



Incidence and predictors of target lesion failure in patients undergoing contemporary DES implantation—Individual patient data pooled analysis from 6 randomized controlled trials

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Background Drug-eluting stents (DESs) have improved clinical outcomes of patients undergoing percutaneous coronary intervention (PCI). Nevertheless, adverse events related to previously treated lesion still occur. We sought to evaluate the incidence and predictors of target lesion failure (TLF) in patients undergoing contemporary DES implantation.

Methods Patient-level data from 6 prospective, randomized trials were pooled, and DES treatment outcomes were analyzed at up to 5 years. Primary outcome was TLF (cardiac death, target lesion revascularization, or target vessel myocardial infarction). Cox proportional-hazards model was used to identify predictors of TLF.

Results Overall, 10,072 patients were included in the analysis. TLF rate was 1.7%, 4.3%, and 11.9% at 30 days, 1 year, and 5 years, respectively. The only independent predictor of TLF at 30 days was stent length (hazard ratio [HR] 1.017, 95% CI 1.011-1.024, $P < .0001$). Moderate/severe calcification, stent length and post procedural diameter stenosis were predictors between 30 days to 1 year but not at 1 to 5 years. Reference vessel diameter was the only lesion-related predictor at 5 years ($P = .003$). Clinical predictors of TLF between 30 days and 1 year were diabetes and hypertension ($P < .01$ for both), and between 1 and 5 years, diabetes (HR 1.40, 95% CI 1.13-1.73, $P = .002$), prior coronary artery bypass grafting (HR 2.52, 95% CI 1.92-3.30, $P < .0001$), and prior PCI (HR 1.29, 95% CI 1.02-1.64, $P = .04$) predicted TLF.

Conclusions Predictors of TLF vary in the early, late, and very late postprocedural periods. Reference vessel diameter was the only lesion-related predictor of long-term TLF; clinical predictors were diabetes, prior coronary artery bypass grafting, and prior PCI. (*Am Heart J* 2019;213:105-11.)

Although drug-eluting stents (DESs) have significantly improved angiographic and clinical outcomes in many patients and lesion subsets,¹⁻⁴ stent failure remains a clinical reality. In fact, rates of stent failure with first-generation DESs were reported to be around 10% at

1 year and around 20% at 5 years.^{5,6} Numerous factors have been suggested as underlying causes of events related to previously treated lesions. These include biological factors such as resistance to antiproliferative drugs and hypersensitivity reactions; mechanical factors such as stent fracture, polymer peeling, and nonuniform polymer/drug deposition; and technical aspects including incomplete stent expansion, malapposition, and vascular injury to unstented segments.⁷ Several studies have aimed to identify patient and lesion characteristics that may predict elevated risk of restenosis and stent failure.^{4,8-11} Some of the patient-related predictors suggested by these studies include younger age, diabetes mellitus, and prior percutaneous coronary intervention (PCI), whereas lesion length, location in a vein graft, and minimal stent diameter have been identified as possible lesion-related predictors of stent failure.^{8,10} Although these factors now

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Table I. Description of the prospective randomized pooled studies

Study	Author, year	Second-generation drug-eluting study stent	No. of patients in the pooled analysis	End point	
				Clinical end point	Time point
COMPARE ¹²	Kedhi et al, 2010	EES (XIENCE)	8.9% (897/10,072)	Death, MI, TVR	1 y
COMPARE II ¹³	Smits et al, 2013	BES (Nobori), EES (XIENCE/Promus)	26.9% (2,707/10,072)	Cardiac death, MI, TVF	1 y
PLATINUM ¹⁴	Stone et al, 2011	EES (Promus)	15.2% (1,530/10,072)	TLF	1 y
SPIRIT III ¹⁵	Stone et al, 2008	EES (XIENCE)	6.6% (669/10,072)	In-segment late lumen loss	9 m
SPIRIT IV ¹⁶	Stone et al, 2010	EES (XIENCE)	24.4% (2,458/10,072)	TLF	1 y
TWENTE II ¹⁷	von Birgelen et al, 2014	ZES (Resolute), EES (Promus)	18.0% (1,811/10,072)	TVF	1 y

EES, everolimus-eluting stent; BES, biolimus-eluting stent; ZES, zotarolimus-eluting stent.

impact clinical care, the predominance of data come from studies of bare metal stents (BMSs) and first-generation DESs and may thus be outdated with current-generation DES technology. Predictors of target lesion failure (TLF) in the contemporary era have not been well described. We therefore sought to determine the incidence and predictors of TLF from a large patient-level pooled database of 10,072 patients undergoing contemporary DES implantation from 6 prospective, randomized trials.

Methods

Trials and study objectives

To perform a comprehensive, patient-level pooled analysis, we combined data from 6 prospective, randomized, controlled trials maintained at the Cardiovascular Research Foundation (New York, NY) in which follow-up of patients treated with contemporary DES was available for up to 5 years. The designs of these trials have been previously described and are summarized in Table I.¹²⁻¹⁷ As the purpose of the study was to analyze contemporary DES performance, only patients treated with second- or third-generation DES in those studies were included in the present analysis.

Each trial was approved by the institutional review board or ethics committee at the respective participating center, and all patients signed informed, written consent prior to randomization.

End points, definitions, and follow-up

The primary end point was the rate of *TLF*, defined as cardiac death, target vessel myocardial infarction (TV-MI), or ischemia-driven target lesion revascularization (TLR) at 30 days, 1 year, and 5 years. *TLR* was defined as any repeat revascularization procedure (percutaneous or surgical) of the original target lesion site, including the stent and within 5 mm of the proximal and distal stent margins. Secondary end points included rates of *major adverse cardiac events*, defined as the composite of all-cause death, myocardial infarction, or TVR, and *target vessel failure* (TVF), defined as cardiac death, TV-MI, or

target vessel revascularization (TVR). *TVR* was defined as any revascularization procedure occurring within the major epicardial vessel in which the stent was implanted or its branches. Definite and probable stent thromboses were defined according to the Academic Research Consortium definitions.¹⁸ Events as adjudicated in each trial were used for the pooled analysis. All end points were evaluated at 30 days, 1 year, and 5 years.

For the 6 trials¹²⁻¹⁷ included in our analysis, patients from A Trial of Everolimus-Eluting Stents and Paclitaxel-Eluting Stents for Coronary Revascularization in Daily Practice (COMPARE); A Prospective, Randomized, Multi-center Trial to Assess an Everolimus-Eluting Coronary Stent System (PROMUS Element) for the Treatment of up to Two De Novo Coronary Artery Lesions (PLATINUM); A Clinical Evaluation of the Investigational Device XIENCE V Everolimus Eluting Coronary Stent System (EECSS) in the Treatment of Subjects With de Novo Native Coronary Artery Lesions (SPIRIT III); and DURable Polymer-based STent CHallenge of Promus Element Versus ReSolute Integrity (DUTCH PEERS): Randomized Multicenter Trial in All Comers Population Treated Within Eastern NeThErlands-2 (TWENTE II) were followed up to 5 years, although the primary end points were earlier. Patients from Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Subjects With de Novo Native Coronary Artery Lesions (SPIRIT IV) and Comparison of the Everolimus Eluting (XIENCE-V, XIENCE-Prime or PROMUS Stent) With the Biolimus A9 Eluting NOBORI Stent in All-comers (COMPARE II) had 4-year and 3-year follow-up available separately. Those patients were censored at the maximum follow-up time and included in the 5-year analysis.

Statistical analysis

Continuous data are presented as mean \pm SD, and statistical differences were assessed with the Student *t* test. Categorical data are presented as percentage and count, and differences were assessed with the χ^2 test. Time-to-event data are presented using Kaplan-Meier estimates as percentage with number of events, and differences were assessed with the log-rank test.

Table II. Clinical, angiographic, and procedural characteristics

	TLF (n = 983)	No TLF (n = 9089)	Overall (N = 10,072)	P value
Age, y	64.7 ± 10.9	63.1 ± 10.7	63.3 ± 10.7	<.0001
Male sex	69.3% (681/983)	71.5% (6500/9089)	71.3% (7181/10,072)	.14
Diabetes mellitus	33.0% (324/983)	22.9% (2085/9086)	23.9% (2409/10,069)	<.0001
Insulin treated	12.8% (126/983)	6.2% (563/9086)	6.8% (689/10,069)	<.0001
Current smoker (≤30 d)	24.3% (236/973)	25.3% (2276/9003)	25.2% (2512/9976)	.48
Hypertension	69.5% (683/983)	63.0% (5726/9084)	63.7% (6409/10,067)	<.0001
Hyperlipidemia	65.7% (643/978)	63.2% (5707/9032)	63.4% (6350/10,010)	.11
Prior CABG	13.6% (134/982)	6.4% (580/9086)	7.1% (714/10,068)	<.0001
Prior PCI	23.6% (230/975)	18.1% (1640/9043)	18.7% (1870/10,018)	<.0001
Prior MI	24.9% (240/965)	19.8% (1778/8994)	20.3% (2018/9959)	.0002
Left ventricular ejection fraction, % (n = 1488)	57.8 ± 10.5	59.4 ± 9.7	59.3 ± 9.8	.06
<40%	6.5% (9/138)	4.4% (59/1350)	4.6% (68/1488)	.25
Clinical presentation				
Acute coronary syndromes	43.6% (408/935)	45.8% (3928/8577)	45.6% (4336/9512)	.21
ST-segment elevation myocardial infarction	9.1% (89/983)	12.0% (1090/9089)	11.7% (1179/10,072)	.006
Non-ST-segment elevation myocardial infarction	13.4% (132/983)	13.5% (1225/9089)	13.5% (1357/10,072)	.97
Unstable angina	20.0% (187/935)	18.8% (1613/8577)	18.9% (1800/9512)	.38
Stable coronary artery disease	56.4% (527/935)	54.2% (4649/8577)	54.4% (5176/9512)	.21
Angiographic core laboratory data				
RVD, mm (n = 9186)	2.66 ± 0.53	2.77 ± 0.88	2.76 ± 0.86	.0004
Minimum lumen diameter, mm (n = 7164)	0.71 ± 0.39	0.75 ± 0.43	0.74 ± 0.42	.058
DS, % (n = 9280)	75.8 ± 14.8	76.1 ± 15.9	76.0 ± 15.8	.61
Lesion length, mm (n = 10,797)	18.7 ± 13.3	17.3 ± 11.3	17.4 ± 11.5	.0008
Lesion location				
Left anterior descending	51.0% (501/983)	48.9% (4445/9088)	49.1% (4946/10,071)	.22
Right	38.9% (382/983)	38.8% (3528/9088)	38.8% (3910/10,071)	.98
Left circumflex	34.5% (339/983)	29.6% (2689/9088)	30.1% (3028/10,071)	.001
Left main	1.8% (18/983)	1.1% (101/9088)	1.2% (119/10,071)	.05
Calcification (moderate/severe)	40.8% (401/982)	31.6% (2872/9078)	32.5% (3273/10,060)	<.0001
Tortuosity (moderate/severe)	6.4% (9/141)	8.5% (118/1389)	8.3% (127/1530)	.39
ACC class C	38.3% (376/981)	31.5% (2861/9071)	32.2% (3237/10,052)	<.0001
Procedural and postprocedure data				
Total stent length (per patient)	39.2 ± 28.2	33.2 ± 24.2	33.8 ± 24.7	<.0001
Stent type				
Zotarolimus-eluting stents (Resolute)	8.9% (87/983)	9.0% (819/9089)	9.0% (906/10,072)	.87
Everolimus-eluting stents	74.3% (730/983)	73.1% (6641/9089)	73.2% (7371/10,072)	.42
Biolimus-eluting stents	16.9% (166/983)	17.9% (1629/9089)	17.8% (1795/10,072)	.42
No. of treated lesions	1.4 ± 0.7	1.3 ± 0.5	1.3 ± 0.6	<.0001
TIMI flow III	98.5% (966/981)	99.1% (8990/9074)	99.0% (9956/10,055)	.07
Postprocedure minimum lumen diameter, mm	2.25 ± 0.75	2.39 ± 1.15	2.37 ± 1.12	.0009
Postprocedure DS, %	15.2 ± 12.1	13.4 ± 10.5	13.6 ± 10.7	<.0001

Data shown as mean ± SD or % (n/N). TIMI, Thrombolysis in Myocardial Infarction.

Univariable determinates were determined using the Wald χ^2 test from a univariable Cox regression. The independent predictors of events were determined by multivariable Cox regression, adjusted by study, with the number of variables for each model sparingly chosen according to their historical relationship to each outcome measure in prior studies to avoid overfitting (at least 10 events per variable). Variables entered into the model appear at the multivariable analysis table and are as follows: age, sex, diabetes, hypertension, hyperlipidemia, prior coronary artery bypass grafting (CABG), prior MI, prior PCI, body mass index, clinical presentation-ACS, moderate/severe calcification, American College of Cardiology (ACC) class C lesion, reference vessel diameter (RVD), percent diameter stenosis (DS), and total stent length.

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Results

Study population and procedural data

A total of 10,072 patients (age 63.3 ± 10.7) were included in the pooled analysis, with a median follow-up of 1,095 days (interquartile range 1,080-1,799 days). Clinical, angiographic, and procedural characteristics of the study population are presented in Table II. Lesions were predominantly located in the left anterior descending artery (49.1%), and mean lesion length was 17.4 ± 11.5 mm. Thrombolysis in Myocardial

Table III. Short- and long-term clinical outcomes

	30 d	1 y	5 y
TLF	1.7% (172)	4.3% (432)	11.9% (983)
Major adverse cardiac events	1.8% (180)	4.5% (451)	12.8% (1052)
Death	0.2% (25)	1.4% (141)	7.9% (552)
Cardiac	0.2% (18)	0.9% (86)	3.7% (275)
Noncardiac	0.1% (7)	0.6% (55)	4.3% (277)
MI	1.5% (148)	2.2% (218)	5.0% (414)
Target vessel	1.4% (140)	2.0% (197)	3.9% (334)
Any revascularization	1.0% (87)	5.6% (472)	17.7% (1118)
Ischemia-driven TLR	0.6% (58)	2.1% (212)	6.9% (551)
Ischemia-driven TVR	0.7% (45)	3.2% (315)	10.8% (844)
Stent thrombosis*	0.4% (39)	0.6% (61)	1.7% (123)
Definite	0.3% (33)	0.5% (47)	1.3% (96)
Probable	0.1% (6)	0.1% (14)	0.4% (28)

Data are % (n).

*Academic Research Consortium definition definite or probable.

Infarction flow III was achieved in almost all patients at the end of the procedure (99.0%).

Patient and lesion characteristics according to the occurrence of TLF

Clinical, angiographic, and procedural data according to the occurrence of TLF during a follow-up of up to 5 years are presented in [Table II](#). Patients experiencing TLF were older and more frequently diabetic and hypertensive, with a higher prevalence of previous ischemic heart disease. In the TLF group, RVD was smaller and lesions were longer, resulting in longer total stent length, located more commonly in the circumflex artery. Lesions in the TLF group were also more frequently calcified and classified as type C according to ACC classification. Patients in the TLF group also had a higher number of treated lesions with a lower post-procedure minimum lumen diameter and a higher percent DS.

Clinical outcomes

Clinical outcomes at 30 days, 1 year, and 5 years are presented in [Table III](#); [Figure 1, A](#); and [Figure 1, B](#). The rate of TLF was 1.7%, 4.3%, and 11.9% at 30 days, 1 year, and 5 years, respectively. The rate of death was 1.4% at 1 year, with cardiac death accounting for 0.9%. The rate of death was 7.9% at 5 years, with cardiac death accounting for 3.7%. At 5 years, 1,118 patients (17.7%) underwent repeat revascularization, of which 10.8% was ischemia-driven TVR. Stent thrombosis occurred in 0.6% and 1.7% of patients at 1 and 5 years, respectively.

Predictors of TLF

The only lesion-related predictor of TLF at 30 days was total stent length (hazard ratio [HR] 1.02, 95% CI 1.011-1.024, $P < .0001$) ([Table IV](#)). Moderate/severe calcifica-

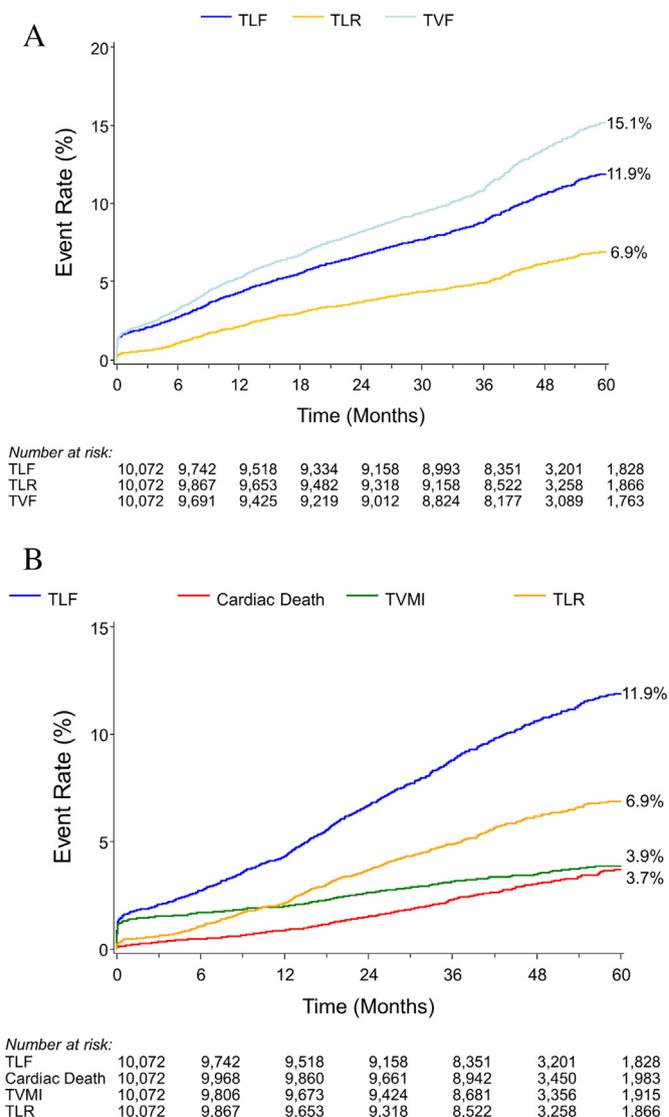
tion, total stent length and post procedural DS predicted TLF between 30 days and 1 year. At both 1 year and 5 years, RVD was identified as a lesion-related predictor. There were no clinical predictors of TLF at 30 days; however, between 30 days and 1 year, diabetes (HR 1.94, 95% CI 1.45-2.61, $P < .0001$) and hypertension (HR 1.59, 95% CI 1.12-2.24, $P = .009$) predicted TLF, and between 1 and 5 years, diabetes (HR 1.40, 95% CI 1.13-1.73, $P = .002$), prior CABG (HR 2.52, 95% CI 1.92-3.30, $P < .0001$), and prior PCI (HR 1.29, CI 1.02-1.64, $P = .04$) predicted TLF.

Discussion

In the present study, pooling data from 6 randomized controlled trials, we aimed to investigate the performance of contemporary DES and to identify lesion-related and clinical predictors of TLF. The main findings of the analysis may be summarized as follows: First, among patients undergoing PCI with implantation of contemporary DES, <5% experience TLF at 1 year, whereas 5-year TLF rates approach 12%. Second, at 30 days, the only lesion-related predictor of TLF was total stent length, whereas both moderate/severe calcification, post procedural DS and total stent length predicted TLF between 30 days to 1 year, and RVD predicted TLF at both 1 year and 5 years. Third, although there were no clinical predictors of TLF at 30 days, diabetes and hypertension were predictors between 30 days and 1 year, and between 1 and 5 years, diabetes, prior CABG, and prior PCI predicted TLF.

The introduction of DESs has significantly improved clinical outcomes of patients undergoing PCI^{1,2,7,15,16}; however, despite the improved performance of modern DESs, stent failure still occurs, leading to adverse cardiac events. Our reported rates of TLF at 1 year are lower than those reported for first-generation DESs^{6,19} and closely resemble those recently reported for contemporary DESs.^{17,20-23} The mechanism by which DESs fail in some patients, and in some segments within the same patient, is unclear and likely multifactorial. Multiple biological, mechanical, and technical causes have been suggested in this regard, such as drug resistance or hypersensitivity to stents components, stent underexpansion or fracture, stent gap, and residual uncovered plaques.^{7,24} In addition, several studies have attempted to identify patient- and lesion-related factors that may predict stent failure. In the BMS era, Singh et al¹¹ identified diabetes mellitus, prior PCI, nonsmoking, small vessel size, long lesions, and ostial lesions as predictors of restenosis among 1,312 patients undergoing angiographic follow-up. Cassese et al⁴ evaluated the incidence and predictors of restenosis among 10,004 patients undergoing implantation of BMS or first-/second-generation DES. In surveillance angiography, binary restenosis was detected in 26.4% of patients. By multivariable analysis, smaller vessel size, total stent length, complex lesion

Figure 1



Clinical outcomes at 5 years. **A**, TLF, TLR, and TVF. **B**, The rate of TLF and its components.

morphology, presence of diabetes mellitus, and history of bypass surgery were independently associated with restenosis and were similar across the spectrum of stent devices. In the Evaluation of Drug Eluting Stents and Ischemic Events (EVENT) registry, which included patients implanted with BMS and DES, identified predictors of DES TLR were age < 60 years, prior PCI, unprotected left main PCI, saphenous vein graft PCI, minimum stent diameter \leq 2.5 mm, and total stent length \geq 40 mm.²⁵ In another study analyzing the incidence of TLR among 2,691 patients with 3,401 lesions undergoing implantation of first-generation DESs, younger age, diabetes mellitus, PCI to vein graft, and prior PCI were found to independently predict TLR.⁸

Our study differs from the above-mentioned studies in several aspects. First, and most importantly, our study includes only patients treated with contemporary DESs, thus representing current clinical practice. Second, to the best of our understanding, this is the largest study to date aiming to identify predictors of stent failure using pooled patient-level data derived exclusively from randomized controlled trials. Third, in contrast to the studies of Singh et al¹¹ and Cassese et al,⁴ the end point of our study is clinical and not angiographic. Finally, as we aimed to identify long- and short-term predictors of TLF, we performed the multivariable analysis for different time points: 0 to 30 days, 30 days to 1 year, and 1 to 5 years. Nevertheless, despite these differences, the predictors

Table IV. Multivariable analysis for independent predictors of TLF

	HR (95% CI)	P value
0-30 d		
Age (per year)	1.012 (0.994-1.031)	.19
Diabetes	0.881 (0.567-1.368)	.57
Male sex	0.698 (0.472-1.031)	.07
Hypertension	0.866 (0.580-1.292)	.48
Hyperlipidemia	1.410 (0.933-2.132)	.10
Prior CABG	0.868 (0.431-1.748)	.69
Prior MI	1.190 (0.758-1.868)	.45
Prior PCI	0.659 (0.380-1.144)	.14
Body mass index (per kg/m ²)	1.012 (0.977-1.049)	.51
Acute coronary syndromes	0.989 (0.677-1.443)	.95
Moderate/severe calcification	0.988 (0.669-1.460)	.95
ACC class C lesion	1.464 (0.963-2.227)	.07
RVD (per mm)	0.796 (0.551-1.149)	.22
DS (postprocedure) (per %)	1.012 (0.997-1.028)	.12
Total stent length (per mm)	1.017 (1.011-1.024)	<.0001
30 d to 1 y		
Age (per year)	0.999 (0.985-1.013)	.87
Diabetes	1.944 (1.446-2.613)	<.0001
Male sex	0.966 (0.707-1.320)	.83
Hypertension	1.585 (1.121-2.242)	.009
Hyperlipidemia	0.882 (0.645-1.208)	.44
Prior CABG	1.449 (0.937-2.239)	.10
Prior MI	1.266 (0.910-1.761)	.16
Prior PCI	1.266 (0.898-1.784)	.18
Body mass index (per kg/m ²)	0.999 (0.972-1.027)	.96
Acute coronary syndromes	1.231 (0.922-1.643)	.16
Moderate/severe calcification	1.379 (1.025-1.854)	.03
ACC class C lesion	0.741 (0.524-1.049)	.09
RVD (per mm)	0.740 (0.558-0.982)	.04
DS (postprocedure) (per %)	1.013 (1.001-1.025)	.03
Total stent length (per mm)	1.010 (1.005-1.016)	.0005
1 to 5 y		
Age (per year)	1.005 (0.995-1.015)	.30
Diabetes	1.397 (1.128-1.730)	.002
Male sex	1.035 (0.835-1.283)	.75
Hypertension	1.094 (0.875-1.367)	.43
Hyperlipidemia	0.849 (0.684-1.054)	.14
Prior CABG	2.516 (1.919-3.300)	<.0001
Prior MI	0.980 (0.771-1.246)	.87
Prior PCI	1.291 (1.016-1.641)	.04
Body mass index (per kg/m ²)	1.012 (0.994-1.031)	.20
Acute coronary syndromes	1.078 (0.881-1.319)	.47
Moderate/severe calcification	1.140 (0.928-1.401)	.21
ACC class C lesion	1.086 (0.863-1.367)	.48
RVD (per mm)	0.745 (0.614-0.904)	.003
DS (postprocedure) (per %)	1.008 (0.999-1.017)	.09
Total stent length (per mm)	1.004 (1.000-1.009)	.07

identified in our study are highly concordant with previous studies. Thus, patient-related factors, such as diabetes mellitus, prior CABG, and prior PCI, represent patient populations with accelerated vascular disease that are prone to more frequent stent failure and repeat revascularization. Lesion-related factors—small RVD, total stent length, moderate/severe calcification, and postprocedural DS—were also previously suggested to predict stent failure. Importantly, during the first month, no patient-related predictors were identified, suggesting

that events occurring in the immediate period following stent implantation may be more related to technical aspects, whereas in the long term, patient-related factors become more pertinent, contributing to the underlying processes of neointimal growth and neoatherosclerosis.

Study limitations

Several limitations should be acknowledged. First, as our primary end point of TLF includes the rates of TV-MI, our finding may be imprecise due to minor interstudy variations in the definition of myocardial infarction. Also, interstudy variations in inclusion/exclusion criteria, duration of follow-up, type of stents used, and other available technologies may have introduced heterogeneity and influenced the outcomes reported in this study. Second, one of the studies included in the analysis (SPIRIT III) had a planned 9-month angiographic follow-up, which may have influenced the clinical outcomes of the trial; however, this study contributed only 7% of our overall study population and likely did not affect our conclusions. Third, we did not have available data regarding compliance with dual antiplatelet therapy or the use of prasugrel and ticagrelor, which are currently widely used following PCI. Fourth, our study population includes only patients enrolled in randomized controlled trials, and therefore, we were unable to examine factors that may play a role in real-world population, such as intervention in specific risk groups such as end-stage renal disease or PCI to vein grafts or to the left main coronary artery. Finally, we did not have angiographic follow-up in most studies; therefore, we were unable to study the predictors of in-stent restenosis.

Conclusions

In this large study evaluating the short- and long-term performance of contemporary DESs, the predictors of TLF vary in the early, late, and very late postprocedural periods. Long-term lesion-related predictor of TLF was RVD, and clinical predictors were diabetes, prior CABG, and prior PCI.

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References

1. Brilakis ES, Lichtenwalter C, Abdel-karim AR, et al. Continued benefit from paclitaxel-eluting compared with bare-metal stent implantation in saphenous vein graft lesions during long-term follow-up of the SOS (Stenting of Saphenous Vein Grafts) trial. *JACC Cardiovasc Interv* 2011;4:176-82.
2. Sabate M, Jimenez-Quevedo P, Angiolillo DJ, et al. Randomized comparison of sirolimus-eluting stent versus standard stent for percutaneous coronary revascularization in diabetic patients:

- the diabetes and sirolimus-eluting stent (DIABETES) trial. *Circulation* 2005;112:2175-83.
3. Schofer J, Schluter M, Gershlick AH, et al. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). *Lancet* 2003;362:1093-9.
 4. Cassese S, Byrne RA, Tada T, et al. Incidence and predictors of restenosis after coronary stenting in 10 004 patients with surveillance angiography. *Heart* 2014;100:153-9.
 5. Kirtane AJ, Leon MB, Ball MW, et al. The "final" 5-year follow-up from the ENDEAVOR IV trial comparing a zotarolimus-eluting stent with a paclitaxel-eluting stent. *JACC Cardiovasc Interv* 2013;6:325-33.
 6. Gada H, Kirtane AJ, Newman W, et al. 5-year results of a randomized comparison of XIENCE V everolimus-eluting and TAXUS paclitaxel-eluting stents: final results from the SPIRIT III trial (clinical evaluation of the XIENCE V everolimus eluting coronary stent system in the treatment of patients with de novo native coronary artery lesions). *JACC Cardiovasc Interv* 2013;6:1263-6.
 7. Garg S, Serruys PW. Coronary stents: current status. *J Am Coll Cardiol* 2010;56:S1-42.
 8. Al Muradi H, Mehra A, Okolo J, et al. Clinical presentation and predictors of target vessel revascularization after drug-eluting stent implantation. *Cardiovasc Revasc Med* 2012;13:311-5.
 9. Kastrati A, Dibra A, Mehilli J, et al. Predictive factors of restenosis after coronary implantation of sirolimus- or paclitaxel-eluting stents. *Circulation* 2006;113:2293-300.
 10. Kedhi E, Genereux P, Palmerini T, et al. Impact of coronary lesion complexity on drug-eluting stent outcomes in patients with and without diabetes mellitus: analysis from 18 pooled randomized trials. *J Am Coll Cardiol* 2014;63:2111-8.
 11. Singh M, Gersh BJ, McClelland RL, et al. Clinical and angiographic predictors of restenosis after percutaneous coronary intervention: insights from the Prevention of Restenosis With Tranilast and Its Outcomes (PRESTO) trial. *Circulation* 2004;109:2727-31.
 12. 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.
 13. Smits PC, Hofma S, Togni M, et al. Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent (COMPARE II): a randomised, controlled, non-inferiority trial. *Lancet* 2013;381:651-60.
 14. Stone GW, Teirstein PS, Meredith IT, et al. A prospective, randomized evaluation of a novel everolimus-eluting coronary stent: the PLATINUM (a Prospective, Randomized, Multicenter Trial to Assess an Everolimus-Eluting Coronary Stent System [PROMUS Element] for the Treatment of Up to Two de Novo Coronary Artery Lesions) trial. *J Am Coll Cardiol* 2011;57:1700-8.
 15. 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.
 16. 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.
 17. von Birgelen C, Sen H, Lam MK, et al. Third-generation zotarolimus-eluting and everolimus-eluting stents in all-comer patients requiring a percutaneous coronary intervention (DUTCH PEERS): a randomised, single-blind, multicentre, non-inferiority trial. *Lancet* 2014;383:413-23.
 18. 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.
 19. Leon MB, Mauri L, Popma JJ, et al. A randomized comparison of the Endeavor zotarolimus-eluting stent versus the TAXUS paclitaxel-eluting stent in de novo native coronary lesions 12-month outcomes from the ENDEAVOR IV trial. *J Am Coll Cardiol* 2010;55:543-54.
 20. Godino C, Pivato CA, Chiarito M, et al. Polymer-free amphimus-eluting stent versus biodegradable polymer biolimus-eluting stent in patients with and without diabetes mellitus. *Int J Cardiol* 2017;245:69-76.
 21. Guan C, Xu B, Qiao S, et al. Comparison of two biodegradable-polymer-based sirolimus-eluting stents with varying elution and absorption kinetics in patients with acute myocardial infarction: A subgroup analysis of the PANDA III trial. *Catheter Cardiovasc Interv* 2017;89:520-7.
 22. Kandzari DE, Smits PC, Love MP, et al. Randomized comparison of ridaforolimus- and zotarolimus-eluting coronary stents in patients with coronary artery disease: primary results from the BIONICS trial (BioNIR Ridaforolimus-Eluting Coronary Stent System in Coronary Stenosis). *Circulation* 2017;136:1304-14.
 23. Xu B, Gao R, Yang Y, et al. Biodegradable polymer-based sirolimus-eluting stents with differing elution and absorption kinetics: the PANDA III trial. *J Am Coll Cardiol* 2016;67:2249-58.
 24. Dangas GD, Claessen BE, Caixeta A, et al. In-stent restenosis in the drug-eluting stent era. *J Am Coll Cardiol* 2010;56:1897-907.
 25. Stolker JM, Kennedy KF, Lindsey JB, et al. Predicting restenosis of drug-eluting stents placed in real-world clinical practice: derivation and validation of a risk model from the EVENT registry. *Circ Cardiovasc Interv* 2010;3:327-34.