JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 4, NO. 9, 2011

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
DOI: 10.1016/j.jcin.2011.03.021

CVN Interview

CLINICAL RESEARCH

Long-Term Outcome of Percutaneous Coronary Intervention for Chronic Total Occlusions

Roxana Mehran, MD,* Bimmer E. Claessen, MD,†§ Cosmo Godino, MD,‡ George D. Dangas, MD, PhD,* Kotaro Obunai, MD,† Sunil Kanwal, MD,† Mauro Carlino, MD,‡ José P. S. Henriques, MD, PhD,§ Carlo Di Mario, MD,‖ Young-Hak Kim, MD,¶ Seung-Jung Park, MD,¶ Gregg W. Stone, MD,† Martin B. Leon, MD,† Jeffrey W. Moses, MD,† Antonio Colombo, MD,‡ on behalf of the Multinational Chronic Total Occlusion Registry

New York, New York; Milan, Italy; Amsterdam, the Netherlands; London, United Kingdom; and Seoul, South Korea

Objectives The aim of this study was to evaluate long-term clinical outcomes after percutaneous coronary intervention (PCI) for chronic total occlusions (CTO).

Background Despite technical advancements, there is a paucity of data on long-term outcomes after PCI of CTO.

Methods We evaluated long-term clinical outcomes in 1,791 patients who underwent PCI of 1,852 CTO at 3 tertiary care centers in the United States, South Korea, and Italy between 1998 and 2007. Median follow-up was 2.9 years (interquartile range: 1.5 to 4.6 years).

Results Procedural success was obtained in 1,226 (68%) patients. Stents were implanted in 1,160 patients (95%); 396 patients (34%) received bare-metal stents (BMS), and 764 patients (66%) received drug-eluting stents (DES). After multivariable analysis, successful CTO PCI was an independent predictor of a lower cardiac mortality (hazard ratio [HR]: 0.40, 95% confidence interval [CI]: 0.21 to 0.75, $p < 0.01$) and reduced need for coronary artery bypass graft surgery (HR: 0.21, 95% CI: 0.13 to 0.40, $p < 0.01$); it also correlated with a strong trend toward lower all-cause mortality (HR: 0.63, 95% CI: 0.40 to 1.00, $p = 0.05$) at 5-year follow-up. Among patients who underwent stent implantation, treatment with DES rather than BMS resulted in less target vessel revascularization at long-term follow-up (17.2% vs. 31.1%, $p < 0.01$); definite/probable stent thrombosis rates were similar (DES 1.7%, BMS 2.3%, $p = 0.58$). Within the DES subgroup, patients treated with paclitaxel-eluting stents and sirolimus-eluting stents had similar clinical outcomes.

Conclusions Successful CTO PCI is associated with reduced long-term cardiac mortality and need for coronary artery bypass graft surgery. Treatment of CTO with DES rather than BMS is associated with a significant reduction in target vessel revascularization with similar rates of stent thrombosis. Paclitaxel-eluting stents and sirolimus-eluting stents had similar long-term safety and efficacy outcomes. (J Am Coll Cardiol Intv 2011;4: 952–61) © 2011 by the American College of Cardiology Foundation

From the *Mount Sinai Medical Center and the Cardiovascular Research Foundation, New York, New York; †Columbia University Medical Center and the Cardiovascular Research Foundation, New York, New York; ‡San Raffaele Scientific Institute, Milan, Italy; §Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands; ‖Royal Brompton Hospital & Imperial College London, London, United Kingdom; and the ¶Asan Medical Center, Seoul, South Korea. Dr. Mehran has received research support from BMS/Sanofi-Aventis; and consulting fees from Abbott Vascular, AstraZeneca, Cerdiva, Cordis, The Medicines Co., and Regado Biosciences. Dr. Dangas is an investigator in a clinical trial sponsored by Medtronic, Boston Scientific, and Abbott; has received speaker honoraria from Cordis; and whose spouse is an advisory board member for Abbott. Dr. Stone is a consultant for Abbott Vascular, Boston Scientific, and Medtronic. Dr. Colombo is a minor shareholder in Cappella Inc. Dr. Leon is on the scientific advisory board for Medtronic, Boston Scientific, and Abbott. Dr. Moses is a consultant for Boston Scientific and Cordis. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Drs. Mehran and Claessen contributed equally to this work.

Manuscript received December 26, 2010; revised manuscript received March 4, 2011, accepted March 16, 2011.

The percutaneous treatment of chronic total occlusions (CTO) is 1 of the major challenges in contemporary interventional cardiology. These complex lesions are identified in 15% to 30% of all patients referred for coronary angiography (1,2). Percutaneous coronary intervention (PCI) of CTOs is technically challenging and requires familiarity with advanced interventional techniques as well as specialty

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equipment. The complexity of percutaneous treatment of CTOs is illustrated by the relatively low procedural success rates (70% to 86%), compared with subtotal stenoses (98%) (3–6). Moreover, even in case of a successful procedure, PCI of a CTO is hampered by high restenosis rates. Nonetheless, successful PCI of a CTO can be associated with symptom relief, lower rate of subsequent myocardial infarction (MI), coronary artery bypass graft (CABG) surgery, and improved long-term survival, compared with unsuccessful PCI (7–11). Most of these studies, however, were not randomized, and many of them were performed with balloon-angioplasty or bare-metal stents (BMS), possibly explaining the relatively high re-occlusion rates.

The introduction of drug-eluting stents (DES) has dramatically reduced restenosis rates after PCI, compared with BMS, and might also have also impacted the percutaneous treatment of CTOs (12). A recent meta-analysis showed DES use in CTO recanalization is associated with lower target vessel revascularization (TVR) (13). However, there was also a statistical trend toward a higher risk of stent thrombosis with DES, compared with BMS. Currently, long-term data on clinical outcomes after CTO recanalization are scarce. Therefore, the aim of the current study was to identify the long-term clinical outcome of patients with successful versus failed CTO recanalization and the long-term safety and efficacy of DES versus BMS in CTOs.

Methods

All patients who underwent PCI for at least 1 CTO at 3 tertiary care hospitals between 1998 and 2007 were included in this study. A CTO was defined as a coronary artery obstruction with a Thrombolysis In Myocardial Infarction (TIMI) flow grade 0. All patients included had a native vessel occlusion estimated to be of at least 3-month duration on the basis of a history of sudden chest pain, a previous MI in the same target vessel territory, or the time between diagnosis made on coronary angiography and PCI. All patients had symptomatic angina and/or a positive functional ischemia study.

The PCI and stent implantation were performed in a standard manner. Heparin was administered to maintain an activated clotting time >250 s. The use of BMS or DES as well as the use of glycoprotein IIb/IIIa inhibitors was left to the discretion of the treating physician. The PCI of the CTO was performed with contemporary techniques such as bilateral injection; specialized hydrophilic, tapered tip, and stiff wires; parallel wires; microcatheters; and retrograde approach when they became available. After PCI, all patients were prescribed lifelong aspirin; in addition clopidogrel was prescribed for at least 3 months after DES implantation in Italy and South Korea and for at least 12 months in the United States and at least 1 month after BMS implantation in all participating sites.

Demographic and procedural data with regard to all patients undergoing PCI at the 3 participating centers were prospectively entered into a dedicated database. Angiographic analyses were performed by online QCA assessment by the operators. Patients were followed prospectively by telephone interview or outpatient visit after 30 days and yearly thereafter. The following endpoints were evaluated to compare patients with a failed versus a successful procedure: all-cause death, cardiac death, MI, and CABG. To compare patients treated with a DES versus BMS the following endpoints were evaluated: the composite clinical endpoint of major adverse cardiac events (MACE) (all-cause death, MI, or TVR), all-cause death, cardiac death, MI, TVR, and definite/probable stent thrombosis according to the Academic Research Consortium definitions (14). The following definitions were used: cardiac death was defined as death within 7 days after MI or stroke, death associated with cardiovascular interventions within 30 days after CABG or within 7 days after PCI, or unexpected death presumed to be due to ischemic cardiovascular disease and occurring within 24 h after the onset of symptoms without clinical or postmortem evidence of another cause. Death from uncertain causes was also classified as cardiac death. In-hospital MI was defined as a rise of creatine phosphokinase or creatine kinase-myocardial band isoenzyme >3× upper limit of normal. Multivessel disease was defined as the presence of at least 1 stenosis ≥70% by visual assessment in another major epicardial vessel or its sidebranches than that where the CTO was located. Procedural success was defined as successful recanalization and dilation of at least 1 CTO/

Abbreviations and Acronyms

BMS = bare-metal stent(s)
CABG = coronary artery bypass graft surgery
CI = confidence interval
CTO = chronic total occlusion
DES = drug-eluting stent(s)
HR = hazard ratio
LAD = left anterior descending coronary artery
LVEF = left ventricular ejection fraction
MACE = major adverse cardiac event(s)
MI = myocardial infarction
PCI = percutaneous coronary intervention
PES = paclitaxel-eluting stent(s)
SES = sirolimus-eluting stent(s)
TIMI = Thrombolysis In Myocardial Infarction
TVR = target vessel revascularization

patient with or without stent implantation, residual stenosis of <50%, and TIMI flow grade ≥2.

Data are presented as the mean ± SD or as percentages. Event rates were estimated with the Kaplan-Meier method. Follow-up was censored at date of last follow-up or at 5 years, whichever came first. Survival curves with all available follow-up data were constructed for time-to-event variables with Kaplan-Meier methodology and compared by log-rank test. Data on patients who were lost to follow-up were censored at the time of the last contact. Cox proportional hazards methods were used to identify the predictors of all-cause mortality, cardiac mortality, MI, and CABG at 5 years among patients with successful versus unsuccessful PCI and TVR at 5 years in patients undergoing successful PCI with BMS versus DES. The multivariable model was built by stepwise variable selection with entry and exit criteria set at the $p = 0.1$ level. The following patient level candidate predictors were evaluated: age (per-year increment), sex, hypercholesterolemia, hypertension, diabetes mellitus, smoking, chronic kidney disease, pre-procedural left ventricular ejection fraction (LVEF) (per-10%), prior MI, multivessel disease, CTO located in the left anterior descending coronary artery (LAD), total CTO length (mm), and total stent length (mm). A smaller number of covariates were evaluated for the low-frequency endpoint of cardiac death (age, LVEF, diabetes mellitus, chronic kidney disease, prior MI, and CTO located in LAD). This selection was made on the basis of the well-known association of these covariates with cardiac mortality. Statistical analyses were performed with SPSS (version 17.0, SPSS, Inc., Chicago, Illinois).

Results

Between 1998 and 2007, a total of 1,852 CTO lesions were attempted in 1,791 patients. Figure 1 shows the patient

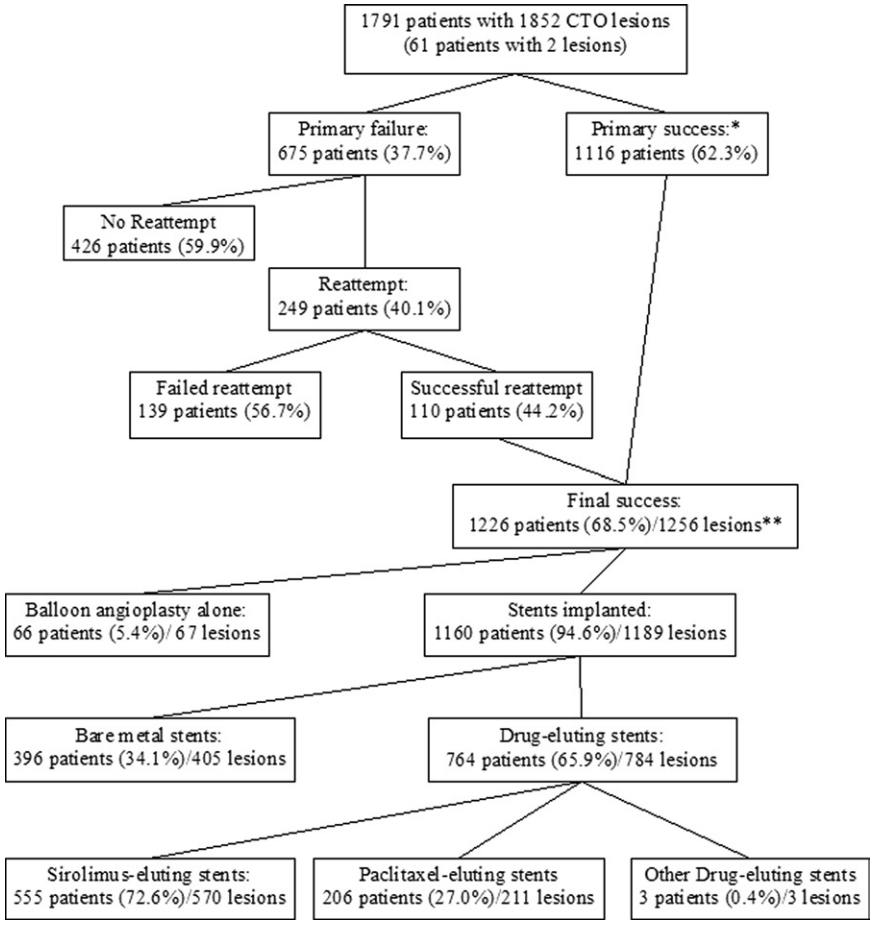

Figure 1. Study Flow Chart

*Procedural success was defined as successful recanalization and dilation of at least 1 chronic total occlusion (CTO)/patient with or without stent implantation, residual stenosis of <50%, and Thrombolysis In Myocardial Infarction flow grade ≥2. **Includes 23 patients with 2 attempted CTOs, of which 1 CTO lesion was successful, and the recanalization of the other failed.

treatment flow. Baseline characteristics of all patients are summarized in Table 1. Procedural success (after reattempts) was obtained in 1,226 patients (68%). Annual success rates ranged from 51.4% to 77.1%, and there was a significant statistical trend indicating success rates increased over time ($p < 0.01$) (Fig. 2). Among the 61 patients with 2 attempted CTO lesions, the procedural outcome was successful PCI of both lesions in 30 patients (49%), successful PCI of only 1 lesion in 23 patients (38%), and failed PCI of both lesions in 8 patients (13%). Success rates after reattempts were 73.0% (276 of 378 patients) in Columbia University Medical Center, 81.3% in Asan Medical Center (217 of 267 patients), and 64.0% in San Raffaele Hospital, Milan (733 of 1,146 patients). Compared with patients who had a successful procedure, patients who had a failed procedure were more often male and smokers, more often had a history of prior MI and prior CABG, less often had hypercholesterolemia, and had a lower pre-procedural LVEF. Furthermore, they more often had multivessel coronary artery disease, longer occlusion lengths, and more often had complicated procedures with coronary dissections and perforations. After successful recanalization, stents were implanted in 1,160 patients (95%). Drug-eluting stents were used in 764 of the 1,160 patients who received a stent (66%).

Table 1. Baseline Demographic, Angiographic, and Procedural Characteristics of Patients Who Underwent Successful and Unsuccessful PCI of a CTO

	Successful PCI (n = 1,226)	Failed PCI (n = 565)	p Value
Baseline characteristics			
Age (yrs)	61.2 ± 10.7	62.1 ± 10.4	0.10
Male	84.8%	89.0%	0.02
Hypertension	60.0%	59.2%	0.79
Smoking	23.0%	28.0%	0.03
Diabetes mellitus	23.1%	21.9%	0.58
Hypercholesterolemia	66.2%	60.7%	0.03
Prior MI	46.7%	56.4%	<0.01
Prior CABG	13.6%	20.9%	<0.01
Ejection fraction (%)	53.8 ± 10.0	52.6 ± 10.7	0.04
CKD	3.1%	4.0%	0.32
Angiographic and procedural characteristics			
Number of CTOs attempted/patient	1.02 ± 0.15	1.05 ± 0.22	<0.01
Number of CTOs revascularized	1,256	0	
CTO located in			0.12
LAD	37.0%	28.4%	
Circumflex	24.0%	23.9%	
RCA	40.9%	48.5%	
Left main	0.4%	0.3%	
Multivessel disease	64.9%	75.3%	<0.01
CTO length (mm)	22.3 ± 15.6	26.3 ± 14.3	<0.01
Number of stents*	1.6 ± 1.0	NA	NA
Stent length (mm)*	40.8 ± 24.9	NA	NA
Stent type*			
BMS	34.1%	NA	NA
SES	47.8%	NA	NA
PES	17.8%	NA	NA
Other DES type	0.3%	NA	NA
Double coronary injection	27.8%	23.9%	0.09
Residual dissection	4.3%	9.4%	<0.01
Coronary perforation during procedure	1.7%	7.4%	<0.01
Total amount of contrast used	433 ± 232	481 ± 222	0.46

Values are mean ± SD or %. *Values apply to 1,160 patients who received stents.

BMS = bare-metal stent(s); CABG = coronary artery bypass surgery; CKD = chronic kidney disease; CTO = chronic total occlusion; DES = drug-eluting stent(s); LAD = left anterior descending coronary artery; MI = myocardial infarction; PCI = percutaneous coronary intervention; PES = paclitaxel-eluting stent(s); RCA = right coronary artery; SES = sirolimus-eluting stent(s).

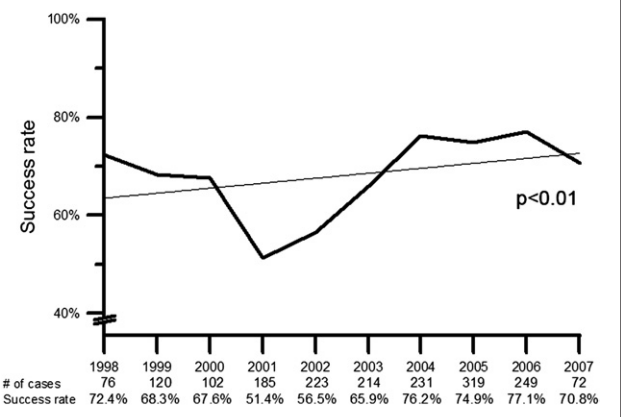

Figure 2. Annual Success Rates of CTO PCI in the Multinational CTO Registry

Success rates after reattempts ranged from 51.4% to 77.1%; there was a significant statistical trend indicating success rates increased over time. CTO = chronic total occlusion; PCI = percutaneous coronary intervention.

Median follow-up in this cohort was 2.9 years (interquartile range: 1.5 to 4.6 years). Kaplan-Meier curves for clinical endpoints at 5 years are shown in Figure 3. Patients with successful CTO PCI had significantly lower rates of all-cause mortality (6.0% vs. 8.6%, $p = 0.01$), cardiac mortality (3.0% vs. 5.8%, $p < 0.01$), and CABG (3.2% vs. 13.3%, $p < 0.01$).

Table 2 shows independent predictors of all-cause mortality, cardiac mortality, MI, and CABG at 5-year follow-up. Successful PCI of a CTO continued to be associated with lower cardiac mortality (hazard ratio [HR]: 0.40, 95% confidence interval [CI]: 0.21 to 0.75, $p < 0.01$) and a reduced need for CABG (HR: 0.21, 95% CI: 0.13 to 0.40, $p < 0.01$). Moreover, we observed a trend toward lower all-cause mortality with successful PCI (HR: 0.63, 95% CI: 0.40 to 1.00, $p = 0.05$).

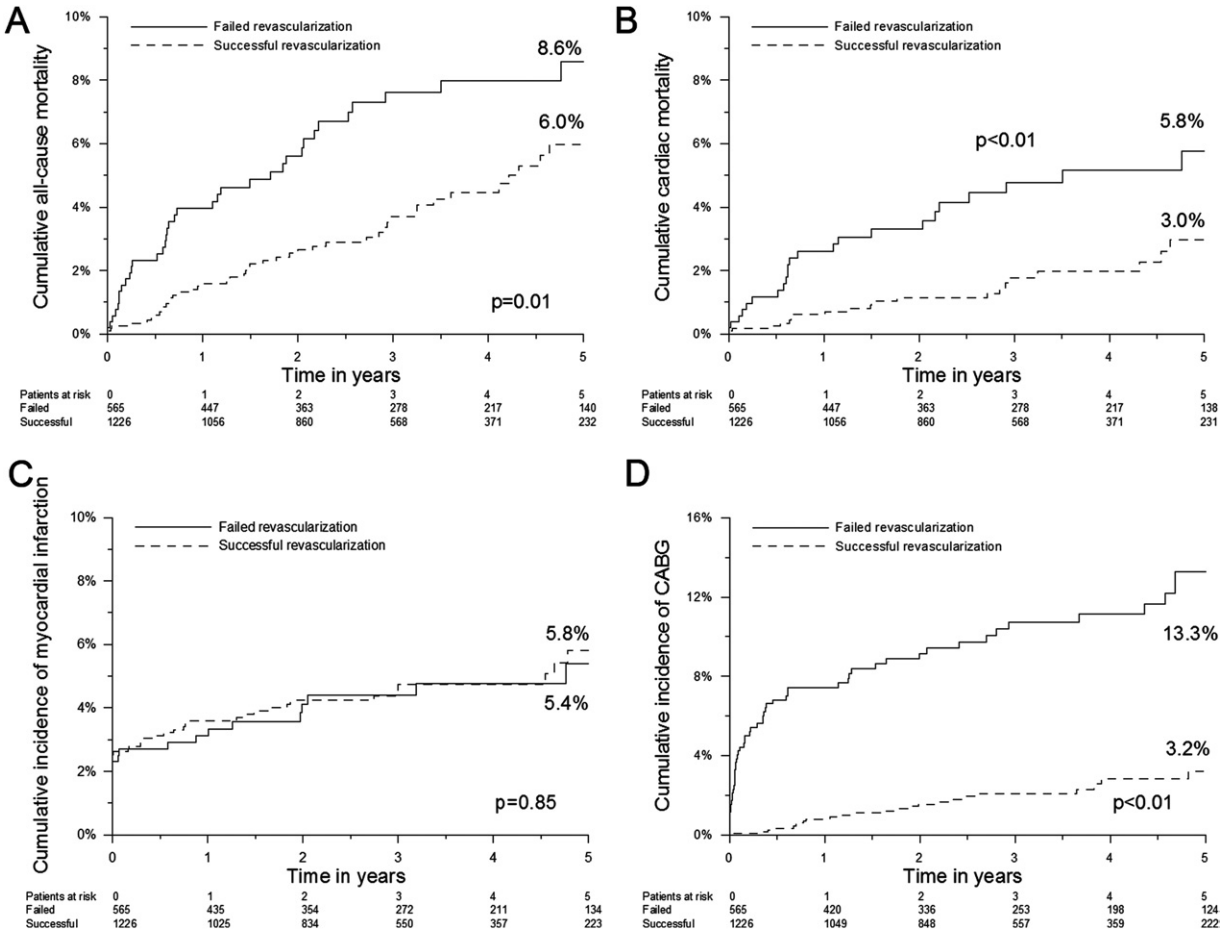

Figure 3. Clinical Event Rates in Patients Who Underwent Successful and Failed PCI of a CTO

Unadjusted Kaplan-Meier rates plotted. CABG = coronary artery bypass graft surgery; other abbreviations as in Figure 2.

We compared, as a secondary analysis, long-term clinical outcomes in patients with failed CTO PCI who subsequently underwent CABG (n = 59, 11.3%) versus those who did not (n = 461, 88.7%). There were no differences in mortality (CABG 6.9% vs. no CABG 8.8%, p = 0.99) or MI (CABG 5.9% vs. no CABG 5.3%, p = 0.78) at long-term follow-up among patients who underwent CABG and those who did not.

DES versus BMS for PCI of a CTO. The temporal relation of stent use was as follows: BMS exclusively 1998 to January 2002 (n = 258), and DES predominantly after they became available (2002 to 2007, n = 764 DES, n = 204 BMS). Baseline characteristics of patients who underwent successful PCI of a CTO and underwent DES or BMS implantation are shown in Table 3. Of 764 patients treated with DES, 555 (72.6%) received Cypher sirolimus-eluting stents (SES) (Cordis, Warren, New Jersey), 206 (27.0%) received Taxus paclitaxel-eluting stents (PES) (Boston Scientific, Natick, Massachusetts), 2 patients received Endeavor zotarolimus-eluting stents (Medtronic, Santa Rosa, California), and 1 patient received a Costar PES (Cordis). When compared with BMS-treated patients, DES-treated patients more often had diabetes mellitus, hypertension, smoking, hypercholesterolemia, and chronic kidney disease and less often had a prior MI.

The median follow-up duration for patients who underwent successful PCI of a CTO was 3.0 years (interquartile range: 2.0 to 4.5 years). Kaplan-Meier curves of 5-year clinical event rates are shown in Figure 4. The long-term MACE rate was significantly lower among patients treated with DES (24.3% vs. 36.9%, p < 0.01), entirely due to a reduced need for TVR (31.1% vs. 17.0%, p < 0.01). The incidence of definite/probable stent thrombosis at 5-year follow-up was similar in both groups (DES 1.8% vs. BMS 2.3%, p = 0.58). Rates of very late (>1 year) definite/probable stent thrombosis were also similar between both groups (DES 1.3% vs. BMS 1.8%, p = 0.75). By multivariable analysis, DES use was the only significant independent

Table 2. Independent Predictors of All-Cause Mortality, Cardiac Mortality, MI, and CABG up to 5-Year Follow-Up in All Patients Who Underwent Attempted PCI of a CTO

	HR	95% CI	p Value
Independent predictors of all-cause mortality			
CKD	2.72	1.37–5.39	<0.01
Diabetes mellitus	2.02	1.25–3.26	<0.01
Age (per-yr increment)	1.09	1.06–1.11	<0.01
Procedural success of CTO	0.63	0.40–1.00	0.05
Independent predictors of cardiac mortality			
CKD	6.34	2.87–14.03	<0.01
Age (per-yr increment)	1.07	1.03–1.10	<0.01
Baseline LVEF (per-10% increment)	0.93	0.91–0.95	<0.01
Procedural success of CTO	0.40	0.21–0.75	<0.01
Independent predictors of MI			
CKD	2.50	1.08–5.75	0.03
Independent predictors of CABG			
CTO located in LAD	1.88	1.16–3.06	0.01
Hypercholesterolemia	0.56	0.35–0.91	0.02
Procedural Success of CTO	0.21	0.13–0.36	<0.01

CI = confidence interval; HR = hazard ratio; LVEF = left ventricular ejection fraction; other abbreviations as in Table 1.

predictor of freedom from TVR up to 5 years (HR: 0.52, 95% CI: 0.39 to 0.70, $p < 0.01$).

PES versus SES. Table 4 shows baseline demographic, angiographic, and procedural characteristics for patients treated with PES (n = 206) or SES (n = 555). Compared with patients treated with SES, patients treated with PES were more likely to have hypertension and a history of a prior MI. Moreover, patients treated with PES had shorter occlusion lengths and a smaller amount of contrast medium usage. Kaplan-Meier estimates of the various long-term clinical event rates were similar for patients treated with PES and SES.

Discussion

The main findings of this analysis in a large prospective multinational CTO registry are: 1) after multivariate analysis, successful CTO PCI was associated with reduced cardiac mortality and a trend toward lower all-cause mortality at long-term follow-up; 2) successful CTO PCI is an independent predictor of a reduced rate of CABG up to long-term follow-up; 3) use of DES compared with BMS is associated with a 48% reduction in the need for TVR at long-term follow-up; 4) rates of overall and very late definite/probable stent thrombosis were similar for patients treated with DES and BMS; and 5) the long-term clinical outcome was similar for patients treated with PES and SES.

Thus far, no randomized controlled trial has been conducted to investigate the effect of CTO recanalization on clinical endpoints. Previous cohort studies have reported inconsistent results with regard to improved survival with successful versus failed CTO PCI (3,9,10,15). A recent meta-analysis on mortality with successful versus failed CTO PCI in 13 nonrandomized cohort studies showed a significant 44% reduction in mortality with successful CTO PCI (11). However, due to the nature of such an analysis of nonrandomized cohort studies, this might at least in part be a result of a less favorable clinical profile of patients with failed PCI rather than the beneficial effect of recanalizing a CTO. The results from the present study reinforce this hypothesis, because unadjusted 5-year Kaplan-Meier estimates of mortality were significantly lower in successful PCI, whereas only a strong trend toward lower mortality remained after multivariate adjustment. The large Open Artery Trial randomized recent rather than "chronic" occlusions and reported no benefit after PCI of occluded infarct-related arteries (16). By contrast, CTO revascularization has been shown to improve left ventricular function and reduce predisposition to ventricular arrhythmias (17–19). More-

Table 3. Baseline Demographic, Angiographic, and Procedural Characteristics of Patients With Successful PCI of a CTO Treated With BMS and DES

	BMS (n = 396)	DES (n = 764)	p Value
Baseline characteristics			
Age (yrs)	61.8 ± 11.1	61.0 ± 10.7	0.38
Male	87.6%	83.8%	0.08
Hypertension	52.3%	64.9%	<0.01
Smoking	11.9%	37.9%	<0.01
Diabetes mellitus	15.9%	27.7%	<0.01
Hypercholesterolemia	53.8%	76.2%	<0.01
Prior MI	64.4%	36.0%	<0.01
Prior CABG	14.4%	12.8%	0.46
Ejection fraction	53.8 ± 10.5	53.9 ± 9.7	0.86
CKD	1.3%	4.2%	0.01
Angiographic and procedural characteristics			
Number of revascularized CTOs	1.02 ± 0.15	1.03 ± 0.16	0.48
CTO located in			0.33
LAD	34.8%	38.2%	
Circumflex	27.0%	21.7%	
RCA	39.6%	42.1%	
Left main	0.5%	0.4%	
Multivessel disease	73.2%	59.4%	<0.01
CTO length (mm)	17.1 ± 10.4	23.5 ± 16.4	<0.01
Number of stents	1.3 ± 0.9	1.8 ± 0.9	<0.01
Stent length (mm)	27.4 ± 19.7	48.4 ± 24.4	<0.01
Double coronary injection	17.0%	34.8%	<0.01
Residual dissection	4.0%	4.1%	0.97
Coronary perforation during procedure	0.5%	2.4%	0.02
Total amount of contrast used	383 ± 113	480 ± 220	0.12

Values are mean ± SD or %.
Abbreviations as in Table 1.

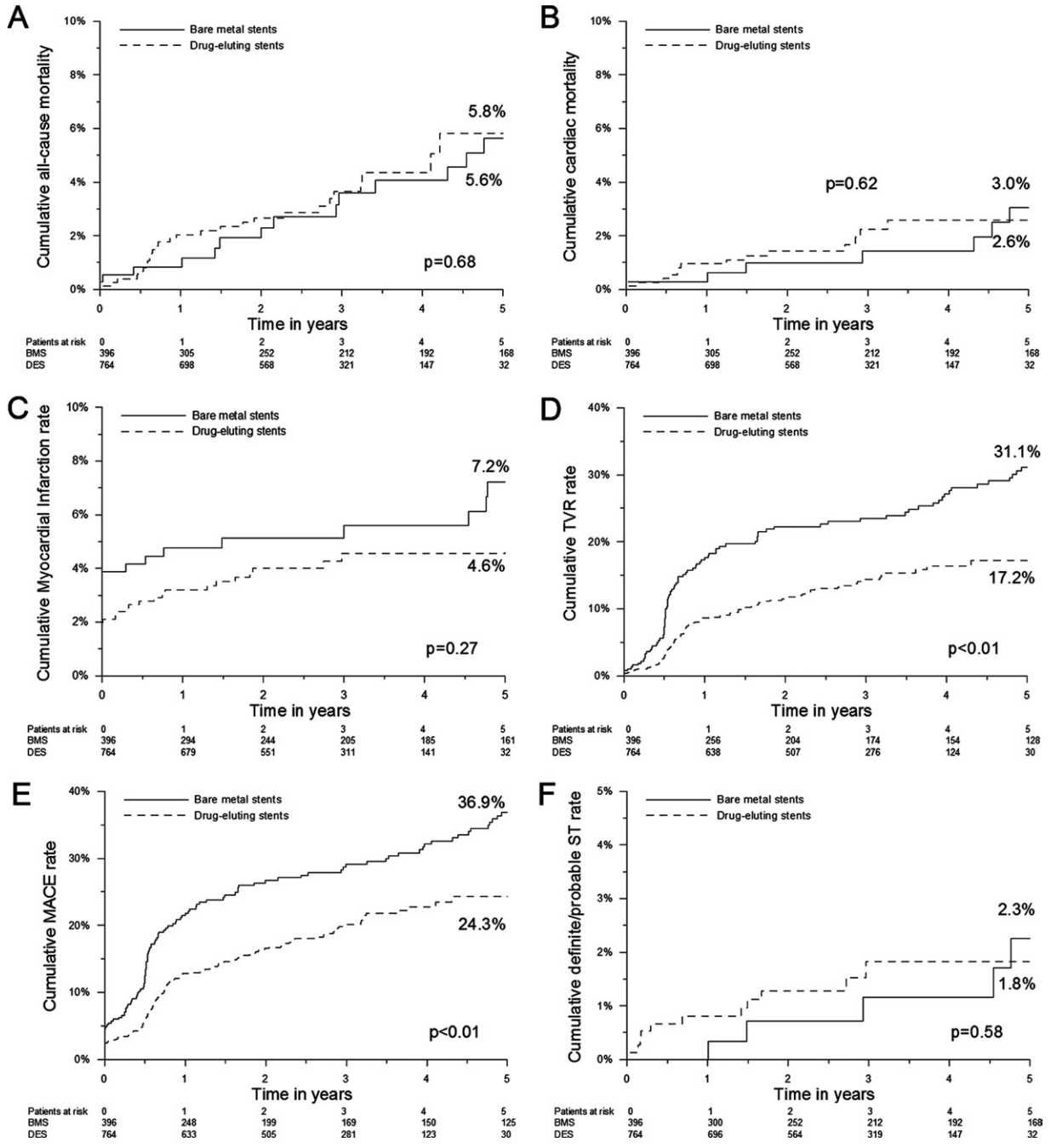

Figure 4. Clinical Event Rates in Patients Who Underwent Successful PCI and Were Treated With BMS and DES

Unadjusted Kaplan-Meier rates plotted. BMS = bare-metal stent(s); DES = drug-eluting stent(s); PCI = percutaneous coronary intervention; MACE = major adverse cardiac events; TVR = target vessel revascularization; ST = stent thrombosis.

over, this is consistent with our finding of reduced cardiac mortality after successful CTO procedures.

It is possible that a survival benefit after successful recanalization of a CTO might be limited to certain subgroups. Safley et al. (20) reported a significant benefit in survival after successful PCI of a CTO located in the LAD but not after successful PCI of a CTO located in the circumflex or right coronary arteries. Moreover, the presence of a CTO in a noninfarct-related artery was recently identified as an independent predictor of mortality after ST-segment elevation MI, and a multicenter randomized trial is currently ongoing to investigate a clinical benefit of

Table 4. Baseline Demographic, Angiographic, and Procedural Characteristics of Patients With Successful PCI of a CTO Treated With PES or SES

	PES (n = 206)	SES (n = 555)	p Value
Baseline characteristics			
Age (yrs)	61.3 ± 10.6	60.9 ± 10.7	0.98
Male	80.6%	84.9%	0.16
Hypertension	71.4%	62.4%	0.03
Smoking	35.0%	39.0%	0.32
Diabetes mellitus	31.0%	26.4%	0.21
Hypercholesterolemia	74.5%	76.4%	0.59
Prior MI	43.6%	33.1%	0.01
Prior CABG	14.1%	12.4%	0.53
Ejection fraction (%)	53.2 ± 9.1	54.1 ± 10.0	0.47
CKD	4.5%	4.2%	0.85
Angiographic and procedural characteristics			
Number of revascularized CTOs	1.02 ± 0.15	1.03 ± 0.16	0.67
CTO located in			0.21
LAD	33.0%	40.2%	
Circumflex	21.4%	21.8%	
RCA	48.1%	40.0%	
Left main	0%	0.5%	
Multivessel disease	62.8%	57.8%	0.25
CTO length (mm)	20.4 ± 13.3	24.4 ± 17.0	0.01
Number of stents	1.8 ± 1.0	1.9 ± 0.9	0.79
Stent length (mm)	45.6 ± 23.6	49.6 ± 24.6	0.31
Double coronary injection	32.4%	35.8%	0.38
Residual dissection	5.9%	3.4%	0.13
Coronary perforation during procedure	3.4%	2.0%	0.25
Total amount of contrast used (ml)	455 ± 197	486 ± 227	0.03
Kaplan-Meier estimates of 5-yr clinical outcomes			
Major adverse cardiovascular events	22.5%	24.4%	0.73
Death	2.1%	6.9%	0.21
MI	6.5%	3.9%	0.49
Target vessel revascularization	16.2%	17.2%	0.77
Definite/probable stent thrombosis	1.2%	2.1%	0.19

Values are mean ± SD or %.
Abbreviations as in Table 1.

opening a CTO within 1 week after an acute ST-segment elevation MI (21,22).

Successful CTO PCI in the current study was associated with a reduced need for subsequent CABG (11), consistent with previous publications. This reduction in subsequent CABG can, for the greatest part, be explained by the fact that patients with failed percutaneous revascularization are more likely to be referred for surgical revascularization than to be treated medically. This validates the clinical need for having appropriately attempted the CTO PCI procedure.

Clinical outcome with BMS versus DES for CTOs. The current article is the first to report on long-term 5-year safety and efficacy outcomes of DES for the treatment of CTOs. At long-term follow-up, the use of DES compared with BMS was associated with significantly reduced rates of MACE, entirely due to lower rates of TVR. A meta-analysis of 14 nonrandomized studies comparing BMS and DES in CTOs reported a significant 60% reduction in TVR, in accordance with this study, but there was a strong trend toward higher rates of stent thrombosis up to 3-year follow-up after DES, not observed in this study (13). A recent study by Han et al. (23) reported a comparable 5-year TVR rate of 18.4% with DES (SES and PES) for the treatment of CTOs. However, these investigators did not report stent thrombosis rates. The 5-year incidence of definite/probable stent thrombosis in the present study was comparable between DES and BMS. A differential use of dual antiplatelet therapy (longer after DES) as well as a different sensitivity to detect late stent thrombosis (lower in BMS era) might have affected our results in both directions.

Clinical outcome with SES versus PES in CTOs. Only 2 previous small-sized cohort studies compared the use of SES versus PES for the treatment of CTO (24). At a mean follow-up of 2 years, Lee et al. (24) reported significantly reduced rates of TVR (SES 9.7% vs. PES 23.9%, p = 0.01) and MI (SES 3.1% vs. PES 7.6%, p = 0.04) with SES in a cohort of 200 patients. The other study, which compared 76 patients treated with SES and 57 patients with PES, showed no differences in TVR at 400-day follow-up between SES and PES (2.6% and 3.6%, respectively) (25). Likewise, in the present report, we observed no significant differences in clinical TVR and MI with PES or SES in a significantly larger cohort (n = 761). Our result might differ from those by Lee et al. (24) at least in part, due to the lack of routine angiographic follow-up in the current study compared with a 58% routine angiographic follow-up in the study by Lee et al. (24). The PES are known to cause higher late loss in a more diffuse pattern and therefore might be more susceptible to the "oculostenotic reflex" than SES. At the same time, the PES group in our study had shorter lesions at baseline, which should have theoretically predisposed to a lower restenosis risk.

Data on the use of PES versus BMS in CTO are scarce but consistent; Werner et al. (26) reported significantly reduced 1-year MACE rates in a cohort of 48 PES-treated CTO patients and 48 matched BMS-treated CTO patients (PES 12.5% vs. BMS 47.9%). More data are available on the use of SES in CTOs; 2 randomized trials showed reduced rates of TVR with SES compared with BMS up to 2-year and 3-year follow-up, respectively (27,28). Stent thrombosis rates with SES in these studies were 1.4% and 5%, respectively. In light of the wide range of stent thrombosis rates reported in randomized clinical trials and the scarcity of long-term data on the use of PES and SES in CTOs, our data show that the use of PES and SES result in similar clinical outcome and have similar, acceptable rates of stent thrombosis at long-term follow-up.

Study limitations. This study was not a randomized study but a registry with prospectively collected data from 3 tertiary referral centers around the world. We had no information on earlier CTO attempts in other hospitals. Moreover, no information on fluoroscopy time was available in our database. Detailed information on peri- and post-procedural medical therapy was not available; therefore we were not able to assess adherence to guideline-based post-PCI therapies. Although we used multivariate Cox regression analysis including a large number of covariates to adjust for differences in baseline characteristics, it is still possible that we did not include potentially unknown confounding variables in the multivariate model. This is a particularly important limitation for the DES versus BMS analysis, because the choice to implant a BMS in the DES era is often because of a contra-indication to prolonged dual antiplatelet therapy or significant comorbidity. Nonetheless, the acceptable stent thrombosis rates in both DES and BMS in this very large cohort of patients with CTO PCI indicate the long-term safety of DES in these complex lesions, often requiring multiple long stents. Finally, the safety and efficacy of next-generation DES might differ from that of the first-generation SES and PES, which were predominantly used in this multinational registry.

Conclusions

Successful CTO PCI is associated with reduced long-term cardiac mortality and reduced need for CABG. Treatment of CTO with DES rather than BMS is associated with a significant reduction in TVR with similar rates of stent thrombosis. The PES and SES had similar long-term safety and efficacy outcomes.

Reprint requests and correspondence: Dr. Roxana Mehran, Mount Sinai Medical Center, Cardiovascular Institute, One Gustave L. Levy Place, Box 1030, New York, New York 10029. E-mail: rmehran@crf.org.

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Key Words: chronic total occlusions ■ drug-eluting stents ■ long-term outcomes ■ percutaneous coronary intervention.