of ST in patients with STEMI treated with second generation DES or Cobalt–Chromium BMS is relatively low; 2) nevertheless, it represents a devastating complication, being associated with high rate of cardiac events; and 3) BMS implantation at the index procedure, lack of ST segment resolution of at least 70% and Killip class appear as independent predictors of ST in this population.

STEMI presentation is known to be one of the most powerful predictors of ST, due to the thrombotic burden, which can enhance inflammatory response and stent malapposition with subsequent thrombosis [22]. In the Swedish Coronary Angiography and Angioplasty Registry, for example, the risk of stent thrombosis in STEMI was increased 2.5 fold relative to patients without STEMI [23]. For all these reasons, much attention has been focused on stent thrombosis rate in various STEMI trials comparing coronary stents. Overall, within STEMI patients the reported 1-year rate of stent thrombosis from several modest-sized randomized trials of DES vs. BMS ranged from 1% to as high 3–4% [2,24,25]. In particular, in the HORIZONS-AMI, one of the largest trials

Table 3
Cases of definite stent thrombosis.

Case	Type of stent	Location MI	Timing of ST (days after the primary procedure)	Killip class on admission	Antiplatelet regimen at the time of ST	Ejection fraction (%)
1	BMS	LAD	1	1	ASA + clopidogrel	61
2	BMS	LAD	1	2	ASA + clopidogrel	50
3	BMS	RCA	0	2	ASA + clopidogrel	39
4	BMS	RCA	0	4	ASA + clopidogrel	69
5	EES	LCx	35	1	ASA + clopidogrel	55
6	EES	RCA	1	2	ASA + clopidogrel	35
7	BMS	LAD	8	1	ASA + clopidogrel	50
8	BMS	LAD	6	4	ASA + clopidogrel	55
9	BMS	RCA	10	1	ASA + clopidogrel	45
10	EES	RCA	0	1	ASA + clopidogrel	50
11	BMS	LAD	29	1	ASA + clopidogrel	63
12	BMS	RCA	255	1	ASA + clopidogrel	54
13	EES	LAD	28	1	ASA + clopidogrel	50
14	BMS	LAD	0	1	ASA + clopidogrel	59
15	BMS	LAD	7	1	ASA + clopidogrel	38
16	BMS	RCA	25	1	ASA + clopidogrel	42
17	BMS	RCA	1	3	ASA + clopidogrel	40
18	BMS	LAD	141	1	ASA + clopidogrel	58

BMS = bare metal stent; EES = everolimus eluting stent; MI = myocardial infarction; LAD = left anterior descending artery; LCx = left circumflex artery; RCA = right coronary artery; ST = stent thrombosis; ASA = aspirin.

Table 4
Predictors of definite/probable stent thrombosis at 1 year.

Variables	Hazard ratio	p-value
Model 1 (AIC: 242.56)		
Age	1.01 [0.98–1.04]	0.492
Diabetes mellitus	0.73 [0.24–2.22]	0.581
Killip class on admission	2.52 [1.65–3.85]	<0.001
ST-resolution > 70%	0.29 [0.12–0.68]	0.005
BMS implanted at the index procedure	3.41 [1.34–8.67]	0.010
Use of IIb/IIIa at the index procedure	0.83 [0.36–1.90]	0.658
Total stent length	0.99 [0.96–1.03]	0.800
Maximum stent diameter	1.90 [0.73–4.95]	0.189
Model 2 (AIC: 65.17)		
Killip class on admission	2.57 [1.70–3.90]	<0.001
ST-resolution > 70%	0.30 [0.13–0.70]	0.005
BMS implanted at the index procedure	3.41 [1.35–8.60]	0.010

AIC = Akaike information criterion; BMS = bare metal stent.

comparing first generation DES vs. BMS, the definite/probable stent thrombosis rate within 1 year was 3.4% [26].

Compared to these previous observations, the EXAMINATION trial was the first trial randomly comparing second generation everolimus-eluting DES vs. Cobalt–Chromium BMS, enrolling a wide all-comer STEMI population (70% of all the STEMI screened) with high usage of thrombectomy device (65%). Under these conditions, it showed an overall 1-year definite/probable stent thrombosis rate of 1.7%, lower than that previously reported [17]. The high use of thrombectomy devices, the usage of second generation coronary devices either drug eluting or not, and the difference in polymer matrix, in anti-proliferative drug dose and in release kinetics between 1st and 2nd generation DES may explain these differing findings as compared to previous reports [27].

Nevertheless, despite very low occurrence, stent thrombosis confirmed to be a devastating complication, being significantly associated with high rate of cardiac death, myocardial infarction and target vessel revascularization (Fig. 1) [28,29]. Identification of safety factors, which can prevent stent thrombosis with subsequent reduction of its clinical meaning, appears therefore appealing. Although the EXAMINATION trial was not powered to demonstrate difference in ST between EES and BMS, it showed a significant unadjusted difference in ST rate between the two stents compared [17]. This finding was already important, especially in light of a previous meta-analysis comparing first-generation DES with BMS in STEMI patients, which failed to show a difference in ST rate between groups [30]. In the present report, we showed that in a statistically adjusted analysis three factors appear to be independent predictors of ST in STEMI population from the EXAMINATION trial: high Killip class at the admission, lack of ST-segment resolution > 70% and use of BMS.

Killip class has been previously associated to early ST in patients with acute coronary syndromes [31,32]. Our finding confirms therefore that STEMI patients with a bad clinical profile at admission, resulting in a low ejection fraction and bad myocardial perfusion, have a high risk of ST within 1-year follow-up. The association between lack of ST-segment resolution > 70% in the EKG post-primary PCI and stent thrombosis supports furthermore the role of myocardial perfusion in primary PCI, which should aim to obtain a TIMI 3 flow, avoiding the no-reflow phenomenon and therefore ensuring a good outcome to STEMI patients.

In addition to these two factors, BMS implantation, as compared to EES, at the index procedure resulted in the most powerful independent predictor of ST. Recent reports support the low thrombogenicity of EES in comparison not only to BMS, but also to 1st generation DES [33,34]. These findings, however, come from studies and meta-analysis including every type of patients either with stable angina or with acute coronary syndromes [13,33–36]. In addition, it is noteworthy that in contrast to previous reports comparing EES with other DES or BMS, the EXAMINATION trial compared two stents (Xience™ V and Multilink® Vision), which share the same stent platform and differ only for the presence of polymer and drug. Through speculative, the mechanisms underlying this lower risk of ST with EES in STEMI patients may be therefore related to these characteristics of manufacturing. In particular, Kolandaivelu et al. showed that drug/polymer coating does not increase acute stent clotting, but conversely decrease thrombosis: the fluorinated copolymer, present in the EES, may indeed confer a certain degree of thromboresistance, reducing inflammatory reactions and improving endothelialization [37]. This can be especially relevant in the context of STEMI where the presence of the copolymer may neutralize the detrimental effects due to the eventual dissolution of the thrombus behind the struts, which leads to a high incidence of late acquired malapposition and stent thrombosis [37,38]. The copolymer may also potentially neutralize any possible toxic effects of the everolimus, whose dose and release kinetics are however known as better than other drugs previously used in stent manufacture. A significantly lower rate of uncovered struts and of intracoronary masses, compatible with thrombus has been, for example, reported in a non randomized optical coherence tomography comparison between EES and sirolimus-eluting stents [39].

Of note is that compliance to dual antiplatelet therapy was very high in both groups and none of the patients with stent thrombosis have prematurely stopped the dual antiplatelet therapy. No differences were also found in terms of peri-procedural antithrombotic or antiplatelet (e.g. clopidogrel loading dose) regimen between groups.

4.1. Limitations

This analysis has several limitations. First, as it is a post-hoc analysis, it has all the limitation inherently to it. Second, the trial was not powered to detect differences in ST between the two groups, which could be play of chance. In addition, although only three variables

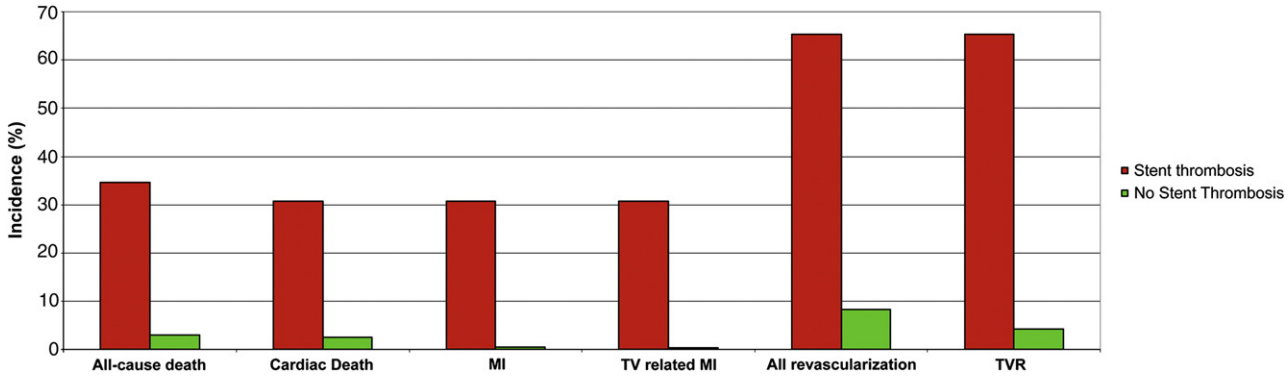

Fig. 1. One-year incidence of the various endpoints, according to the presence of stent thrombosis. Development of stent thrombosis is associated with higher rate of the various clinical endpoints as compared to its absence. All p-value are <0.001. MI = myocardial infarction; TV = target vessel; TVR = target vessel revascularization.

were included in the final model of the multivariate analysis due to the few number of events, the model may be overfitted. Nevertheless, it currently represents the only data existing on ST of EES in the clinical context of STEMI patients and corroborates data recently published in other scenarios [31–34]. Third, a longer follow-up would be needed to rule out all late safety concerns specific to EES in STEMI.

5. Conclusions

In STEMI patients undergoing primary PCI, BMS implantation, ST-segment resolution > 70% and Killip class, represent independent predictors of 1-year stent thrombosis. The concept of a polymer-coated DES being safer than a BMS in STEMI patients may represent a paradigm shift in their treatment and need to be confirmed in a trial adequately powered with longer follow-up.

References

[1] Wijns W, Kolh P, Danchin N, et al. Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2010;31:2501–55.

[2] Spaulding C, Henry P, Teiger E, et al. Sirolimus-eluting versus uncoated stents in acute myocardial infarction. N Engl J Med 2006;355:1093–104.

[3] Spaulding C, Teiger E, Commeau P, et al. Four-year follow-up of TYPHOON (trial to assess the use of the CYPHer sirolimus-eluting coronary stent in acute myocardial infarction treated with BallOON angioplasty). JACC Cardiovasc Interv 2011;4:14–23.

[4] Kastrati A, Mehilli J, Pache J, et al. Analysis of 14 trials comparing sirolimus-eluting stents with bare-metal stents. N Engl J Med 2007;356:1030–9.

[5] Daemen J, Wenaweser P, Tsuchida K, et al. Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study. Lancet 2007;369:667–78.

[6] Mauri L, Hsieh WH, Massaro JM, Ho KK, D'Agostino R, Cutlip DE. Stent thrombosis in randomized clinical trials of drug-eluting stents. N Engl J Med 2007;356:1020–9.

[7] Sianos G, Papafaklis MI, Daemen J, et al. Angiographic stent thrombosis after routine use of drug-eluting stents in ST-segment elevation myocardial infarction: the importance of thrombus burden. J Am Coll Cardiol 2007;50:573–83.

[8] Nakazawa G, Finn AV, Vorpahl M, et al. Incidence and predictors of drug-eluting stent fracture in human coronary artery a pathologic analysis. J Am Coll Cardiol 2009;54:1924–31.

[9] Gonzalo N, Barlis P, Serruys PW, et al. Incomplete stent apposition and delayed tissue coverage are more frequent in drug-eluting stents implanted during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction than in drug-eluting stents implanted for stable/unstable angina: insights from optical coherence tomography. JACC Cardiovasc Interv 2009;2:445–52.

[10] Pfisterer M, Brunner-La Rocca HP, Buser PT, et al. Late clinical events after clopidogrel discontinuation may limit the benefit of drug-eluting stents: an observational study of drug-eluting versus bare-metal stents. J Am Coll Cardiol 2006;48:2584–91.

[11] Stone GW, Moses JW, Ellis SG, et al. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. N Engl J Med 2007;356:998–1008.

[12] Jensen LO, Thayssen P, Hansen HS, et al. Randomized comparison of everolimus-eluting and sirolimus-eluting stents in patients treated with percutaneous coronary intervention: the Scandinavian Organization for Randomized Trials with Clinical Outcome IV (SORT OUT IV). Circulation 2012;125:1246–55.

[13] Kedhi E, Joesoef KS, McFadden E, et al. Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice (COMPARE): a randomised trial. Lancet 2010;375:201–9.

[14] Stone GW, Midei M, Newman W, et al. Comparison of an everolimus-eluting stent and a paclitaxel-eluting stent in patients with coronary artery disease: a randomized trial. JAMA 2008;299:1903–13.

[15] Stone GW, Rizvi A, Newman W, et al. Everolimus-eluting versus paclitaxel-eluting stents in coronary artery disease. N Engl J Med 2010;362:1663–74.

[16] Serruys PW, Silber S, Garg S, et al. Comparison of zotarolimus-eluting and everolimus-eluting coronary stents. N Engl J Med 2010;363:136–46.

[17] Sabate M, Cequier A, Iniguez A, et al. Everolimus-eluting stent versus bare-metal stent in ST-segment elevation myocardial infarction (EXAMINATION): 1 year results of a randomised controlled trial. Lancet 2012;380:1482–90.

[18] Dangas GD, Caixeta A, Mehran R, et al. Frequency and predictors of stent thrombosis after percutaneous coronary intervention in acute myocardial infarction. Circulation 2011;123:1745–56.

[19] Sabate M, Cequier A, Iniguez A, et al. Rationale and design of the EXAMINATION trial: a randomised comparison between everolimus-eluting stents and cobalt–chromium bare-metal stents in ST-elevation myocardial infarction. EuroIntervention 2011;7:977–84.

[20] Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007;115:2344–51.

[21] Akaike H. A new look at the statistical model identification. IEEE Trans Autom Control 1974;19:716–23.

[22] Finn AV, Nakazawa G, Joner M, et al. Vascular responses to drug eluting stents: importance of delayed healing. Arterioscler Thromb Vasc Biol 2007;27:1500–10.

[23] Lagerqvist B, Carlsson J, Frobert O, et al. Stent thrombosis in Sweden: a report from the Swedish Coronary Angiography and Angioplasty Registry. Circ Cardiovasc Interv 2009;2:401–8.

[24] Laarman GJ, Suttorp MJ, Dirksen MT, et al. Paclitaxel-eluting versus uncoated stents in primary percutaneous coronary intervention. N Engl J Med 2006;355:1105–13.

[25] Valgimigli M, Campo G, Percoco G, et al. Comparison of angioplasty with infusion of tirofiban or abciximab and with implantation of sirolimus-eluting or uncoated stents for acute myocardial infarction: the MULTISTRATEGY randomized trial. JAMA 2008;299:1788–99.

[26] Stone GW, Witzenbichler B, Guagliumi G, et al. Bivalirudin during primary PCI in acute myocardial infarction. N Engl J Med 2008;358:2218–30.

[27] John MC, Wessely R, Kastrati A, et al. Differential healing responses in polymer- and nonpolymer-based sirolimus-eluting stents. JACC Cardiovasc Interv 2008;1:535–44.

[28] van Werkum JW, Heestermans AA, de Korte FI, et al. Long-term clinical outcome after a first angiographically confirmed coronary stent thrombosis: an analysis of 431 cases. Circulation 2009;119:828–34.

[29] Iakovou I, Schmidt T, Bonizzoni E, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. JAMA 2005;293:2126–30.

[30] Brar SS, Leon MB, Stone GW, et al. Use of drug-eluting stents in acute myocardial infarction: a systematic review and meta-analysis. J Am Coll Cardiol 2009;53:1677–89.

[31] Smit JJ, van 't Hof AW, de Boer MJ, et al. Incidence and predictors of subacute thrombosis in patients undergoing primary angioplasty for an acute myocardial infarction. Thromb Haemost 2006;96:190–5.

[32] Beinart R, Abu Sham'a R, Segev A, et al. The incidence and clinical predictors of early stent thrombosis in patients with acute coronary syndrome. Am Heart J 2010;159:118–24.

[33] Raber L, Magro M, Stefanini GG, et al. Very late coronary stent thrombosis of a newer-generation everolimus-eluting stent compared with early-generation drug-eluting stents: a prospective cohort study. Circulation 2012;125:1110–21.

[34] Palmerini T, Biondi-Zoccai G, Della Riva D, et al. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. Lancet 2012;379:1393–402.

[35] Planer D, Smits PC, Kereiakes DJ, et al. Comparison of everolimus- and paclitaxel-eluting stents in patients with acute and stable coronary syndromes: pooled results from the SPIRIT (A Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) and COMPARE (A Trial of Everolimus-Eluting Stents and Paclitaxel-Eluting Stents for Coronary Revascularization in Daily Practice) Trials. JACC Cardiovasc Interv 2011;4:1104–15.

[36] Bangalore S, Kumar S, Fusaro M, et al. Short and long-term outcomes with drug eluting and bare metal coronary stents: a mixed treatment comparison analysis of 117 762 patient-years of follow-up from randomized trials. Circulation 2012;125:2873–91.

[37] Kolandaivelu K, Swaminathan R, Gibson WJ, et al. Stent thrombogenicity early in high-risk interventional settings is driven by stent design and deployment and protected by polymer–drug coatings. Circulation 2011;123:1400–9.

[38] Guagliumi G, Costa MA, Sirbu V, et al. Strut coverage and late malapposition with paclitaxel-eluting stents compared with bare metal stents in acute myocardial infarction: optical coherence tomography substudy of the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) Trial. Circulation 2011;123:274–81.

[39] Choi HH, Kim JS, Yoon DH, et al. Favorable neointimal coverage in everolimus-eluting stent at 9 months after stent implantation: comparison with sirolimus-eluting stent using optical coherence tomography. Int J Cardiovasc Imaging 2012;28:491–7.