

Long-Term Outcomes After Percutaneous Coronary Intervention in Patients With and Without Diabetes Mellitus in Western Denmark

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Patients with diabetes mellitus have worse outcomes after percutaneous coronary intervention than patients without diabetes mellitus. We compared the risk of stent thrombosis, myocardial infarction, death, and target lesion revascularization in diabetic and nondiabetic patients after implantation of drug-eluting stents or bare metal stents. In the Western Denmark Heart Registry, 12,347 consecutive patients (1,575 with and 10,772 without diabetes) were identified and followed up for 2 years. The 2-year risk of definite stent thrombosis was 0.52% in patients with diabetes mellitus and 0.71% in nondiabetic patients (adjusted relative risk [RR] 0.74, 95% confidence interval [CI] 0.41 to 1.34, $p = 0.321$). The 2-year risk of myocardial infarction was greater in the diabetic patients (6.9%) than in the nondiabetic patients (3.6%; adjusted RR 1.96, 95% CI 1.58 to 2.43; $p < 0.001$). The all-cause 2-year mortality rate was almost twice as great for the diabetic patients compared to the nondiabetic patients (12.4% vs 6.7%; adjusted RR 1.91, 95% CI 1.63 to 2.23; $p < 0.001$). The 2-year risk of target lesion revascularization was 8.5% in the diabetic patients and 6.8% in the nondiabetic patients (adjusted RR 1.28, 95% CI 1.10 to 1.49; $p < 0.001$). In conclusion, 2 years after drug-eluting stent or bare metal stent implantation, diabetic patients had a greater risk than nondiabetic patients of myocardial infarction and death. Drug-eluting stent treatment reduced the risk of target lesion revascularization compared to bare metal stent treatment, regardless of diabetes status. © 2010 Elsevier Inc. All rights reserved. (Am J Cardiol 2010;105:1513–1519)

Patients with diabetes mellitus have tended to have worse outcomes after percutaneous coronary intervention (PCI) than nondiabetic patients.¹ Angiographic and intravascular ultrasound studies have suggested increased late lumen loss² and intimal hyperplasia³ as potential mechanisms underlying the greater restenosis risk. A more diffuse and accelerated form of atherosclerosis in diabetic patients, accompanied by small vessel size, long lesions, and greater plaque burden, might contribute to their well-documented increased risk of restenosis after stent implantation.^{4,5} Drug-eluting stents (DESs) have shown promising results in patients with and without diabetes mellitus.^{6–10} Although the initial use of DESs was not associated with safety concerns, recent studies have reported increased risks of stent throm-

bosis, myocardial infarction (MI), and death associated with the use of DESs compared to bare metal stent (BMS) use.¹¹ The present study examined the influence of diabetes mellitus on the long-term outcomes of patients treated with PCI using DESs or BMSs, with a recommended 12-month duration of dual antiplatelet therapy.

Methods

We conducted the present follow-up study using Western Denmark's healthcare databases, covering the region's entire population (approximately 3.0 million inhabitants; 55% of the Danish population). All patients were followed up for 24 months. A detailed description of the databases has been previously reported.⁶ In brief, the Danish National Health Service provides universal tax-supported healthcare, guaranteeing patients free access to general practitioners and hospitals. Our data came from the Danish Civil Registration System, which has kept electronic records on gender, date of birth, residence, date of emigration, and changes in vital status since 1968.¹² The information on vital status is updated daily. The records include a unique 10-digit civil registration number that is assigned at birth and is used in all public registries, allowing accurate record linkage. The National Registry of Causes of Deaths and National Patient Registry¹³ was used to obtain the causes of death and the diagnoses assigned by the treating physician during hospi-

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Table 1
Patient characteristics

Variable	Diabetic Patients			Nondiabetic Patients		
	DES (n = 593)	BMS (n = 982)	p Value	DES (n = 2,906)	BMS (n = 7,866)	p Value
Men	416 (70.2%)	648 (66.0%)	0.087	2,117 (72.8%)	5,727 (72.8%)	0.993
Age (years)			<0.01			<0.001
Median	62.0	66.0		62.0	64.0	
Interquartile range	56.0–70.0	58.0–73.0		54.0–70.0	56.0–73.0	
Family history	234 (45.5%)	331 (40.6%)	0.075	1,167 (46.5%)	2,860 (42.9%)	0.002
Smoker	170 (30.2%)	255 (31.4%)	0.495	1,009 (40.6%)	2,809 (42.3%)	0.155
Hypertension	345 (64.7%)	490 (57.2%)	0.006	1,056 (41.7%)	2,573 (37.6%)	<0.001
Previous coronary bypass	57 (10.6%)	83 (9.6%)	0.510	180 (7.1%)	400 (5.7%)	0.012
Previous percutaneous coronary intervention	69 (13.5%)	101 (12.1%)	0.472	271 (11.2%)	638 (9.5%)	0.021
Previous myocardial infarction	187 (36.7%)	303 (36.2%)	0.863	604 (24.8%)	2,035 (30.3%)	<0.001
Lipid-lowering therapy	364 (67.8%)	473 (55.0%)	<0.001	1,367 (53.7%)	2,849 (41.6%)	<0.001
Procedure time (minutes)	31.0 ± 19.9	28.3 ± 19.4	0.002	29.8 ± 20.2	27.2 ± 19.3	<0.001
Fluoroscopy time (minutes)	11.1 ± 8.5	10.9 ± 9.7	0.070	10.6 ± 8.4	10.1 ± 9.9	<0.001
Contrast (ml)	163.2 ± 106.1	159.3 ± 110.0	0.270	157.2 ± 97.5	155.1 ± 104.0	<0.001
No. of treated lesions	1.6 ± 0.9	1.4 ± 0.7	<0.001	1.4 ± 0.7	1.3 ± 0.6	0.002
Indication for percutaneous coronary intervention			<0.001			<0.001
Stable angina pectoris	314 (53.0%)	385 (39.2%)		1,271 (43.7%)	2,589 (32.9%)	
Non–ST-segment elevation myocardial infarction/unstable angina pectoris	173 (29.2%)	327 (33.3%)		869 (29.9%)	2,383 (30.3%)	
ST-segment elevation myocardial infarction	84 (14.2%)	237 (24.1%)		675 (23.2%)	2,709 (34.4%)	
Other	22 (3.7%)	33 (3.4%)		92 (3.2%)	184 (2.3%)	
Co-morbidity index score			0.190			0.561
0	295 (49.7%)	535 (54.5%)		1,947 (67.0%)	5,234 (66.5%)	
1–2	244 (41.1%)	366 (37.3%)		805 (27.7%)	2,169 (27.6%)	
3+	54 (9.1%)	81 (8.2%)		155 (5.3%)	462 (5.9%)	

Table 2
Procedure characteristics

Variable	Diabetic Patients			Nondiabetic Patients		
	DES	BMS	p Value	DES	BMS	p Value
No. of lesions	978	1,323		4,439	10,396	
Vessel			<0.001			<0.001
Right	173 (29.2%)	327 (33.3%)		1,078 (24.3%)	4,180 (40.2%)	
Left anterior descending	314 (53.0%)	385 (39.2%)		2,359 (53.1%)	3,787 (26.4%)	
Left circumflex	84 (14.2%)	237 (24.1%)		846 (19.1%)	2,346 (22.6%)	
Left main	22 (3.7%)	33 (3.4%)		156 (3.5%)	83 (0.8%)	
Saphenous vein graft	17 (1.3%)	17 (1.7%)	0.463	39 (0.9%)	93 (0.9%)	0.927
Lesion length (mm)	16.0 ± 9.6	13.5 ± 7.4	<0.001	16.0 ± 9.5	13.5 ± 7.2	<0.001
Lesion type			<0.001			<0.001
A	217 (22.2%)	273 (20.6%)		932 (21.0%)	2,281 (21.9%)	
B1	378 (38.7%)	793 (20.6%)		1,789 (40.3%)	6,115 (58.8%)	
B2	79 (8.1%)	155 (11.7%)		437 (9.8%)	1,157 (11.1%)	
C	304 (31.1%)	102 (7.7%)		1,281 (28.9%)	846 (8.1%)	
Restenotic lesion	11 (0.8%)	21 (2.2%)	0.018	107 (1.0%)	108 (2.4%)	<0.001
Stent length (mm)	19.3 ± 8.8	16.6 ± 7.4	<0.001	19.2 ± 8.6	16.9 ± 7.1	<0.001
Stents used (n)	1.2 ± 0.6	1.2 ± 0.5	0.005	1.2 ± 0.6	1.2 ± 0.5	<0.001
Maximum balloon pressure (atm)	16.3 ± 4.1	15.3 ± 3.6	<0.001	15.9 ± 4.1	15.2 ± 3.5	<0.001
Maximum balloon diameter (mm)	3.3 ± 0.5	3.4 ± 0.6	<0.001	3.3 ± 0.5	3.5 ± 0.6	<0.001
Reference segment (mm)	3.2 ± 0.5	3.3 ± 0.6	0.001	3.2 ± 0.5	3.3 ± 0.6	<0.001
Minimum lumen diameter (mm)	0.46 ± 0.44	0.45 ± 0.53	0.02	0.41 ± 0.47	0.43 ± 0.53	0.499
Stenosis (% luminal diameter)	86.0 ± 12.5	87.1 ± 12.4	0.002	87.8 ± 12.4	87.8 ± 12.7	0.124

Data are presented as n (%) or mean ± SD.

talization and coded according to the *International Classification of Diseases*, eighth revision until the end of 1993 and the tenth revision thereafter.¹³

We used the Western Denmark Heart Registry to identify all PCIs recorded from January 1, 2002 to June 30, 2005. The Western Denmark Heart Registry collects detailed pa-

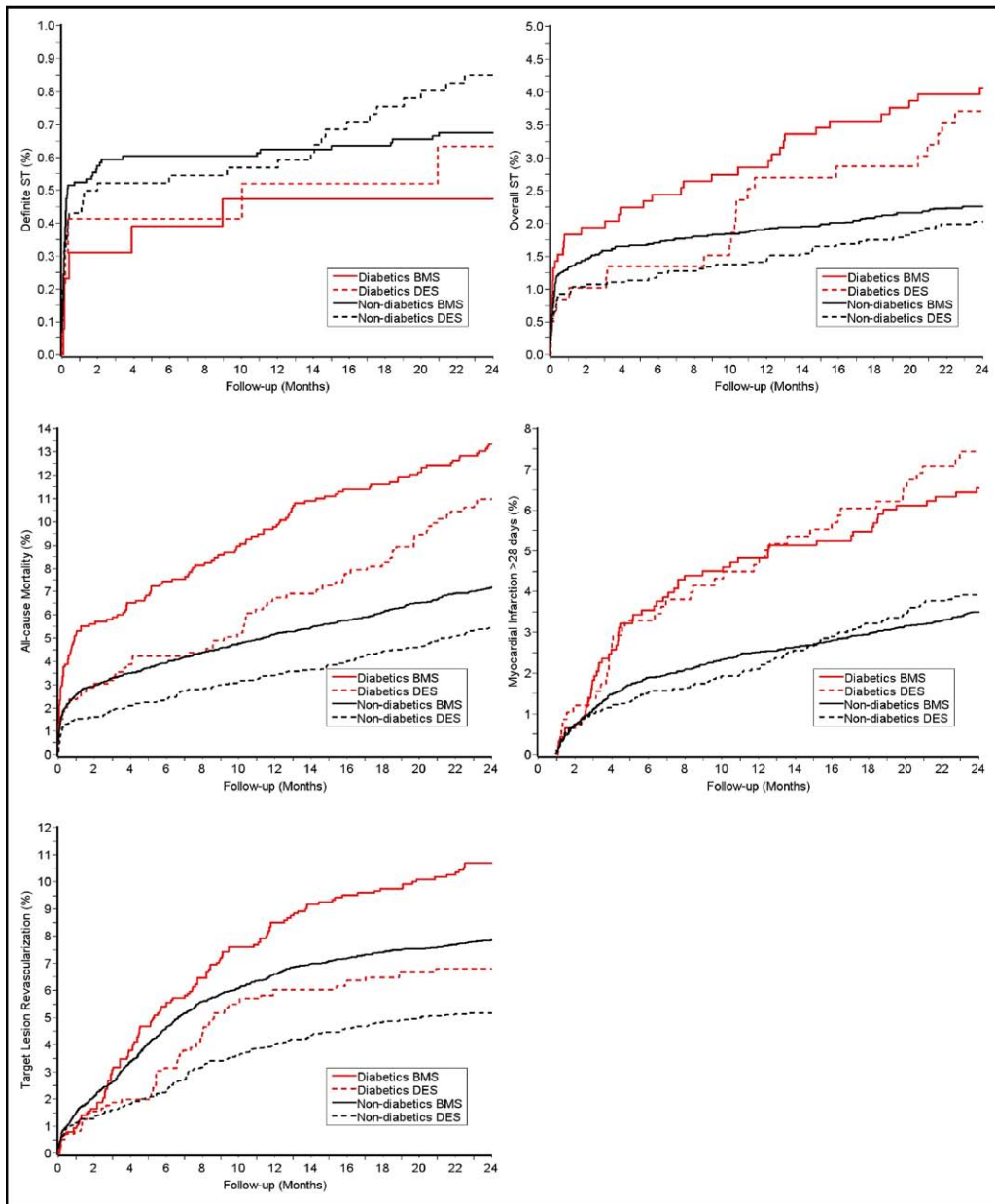


Figure 1. Risk of (A) definite stent thrombosis, (B) overall stent thrombosis (definite, probable or possible stent thrombosis), (C) mortality, (D) MI, and (E) TLR among patients with and without diabetes mellitus treated with DESs or BMSs.

tient and procedure data for all interventions performed in western Denmark's 3 coronary intervention centers (Odense University Hospital, Aarhus University Hospital Skejby, and Aarhus University Hospital Aalborg). For each patient, we included only the first PCI procedure performed during the study period (the index procedure). The DES used was either a Cypher stent or a Taxus Express stent. We excluded patients treated with balloon angioplasty only or a combination of BMSs and DESs ($n = 645$, 4.9%). The post-PCI antiplatelet regimens included lifelong acetylsalicylic acid (75 to 150 mg/day) and clopidogrel (loading dose of 300 mg followed by 75 mg/day). Since November 2002, the recommended duration of clopidogrel treatment has been 12 months for both stent types. Patients were considered to have diabetes if their Western Denmark Heart Registry

records indicated receipt of dietary treatment, oral antidiabetic medication, or insulin.

The study end points were the interval to stent thrombosis (classified as definite, probable, or possible), MI, all-cause mortality, cardiac death, and target lesion revascularization (TLR). The end point events were ascertained from the Western Denmark Heart Registry, the Danish National Patient Registry,¹³ which tracks all hospitalizations in Denmark, and the Danish Registry of Causes of Death.

We defined the types of stent thrombosis according to the Academic Research Consortium definition, with a modification for probable stent thrombosis.¹⁴ Probable stent thrombosis was assumed for any unexplained death within the first 30 days after intracoronary stenting.

Table 3

Relative risk (RR) estimates for death, myocardial infarction (MI), and stent thrombosis (definite, probable, and possible) in patients with (n = 1,575) and without (n = 10,772) diabetes mellitus

Variable	Diabetic Patients		Nondiabetic Patients		Adjusted RR (95% CI) for Diabetes vs No Diabetes	Adjusted RR (95% CI) for DES vs BMS	
	DES	BMS	DES	BMS		Diabetic Patients	Nondiabetic Patients
All-cause death	65 (11.0%)	131 (13.3%)	160 (5.5%)	564 (7.2%)	1.91 (1.63–2.23)	0.80 (0.59–1.08)	0.90 (0.76–1.07)
≤12 months	40 (6.7%)	96 (9.8%)	100 (3.4%)	407 (5.2%)	1.87 (1.55–2.26)	0.67 (0.47–0.98)	0.78 (0.63–0.97)
>12 months	25 (4.5%)	35 (4.0%)	60 (2.1%)	157 (2.1%)	1.98 (1.49–2.63)	1.43 (0.85–2.41)	1.03 (0.76–1.38)
Cardiac death	28 (4.7%)	81 (8.2%)	78 (2.7%)	305 (3.9)	1.99 (1.61–2.46)	0.63 (0.41–0.98)	0.83 (0.64–1.06)
Noncardiac death	30 (5.1%)	44 (4.5%)	66 (2.3%)	217 (2.8)	1.69 (1.31–2.18)	1.09 (0.69–1.74)	0.81 (0.61–1.07)
Myocardial infarction	43 (7.4%)	61 (6.5%)	112 (3.9%)	268 (3.5)	1.96 (1.58–2.43)	1.14 (0.77–1.68)	0.83 (0.64–1.06)
28 days to 12 months	28 (4.8%)	45 (4.8%)	60 (2.1%)	193 (2.5%)	2.01 (1.55–2.61)	0.97 (0.60–1.56)	0.78 (0.63–0.97)
≥12 months	15 (2.8%)	16 (1.9%)	52 (1.9%)	75 (1.0%)	1.85 (1.26–2.73)	1.62 (0.81–3.24)	1.84 (1.29–2.63)
Definite stent thrombosis	6 (0.6%)	6 (0.5%)	37 (0.8%)	69 (0.7%)	0.74 (0.41–1.34)	1.75 (0.55–5.53)	1.25 (0.84–1.86)
Overall stent thrombosis	22 (3.7%)	40 (4.1%)	59 (2.0%)	178 (2.3%)	1.59 (1.20–2.10)	1.01 (0.60–1.71)	0.89 (0.66–1.19)
<30 days	5 (0.8%)	18 (1.5%)	27 (0.9%)	102 (1.3%)	1.02 (0.65–1.59)	0.71 (0.25–2.00)	0.81 (0.53–1.24)
30 days to 24 months	17 (3.0%)	22 (2.4%)	32 (1.1%)	76 (1.1%)	2.56 (1.78–3.69)	1.24 (0.66–2.34)	1.12 (0.74–1.70)
Probable stent thrombosis	1 (0.2%)	15 (1.5%)	10 (0.3%)	51 (0.6%)	2.17 (1.25–3.77)	0.16 (0.02–1.27)	0.75 (0.38–1.48)
Possible stent thrombosis	15 (2.5%)	20 (2.0%)	17 (0.6%)	61 (0.8%)	3.19 (2.14–4.75)	1.20 (0.61–2.35)	0.74 (0.43–1.27)
Target lesion revascularization	64 (6.5%)	132 (10.0%)	224 (5.0%)	789 (7.8%)	1.28 (1.10–1.49)	0.63 (0.47–0.85)	0.65 (0.56–0.75)

Covariates considered in multivariate analyses included age, gender, diabetes mellitus, clinical indication, procedure duration, number of stents, and co-morbidities (and stent length and size of reference vessel in lesion-specific analyses); number of covariates included varied from 0 to 3 between end points because inclusion of covariates determined by change-in-estimate method (see “Methods” section for details).

We defined a new MI as hospitalization for MI occurring >28 days after the index PCI.¹⁵ We ascertained the admissions and readmissions for MI (*International Classification of Diseases*, tenth revision, codes I21 to I21.9) from the National Patient Registry¹³ and deaths from the Civil Registration System.¹² We validated the recorded cause of death using the original death certificates obtained from the National Registry of Causes of Death and classified deaths according to their underlying cause.

From the Western Denmark Heart Registry we ascertained TLR, defined as repeat PCI of the index lesion or coronary artery bypass grafting. For all cases of stent thrombosis, we retrieved the relevant medical records and catheterization films.

From the Western Denmark Heart Registry, we also retrieved data on other potential predictors of subsequent cardiovascular events. For each patient, we also obtained data on all hospital diagnoses from the National Patient Registry and computed the co-morbidity scores using the Charlson Co-morbidity Index,¹⁶ which covers 19 major disease categories, including diabetes mellitus, heart failure, cerebrovascular diseases, and cancer. The index value is a weighted summary of the diagnoses, such that the weight is based on the 1-year mortality associated with each disease in the original Charlson data set.¹⁶ The data for all key patient and procedure characteristics were >95% complete, and the ascertainment of end points (stent thrombosis, death, MI, and TLR) was 100% complete.

The distributions of continuous variables in the 2 groups (with or without diabetes) were compared using either the 2-sample *t* test or the Mann-Whitney *U* test, depending on whether the data followed the normal distribution. We compared the distributions of categorical variables using the chi-square test.

We counted the end point events that occurred during the follow-up period and compared their rates for the 2 cohorts

of patients, with and without diabetes mellitus. Follow-up began on the date of the index PCI procedure. In the analyses with stent thrombosis, MI, or death as the outcome, the follow-up period continued until the date of the respective event, death, emigration, or 24 months after implantation, whichever came first. We constructed Kaplan-Meier curves for patients with and without diabetes, stratified by lesion type treated. We used the life-table method to compute the 2-year risk of each end point (proportion of the population at risk with the outcome of interest). We used Cox proportional hazards regression analysis to estimate the relative risk (RR) for each end point. Because the hazards were not proportional throughout the follow-up period, we estimated the RRs within the periods during which the proportionality assumption held. The RR in these analyses reflected the risk among patients alive and at risk of a specific end point at the start of each period (eg, after 30 days or 1 year of follow-up). In all regression analyses, we included the age, gender, diabetes mellitus status, clinical indication, procedure duration, number of stents, and co-morbidities (and stent length and size of the reference vessel in the lesion-specific analyses). To maximize the precision of the RR estimates, we used the change-in-estimate method, which entailed retaining only those variables that changed the RR estimates for an outcome by >10%. The number of variables included in the final regression models varied from 0 to 3. We used Statistical Analysis Systems software, version 9.2 (SAS Institute, Cary, North Carolina).

Results

We included 12,347 consecutive patients with a total of 17,147 lesions. Of these 12,347 patients, 1,575 (12.8%; total of 2,301 lesions) had diabetes mellitus. The median patient age was 64.3 years (range 56 to 72). The prevalence of patients >75 years old was similar for those with and

without diabetes (18.9% vs 18.6%, $p = 0.756$). The indications for PCI were ST-segment elevation MI (30.0%), non-ST-segment elevation MI/unstable angina (30.4%), stable angina (36.9%), and other (2.7%). The indication for PCI differed between those with and without diabetes. The indication for the diabetic patients was stable angina in 44.3%, non-ST-segment elevation MI in 31.7%, ST-segment elevation MI in 20.4%, and other in 3.4%. The indication for the nondiabetic patients was stable angina in 35.8%, non-ST-segment elevation MI in 30.2%, ST-segment elevation MI in 31.4%, and other in 2.6% ($p < 0.0001$). The baseline patient, procedure, and lesion characteristics differed substantially between those with and without diabetes, and this difference was also seen after stratifying by treatment with DES versus BMS. Patients with diabetes were more likely to have a history of revascularization, smaller vessels (3.2 ± 0.6 vs 3.3 ± 0.6 mm; $p < 0.001$) and a greater rate of DES treatment (42.4% vs 29.9%; $p < 0.001$). They were also slightly older (median age 65.0 years, range 57 to 72 vs 64.0 years, range 56.0 to 72.0; $p = 0.01$) and included more women (32.4% vs 27.2%; $p < 0.01$; Tables 1 and 2).

Comparing the patients with and without diabetes, we found no significant difference in the incidence of definite stent thrombosis, with an occurrence in 12 lesions in 12 diabetic patients (2-year risk 0.52%) and in 106 lesions in 106 patients without diabetes (2-year risk 0.71%, adjusted RR 0.74, 95% CI 0.41 to 1.34). The risk of acute, subacute, and late definite stent thrombosis was also similar between the 2 groups (Figure 1). Very late definite stent thrombosis occurred in 1 lesion in 1 patient with diabetes mellitus (2-year risk 0.04%) and in 17 lesions in 17 patients without diabetes (2-year risk 0.11%). None of the 118 cases of definite stent thrombosis occurred in saphenous vein grafts.

Of the 118 patients who developed definite stent thrombosis, 92 (78%) were receiving dual antiplatelet therapy (aspirin and clopidogrel) at the time of the thrombotic event. Of the 18 patients with very late stent thrombosis, 3 (17%) were receiving dual antiplatelet therapy, 11 (61%) were receiving aspirin only, and 4 (22%) had discontinued both aspirin and clopidogrel.

Definite, probable, or possible stent thrombosis was found in 62 patients with diabetes mellitus (2-year risk 3.9%) and in 237 patients without diabetes mellitus (2-year risk 2.2%, RR 1.83, 95% CI 1.38 to 2.42; Figure 1). Controlling for covariates did not attenuate this estimate (adjusted RR 1.59, 95% CI 1.20 to 2.10; Table 3). Definite, probable, or possible stent thrombosis did not vary according to stent type.

The all-cause 2-year mortality rate was significantly greater in patients with diabetes than in those without diabetes (12.4% vs 6.7%, $p < 0.001$; Figure 1). The difference remained after controlling for covariates (adjusted RR 1.91, 95% CI 1.63 to 2.23). Patients with diabetes were at a greater risk than those without diabetes for both cardiac death (6.7% vs 3.6%, adjusted RR 1.99, 95% CI 1.61 to 2.46; $p < 0.001$) and noncardiac death (4.7% vs 2.6%, adjusted RR 1.69, 95% CI 1.31 to 2.18; $p < 0.001$) during the 2 years of follow-up (Table 3). The risk profiles did not vary according to stent type.

The patients with diabetes more likely than those without diabetes to experience an MI during the follow-up period

(2-year risk 6.9% vs 3.6%, adjusted RR 1.96, 95% CI 1.58 to 2.43, $p < 0.001$; Figure 1 and Table 3). A significant increase in the risk of MI after 12 months of follow-up occurred among DES-treated patients without diabetes (Table 3).

TLR occurred more frequently in the patients with diabetes than those without diabetes (2-year risk 8.5% vs 6.8%, adjusted RR 1.28, 95% CI 1.10 to 1.49, $p < 0.001$; Figure 1). DESs were associated with a decreased risk of TLR compared to BMSs in both diabetic (adjusted RR 0.63, 95% CI 0.47 to 0.85) and nondiabetic (adjusted RR 0.65, 95% CI 0.56 to 0.75) patients.

Discussion

In a "real-world" setting with 2 years of follow-up, we found an increased risk of MI, mortality, and TLR after PCI with DESs or BMSs in patients with and without diabetes. The risk of definite stent thrombosis was low in those with and without diabetes and did not differ significantly between the 2 groups. The risk of definite stent thrombosis after DES versus BMS implantation also did not vary by diabetic status. However, the incidence of very late definite stent thrombosis and MI was significantly greater only in nondiabetic patients treated with DESs, because only 1 diabetic patient developed very late definite stent thrombosis.

Diabetes has been reported to be a predictor of both early and late stent thrombosis in patients treated with DESs.¹⁷ According to data from the Registro Regionale Angioplastiche dell'Emilia-Romagna (REAL Registry),¹⁸ definite stent thrombosis occurred more frequently in diabetic patients treated with DESs than diabetic patients treated with BMSs. The difference was insignificant, however, and was attributable to late and very late stent thrombosis. In contrast, we did not find an increased rate of definite stent thrombosis in diabetic patients compared to nondiabetic patients or an increased risk of stent thrombosis among diabetic patients treated with DESs compared to those treated with BMSs. The patients in our study and in the REAL Registry study differed with respect to the duration of dual antiplatelet therapy. The patients in the REAL registry were given 2 to 6 months of dual antiplatelet therapy. In contrast, in our study, the recommended treatment duration was 12 months. Our estimates differed from other similar studies, such as the e-Cypher¹⁹ or Évaluation coût/efficacité du stent actif au sirolimus chez les patients diabétiques et non diabétiques (EVASTENT).²⁰ For example, in the EVASTENT study,²⁰ a matched multicenter cohort registry, 844 diabetic patients were matched with 887 nondiabetic patients, and both groups underwent revascularization exclusively with sirolimus stents. A total of 45 cases of stent thrombosis were observed during the follow-up period. Of these 45 cases, 30 were definite, 8 were probable, and 7 were possible. At 1 year of follow-up, stent thrombosis had occurred in 3.2% of the diabetic patients and 1.7% of the nondiabetic patients. The greatest rate of stent thrombosis was seen in the diabetic patients with multivessel disease, although on multivariate analysis, diabetes ceased to be a significant predictor of stent thrombosis. Both EVASTENT²⁰ and e-Cypher¹⁹ Registries reported the results for all types of stent thrombosis combined, regardless of the certainty of the event.

Therefore, the extent of the contribution of definite, probable, and possible stent thrombosis in those estimates could not be assessed. The results from the EVASTENT²⁰ Registry regarding all types of stent thrombosis combined are consistent with our findings regarding the increased risk of probable and possible stent thrombosis in diabetic patients. In the EVASTENT²⁰ Registry, 1/4 of the stent thrombosis cases (n = 11) were related to problems with the management of antithrombotic treatment, because 8 of the cases occurred 2 to 10 days after complete withdrawal of dual antiplatelet therapy. Thus, the 12 months of dual antiplatelet treatment might explain the lower rates of definite stent thrombosis observed in our study.

In the diabetic patients, we found an overall increased risk of MI that was not associated with DES use. In contrast, nondiabetic patients treated with DESs had a greater risk of MI than their counterparts treated with BMSs. In studies using the data from the Ontario Registry²¹ and the REAL Registry,¹⁸ the overall rate of MI among diabetic patients did not differ significantly by stent type. In the Ontario Registry study,²¹ patients treated with DESs received a 1-year supply of clopidogrel only if they were >65 years. Despite the longer duration of dual antiplatelet therapy among patients in our study, we found a slightly greater 2-year risk of MI than that reported from the Ontario Registry,²¹ especially among diabetic patients treated with BMSs. Both studies showed a nearly twofold increase in the risk of MI associated with the presence of diabetes. The REAL Registry study did not report the estimates of MI risk.

Our study's results showed that the 2-year all-cause and cardiac mortality was greater among the patients with diabetes than those without this condition, regardless of stent type. Our results agree with those from the Ontario Registry study,²¹ except for their finding, that mortality was significantly lower for nondiabetic patients if they had been treated with DESs instead of BMSs. A meta-analysis by Spaulding et al¹⁷ showed an increased number of cardiovascular and noncardiovascular deaths among diabetic patients treated with sirolimus-eluting stents, with the rates of MI and stent thrombosis similar in the DES and BMS groups. In the randomized Sirolimus-Eluting Stent Compared With Paclitaxel-Eluting Stent For Coronary Revascularization (SIRTAX) trial,²² mortality doubled among diabetic patients after 2 years, in agreement with our results.

Diabetes mellitus is a risk factor for restenosis after PCI, and DES use has been shown to reduce the restenosis rate in these patients.^{7,23-25} However, a meta-analysis of randomized trials²⁶ and a registry study²⁷ have generated evidence that the long-term benefit of DESs in diabetic patients might be limited. Among those with diabetes²⁷ in the Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH)²⁸ and Taxus-Stent Evaluated at Rotterdam Cardiology Hospital (T-SEARCH)²⁹ registries, neither sirolimus-eluting nor paclitaxel-eluting stents appeared superior to BMSs in reducing TLR at 2 years. This contrasts with the findings in our study, in which the effectiveness of DESs was similar in diabetic and nondiabetic patients. The use of DESs was associated with a 47% reduction in clinically driven TLR in diabetic patients and a 43% reduction in TLR in nondiabetic patients after 2 years. Our results are

similar to the DES-associated reduction in revascularization rates among diabetic patients in the recently published Massachusetts Data Analysis Center Registry.³⁰

Our observational study had several limitations. The validity of its findings depends on the data quality and the ability to control for potential confounding. We used the data routinely compiled in computerized registries with complete nationwide coverage, which allowed us to study a well-defined, large population with complete follow-up. However, as with all observational studies, our study was prone to biases from nonrandom assignment of exposure and unmeasured confounding and revascularization treatment strategy was determined by the physician's choice. Finally, we collected data during a 3-year period, during which the prevalence of using DESs increased from 0% to 53%. To reduce bias during this transition period, we followed up every patient for 24 months.

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