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Comparative Effectiveness of Drug-Eluting Versus Bare-Metal Stents in Elderly Patients Undergoing Revascularization of Chronic Total Coronary Occlusions

Results From the National Cardiovascular Data Registry, 2005–2008

Manesh R. Patel, MD,* Steven P. Marso, MD,† David Dai, PHD, MS,* Kevin J. Anstrom, PHD,* Kendrick A. Shunk, MD, PHD,‡ Jeptha P. Curtus, MD,§ J. Matthew Brennan, MD, MPH,* Art Sedrakyan, MD, PHD,‖ John C. Messenger, MD,¶ Pamela S. Douglas, MD*

Durham, North Carolina; Kansas City, Missouri; San Francisco, California; New Haven, Connecticut; New York, New York; and Aurora, Colorado

Objectives This study sought to investigate the long-term effectiveness of drug-eluting stents (DES) versus bare-metal stents (BMS).

Background Improved recanalization techniques have increased interest in percutaneous coronary intervention (PCI) for chronic total coronary occlusion (CTO). The long-term effectiveness of DES and BMS is not known.

Methods We used data from 10,261 stable patients age ≥65 years at 889 U.S. hospitals who underwent CTO PCI from January 1, 2005, to December 31, 2008, in the NCDR (National Cardiovascular Data Registry) CathPCI Registry with linked Medicare inpatient claims for follow-up. Patient and procedural characteristics, and 30-month death, myocardial infarction, revascularization, and hospitalization for bleeding were evaluated by stent type. Outcomes following stenting were adjusted and compared using propensity score matching.

Results DES were used for CTO PCI in 8,218 (80%) and BMS in 2,043 (20%). DES patients were younger (74.0 vs. 75.5 years, $p < 0.001$), had longer lesions (18.8 vs. 16.5 mm, $p < 0.001$), received more stents (≥2 stents in 45.7% vs. 37.9%, $p < 0.001$), and underwent multivessel PCI (18.9% vs. 15.1%, $p < 0.001$). DES implantation was associated with a lower hazard of mortality (hazard ratio [HR]: = 0.72, 95% confidence interval [CI]: 0.60 to 0.86, $p < 0.001$), a similar hazard for myocardial infarction (HR: 0.85, 95% CI: 0.61 to 1.19, $p = 0.35$), and subsequent revascularization (HR: 0.94, 95% CI: 0.79 to 1.12, $p = 0.48$), including PCI (HR: 0.98, 95% CI: 0.83 to 1.19, $p = 0.87$) and coronary artery bypass grafting (HR: 0.71, 95% CI: 0.46 to 1.10, $p = 0.12$). Hospitalization for bleeding was also similar for DES versus BMS (HR: 0.92; 95% CI: 0.61 to 1.39, $p = 0.70$).

Conclusions Compared with BMS, DES use in stable patients undergoing CTO PCI was associated with lower mortality, as well as similar myocardial infarction and repeat revascularization rates without an increase in subsequent bleeding requiring hospitalization. (J Am Coll Cardiol Intv 2012;5:1054–61)

From the *Department of Medicine, Division of Cardiology, Duke Clinical Research Institute, Duke University Medical Center, Durham, North Carolina; †Department of Medicine, Division of Cardiology, Saint Luke's Mid America Heart Institute, Kansas City, Missouri; ‡Veterans Affairs Medical Center and Department of Medicine, Division of Cardiology, University of California-San Francisco, San Francisco, California; §Department of Medicine, Division of Cardiology, Yale University, New Haven, Connecticut; ‖Department of Medicine, Division of Cardiology, Weill Cornell Medical College, New York, New York; and the ¶Division of Cardiology, Department of Medicine, University of Colorado School of Medicine, Aurora, Colorado. This project was sponsored by the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services, Rockville, Maryland, as part of the Cardiovascular Consortium and funded under Project ID 24-EHC-1 and Work Assignment

The benefit of percutaneous revascularization in patients with chronic total coronary occlusions (CTO) depends on both successful recanalization of the vessel and durable long-term patency. These challenges are evident as the presence of a total coronary occlusion increases the complexity score for percutaneous revascularization (1), and presence of a total coronary occlusion remains 1 of the strongest predictors of a referral for coronary bypass surgery. The complexity of this decision is further amplified in elderly patients in whom the risks of revascularization (with either percutaneous coronary intervention [PCI] or bypass surgery) are increased.

Recent advances in percutaneous techniques for recanalization (2) have increased focus on stent choice and the challenge of maintaining patency. Although drug-eluting stents (DES) were approved based on reduced rates of restenosis compared with bare-metal stents (BMS) (3–5), patients with CTO were excluded from these trials. To date, 1 small prospective randomized trial (n = 200) has examined the use of DES compared with BMS in CTO (6). Given the risks of revascularization in the elderly (represented in practice as patients of Medicare age or older) and the greater complexity of CTO, the comparative safety and real-world outcomes of DES and BMS in patients undergoing percutaneous recanalization of total occlusions are needed to inform clinical practice.

We used data from the NCDR (National Cardiovascular Data Registry) CathPCI Registry linked to Centers for Medicare and Medicaid Services's national inpatient claims databases to: 1) examine the clinical and procedural characteristics of elderly patients undergoing recanalization for CTO with DES and BMS; and 2) compare the outcomes of DES versus BMS implantation for CTO after adjusting for differences in baseline demographics and clinical characteristics. Specifically, the short- and long-term rates of death, myocardial infarction (MI), repeat revascularization, and bleeding requiring hospitalization were evaluated.

Methods

Data source. The study cohort was obtained from the CathPCI Registry, a national invasive catheterization registry cosponsored by the American College of Cardiology and the Society for Coronary Angiography and Interventions (7–9). Data on patient and hospital characteristics, clinical presentation, treatments, and in-hospital outcomes for PCI procedures from over 1,000 sites across the United States are entered by sites into NCDR-certified software and exported in a standard format. There is a data quality program that includes both data quality report specifications for data capture and transmission and an auditing program. The prospectively defined variables are available on the NCDR's website (10).

Study population. This study included all Medicare-linked patients ≥65 years of age undergoing PCI who were enrolled in the CathPCI Registry from January 1, 2005, to December 31, 2008, using the version 3 data collection form (11,12). To define a cohort that closely resembles an acceptable clinical working definition of CTO, patients were excluded who had acute coronary syndromes emergent or urgent indications for cardiac catheterization or cardiogenic shock. In addition, subjects were excluded who had congenital heart disease, in-stent PCI, prior coronary artery bypass graft (CABG), or cardiac transplant. Finally, only patients undergoing PCI for native vessel CTO (defined as 100% stenosis in a major epicardial coronary artery) were included in the analysis (Online Fig. 1).

The PCI procedure codes (00.66, 36.0x, 37.22, 37.23, and 88.5x, except 88.59) from the International classification of Diseases-Ninth Revision-Clinical Modification (ICD-9-CM) were used to identify index procedures in the Medicare files that were then linked to NCDR records using indirect identifiers (nonunique fields that when used in combination may identify unique hospitalizations), as previously described (12). Patients receiving >1 stent type (i.e., both BMS and DES) were excluded from the analysis. The Duke University Medical Center Institutional Review Board granted a waiver of informed consent and authorization for this study.

Abbreviations and Acronyms

BMS = bare-metal stent(s)
CABG = coronary artery bypass graft
CI = confidence interval
CTO = chronic total coronary occlusion(s)
DES = drug-eluting stent(s)
HR = hazard ratio
ICD-9-CM = International classification of Diseases-Ninth Revision-Clinical Modification
IPW = inverse probability weighted
MI = myocardial infarction
PCI = percutaneous coronary intervention

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Clinical endpoints. For this study, 4 primary clinical endpoints were evaluated: death, MI, repeat revascularization procedures (including both PCI and CABG after the index hospital stay), and bleeding requiring hospitalization (13). Death was defined both during the index PCI procedure (using CathPCI Registry information) and after discharge (using the Medicare denominator file). Other clinical endpoints were defined after discharge with the Medicare claims file using the primary diagnosis for the hospital admission. The ICD-9-CM diagnosis codes used to identify events were MI (410.X1), major bleeding (430 to 432 [intracerebral], 578.X [gastrointestinal tract], 719.1X [hemarthrosis], 423.0 [hemopericardium], 599.7 [hematuria], 626.2, 626.6, 626.8, 627.0, 627.1 [vaginal], 786.3 [hemoptysis], 784.7 [epistaxis], or 459.0 [hemorrhage not otherwise specified]), and revascularization (ICD-9-CM procedure codes for PCI: 36.00, 36.06, 36.07, 36.09, and CABG: 36.10-19).

Statistical analysis. Baseline characteristics for the CTO population and propensity score-matched cohorts were categorized by stent type (DES vs. BMS) and summarized as counts and percentages for categorical variables and mean ± SD for continuous variables. Differences between groups were compared using chi-square tests for categorical variables and the Wilcoxon rank sum or Kruskal-Wallis test for continuous variables. To examine the amount of bias reduction from the propensity score matching, standardized differences from the overall cohort and the propensity score cohort were plotted for all variables in the propensity score model. Statistical significance was defined as $p < 0.05$, with no correction for multiple comparisons. SAS statistical software (version 9.2, SAS Institute, Cary, North Carolina) was used for all calculations.

Unadjusted estimates of the event rates for clinical endpoints at 1, 12, and 30 months following intervention were based on weights that were functions of Kaplan-Meier censoring estimates (14). The cumulative incidence rates for time-to-event clinical outcomes were estimated by using the Gray method (15). Unadjusted estimates of hazard ratios (HR) comparing DES with BMS were calculated using a Cox model with type of stent as the only covariates.

For adjusted analyses, the propensity score model was created among CTO patients for comparing DES with BMS (16). Propensity scores represent the estimated probabilities of patients receiving 1 device type versus another, in this case conditioned on 77 observed covariates (Online Appendix). The propensity score logistic regression models had C indexes of 0.727. The Greedy 5 → 1 Digit Matching Algorithm was employed to match each pair of device types based on the propensity scores (17). After matching, the distribution of estimated propensity scores for patients with DES closely matched those for patients with BMS, as evidenced by the 5-number summaries (minimum; 25th, 50th, and 75th percentiles; maximum) describing the curves for patients receiving each type of device: DES (29.6%, 62.5%, 72.6%, 82.8%, 97.7%); BMS (27.8%, 62.5%, 72.6%, 82.8%, 97.7%). Adjusted HR comparing each pair of device types for the propensity score-matched cohort were calculated using a Cox proportional hazards model with an indicator variable for DES. An inverse probability weighted (IPW) method was also used as secondary approach to calculate adjusted HR (18).

Results

Study population. From January 1, 2005, to December 31, 2008, 158,422 patients ≥65 years of age underwent elective PCI with stent implantation and 92,069 (58.2%) were linked to Medicare longitudinal records. Of these 92,069 patients, 10,766 (11.7%) met the specified clinical working definition of a CTO. After excluding 505 patients who had both DES and BMS used for PCI, 10,261 patients undergoing elective PCI for CTO formed the analysis cohort. The PCI success rates were 97.05% in the Centers for Medicare and Medicaid Services–matched population and 97.36 in the population that did not match to the Centers for Medicare and Medicaid Services. Compared with the population eligible for Medicare linkage who were unlinked, those linked to Medicare records were slightly older, more often women, and less often insured.

Baseline patient characteristics by stent type. Of the Medicare-linked cohort of stable patients with CTO undergoing elective PCI (n = 10,261), DES was used for CTO PCI in 8,218 (80%) patients, and BMS was used in 2,043 (20%). Propensity matching was done in 4,034 patients (2,017 treated with DES and 2,017 treated with BMS). Unadjusted baseline characteristics by type of stent received are shown in Table 1. Compared with BMS recipients, patients who received a DES for CTO PCI were slightly younger (74.0 vs. 75.5 years, $p < 0.001$) and less likely to have heart failure (57.7% vs. 60.1%, $p = 0.048$), peripheral vascular disease (16.3% vs. 19.9%, $p < 0.001$), or renal failure requiring dialysis (1.4% vs. 3.1%, $p < 0.001$).

Procedural characteristics and outcomes. Procedural characteristics were different between patients undergoing total occlusion PCI with DES than with BMS (Table 1). Patients treated with DES for CTO PCI were likely to have longer lesions (18.8 vs. 16.5 mm, $p < 0.001$), more stents (≥2 stents in 45.7% vs. 37.9%, $p < 0.001$), and undergo multivessel PCI (18.9% vs. 15.1%, $p < 0.001$), when compared with BMS.

Unadjusted procedural outcomes during total occlusion PCI by stent type are presented in Table 2. When comparing patients who received DES versus BMS for CTO PCI, major periprocedural complications were similar, including vascular access complications (0.8% vs. 1.2%, $p = 0.072$), as well as general complications (2.6% vs. 3.2%, $p = 0.13$), including renal failure (0.2% vs. 0.2%, $p = 0.86$) and tamponade (0.2% vs. 0.0%, $p = 0.072$).

Table 1. Baseline Patient and Procedural Characteristics

	All Patients (N = 10,261)	DES (n = 8,218)	BMS (n = 2,043)	p Value
Age, yrs	74.3 ± 6.5	74.0 ± 6.4	75.5 ± 6.9	<0.001
Male	6,996 (68.2)	5,637 (68.6)	1,359 (66.5)	0.072
Caucasian	8,967 (87.5)	7,194 (87.7)	1,773 (86.9)	0.329
Current smoking	1,246 (12.1)	976 (11.9)	270 (13.2)	0.096
CHF	5,966 (58.2)	4,739 (57.7)	1,227 (60.1)	0.048
HTN	8,501 (82.9)	6,787 (82.6)	1,714 (83.9)	0.15
No dialysis renal failure	489 (4.8)	370 (4.5)	119 (5.8)	0.012
Dialysis renal failure	180 (1.8)	117 (1.4)	63 (3.1)	<0.001
PVD	1,747 (17.0)	1,341 (16.3)	406 (19.9)	<0.001
Diabetes				
Noninsulin	2,633 (25.7)	2,127 (25.9)	506 (24.8)	0.306
Insulin	926 (9.0)	738 (9.0)	188 (9.2)	0.751
Stroke	1,543 (15.0)	1,181 (14.4)	362 (17.7)	<0.001
Chronic lung disease	1,762 (17.2)	1,353 (16.5)	409 (20.0)	<0.001
Prior PCI	3,492 (34.0)	2,918 (35.5)	574 (28.1)	<0.001
Prior MI	3,409 (33.2)	3,409 (33.2)	2,710 (33.0)	0.289
Positive noninvasive test	7,254 (86.7)	5,878 (87.4)	1,376 (83.5)	<0.001
Procedural characteristics				
Multivessel PCI	1,859 (18.1)	1,550 (18.9)	309 (15.1)	<0.001
Number of vessels intervened				
1	8,402 (81.9)	6,668 (81.1)	1,734 (84.9)	<0.001
2	1,758 (17.1)	1,466 (17.8)	292 (14.3)	<0.001
3	101 (1.0)	84 (1.0)	17 (0.8)	0.436
Intervened vessel				
LAD	4,757 (46.4)	3,934 (47.9)	823 (40.3)	<0.001
LCX	3,720 (36.3)	2,957 (36.0)	763 (37.3)	0.251
RCA	3,074 (30.0)	2,421 (29.5)	653 (32.0)	0.027
Stents per patient				
1	5,729 (55.8)	4,460 (54.3)	1,269 (62.1)	<0.001
≥2	4,532 (44.2)	3,758 (45.7)	774 (37.9)	<0.001
Lesion length, mm	18.4 ± 10.7	18.8 ± 10.9	16.5 ± 9.5	<0.001

Values are mean ± SD or n (%).

BMS = bare-metal stent(s); CHF = congestive heart failure; DES = drug-eluting stent(s); HTN = hypertension; LAD = left anterior descending; LCX = left circumflex; MI = myocardial infarction; PCI = percutaneous coronary intervention; PVD = peripheral vascular disease; RCA = right coronary artery.

Comparison of DES versus BMS outcomes. MORTALITY AND MYOCARDIAL INFARCTION. Medicare patients undergoing CTO PCI treated with DES rather than BMS had lower unadjusted rates of death (12.3% vs. 21.1%, p < 0.001) (Fig. 1A). Examination of the adjusted analyses, including the propensity score-matched cohort (adjusted HR: 0.72, 95% confidence interval [CI]: 0.60 to 0.86, p < 0.001) and the IPW HR (HR: 0.67, 95% CI: 0.59 to 0.77, p < 0.001) demonstrates findings similar to the unadjusted data (Fig. 2).

The unadjusted incidence of MI at 30 months in patients treated with DES was similar for patients treated with BMS (5.1% vs. 6.3%, p = 0.36) (Fig. 1B). This finding was confirmed with the propensity score-matched adjusted cohort HR (HR: 0.85, 95% CI: 0.61 to 1.19, p = 0.348) and the IPW HR for MI (HR: 0.81, 95% CI: 0.63 to 1.03, p = 0.087) for patients treated with DES compared with BMS (Table 3).

REPEAT REVASCULARIZATION. The unadjusted rates of subsequent revascularization for patients treated with DES versus BMS for CTO PCI was similar at short-term follow-up (1 month rate: 4.1% vs. 3.3%, p = 0.103) and long-term follow-up (30 month rate: 21.7% vs. 20.4%, p = 0.62) (Fig. 1C). Examination of adjusted HR demonstrates similar findings for both short-term and long-term revascularization (Fig. 2).

Subsequent PCI in patients receiving DES versus BMS was higher at 1 month (unadjusted rate: 4.0% vs. 3.0%, p = 0.042), and similar at long-term follow up (30 month unadjusted rate: 18.7% vs. 16.9%, p = 0.44). Examining the propensity score-matched cohort for long-term adjusted comparisons of subsequent PCI procedures, DES implantation was associated with a similar hazard compared with patients receiving BMS (HR: 0.98, 95% CI: 0.81 to 1.19, p = 0.87). Adjustment with the IPW method found that differences in additional PCI rates between DES and BMS were similar to those observed in the propensity score-matched cohort (Fig. 2).

Unadjusted rates for subsequent CABG at long-term follow-up in patients receiving DES versus BMS was similar (3.0% vs. 3.5%, p = 0.66). Propensity score-matched cohort analysis for long-term CABG trended toward lower hazard in patients treated with DES versus BMS (HR: 0.71, 95% CI: 0.46 to 1.10, p = 0.12). After adjusting for baseline differences, the IPW method demonstrated a lower

Table 2. Procedural Outcomes in Patients Undergoing Total Occlusion PCI

	All Patients (N = 10,261)	DES (n = 8,218)	BMS (n = 2,043)	p Value
DES stent type				
Sirolimus-eluting		3,415 (41.6)		
Paclitaxel-eluting		4,164 (50.7)		
Everolimus-eluting		487 (5.9)		
Zotarolimus eluting		288 (3.5)		
Vascular complications	87 (0.8)	63 (0.8)	24 (1.2)	0.072
Access site occlusion	4 (<0.01)	4 (<0.01)	0 (0.0)	0.318
Peripheral embolization	3 (<0.01)	2 (<0.01)	1 (<0.01)	
Dissection	24 (0.2)	18 (0.2)	6 (0.3)	0.533
Pseudoaneurysm	53 (0.5)	37 (0.5)	16 (0.8)	0.061
AV fistula	7 (0.1)	5 (0.1)	2 (0.1)	0.566
Retroperitoneal bleed	22 (0.2)	21 (0.3)	1 (0.0)	0.071
General complications	277 (2.7)	212 (2.6)	65 (3.2)	0.134
Periprocedural MI	130 (1.3)	102 (1.2)	28 (1.4)	0.642
Stroke	15 (0.1)	11 (0.1)	4 (0.2)	0.513
Tamponade	13 (0.1)	13 (0.2)	0 (0.0)	0.072
Renal failure	19 (0.2)	15 (0.2)	4 (0.2)	0.856

Values are n (%).

AV = arteriovenous; other abbreviations as in Table 1.

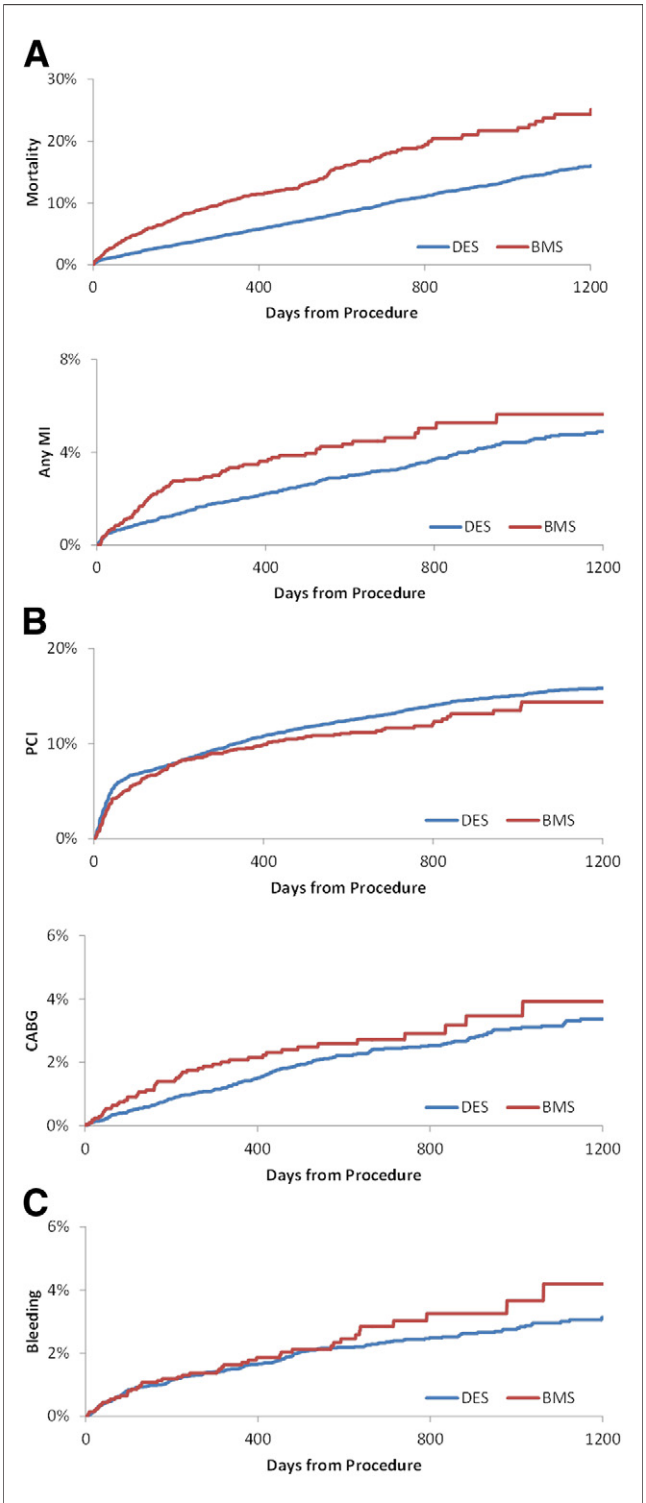

Figure 1. Unadjusted Rates by Stent Type in Patients Undergoing CTO PCI

Unadjusted rates of **(A)** death and myocardial infarction (MI); **(B)** revascularization; and **(C)** bleeding requiring hospitalization for patients getting drug-eluting stents (DES) versus bare-metal stents (BMS) for chronic total coronary occlusion (CTO) percutaneous coronary intervention (PCI).

hazard for subsequent CABG (HR: 0.70, 95% CI: 0.52 to 0.94, p = 0.017).

BLEEDING. DES implantation, compared with BMS implantation, was not associated with a significantly lower incidence of hospitalization for bleeding (unadjusted 30 month rate: 3.1% vs. 4.9%, p = 0.142). Between the propensity score-matched cohort and the IPW-adjusted analysis, there were no significant differences in 30-month bleeding rates between DES and BMS for CTO PCI (Fig. 2).

Discussion

This national observational real-world cohort provides information on greater than 10,000 elderly patients undergo-

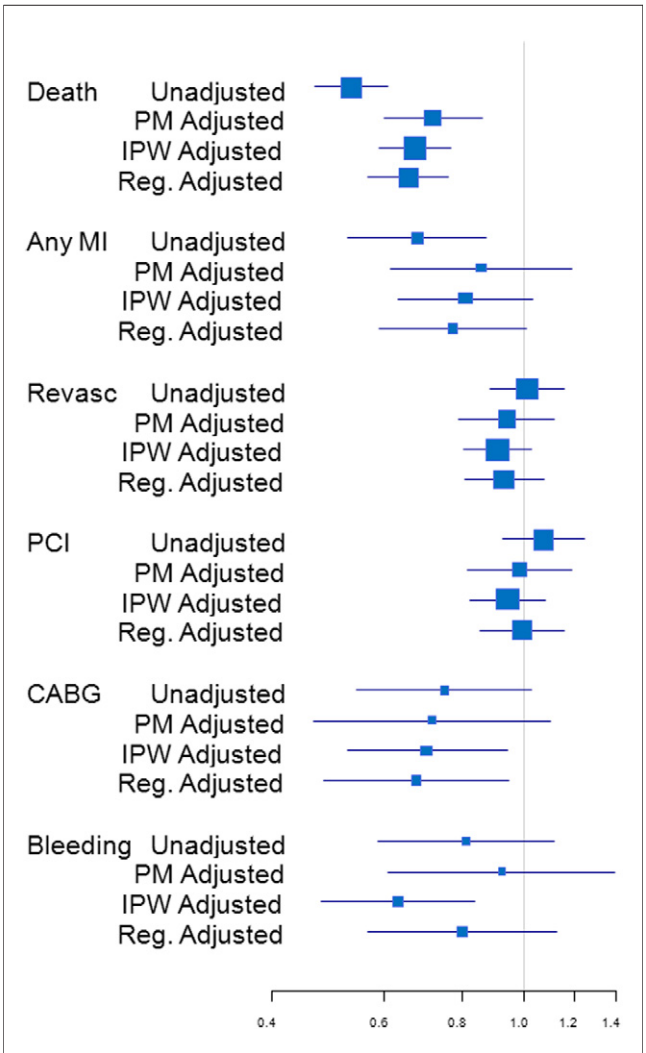

Figure 2. Adjusted Clinical Events for DES Versus BMS

This figure is a Forrest plot of the clinical events for DES and BMS with the effects shown as point estimates after adjustment with propensity methods. CABG = coronary artery bypass graft; IPW = inverse probability weighted; PM = propensity matched; REG = regular; revasc = revascularization; other abbreviations as in Figure 1.

Table 3. Unadjusted and Propensity Score-Matched Event Rates by Stent Type for CTO PCI

	DES			BMS			
Outcomes*	1 Month	12 Months	30 Months	1 Month	12 Months	30 Months	p Value†
Death							
Unadjusted	1.0	5.2	12.3	2.3	11	21.1	<0.001
PS matched	1.1	7.1	15.9	2.2	10.8	20.8	0.014
IPW adjusted	1.0	5.5	13.0	2.0	10.1	17.9	<0.001
MI, rate per 100 patients							
Unadjusted	0.6	2.5	5.1	0.6	3.6	6.3	0.36
PS matched	0.7	3.2	5.7	0.6	3.5	6.3	0.744
IPW adjusted	0.5	2.1	4.4	0.5	3.1	5.2	0.002
Revascularization, rate per 100 pt							
Unadjusted	4.1	12.9	21.7	3.3	12.4	20.4	0.622
PS matched	3.9	12.1	19.3	3.3	12.5	20.5	0.721
IPW adjusted	4.0	11.6	17.3	4.2	13.6	18.3	0.877
Subsequent PCI rate							
Unadjusted	4.0	11.6	18.7	3.0	10.6	16.9	0.443
PS matched	3.7	10.9	16.6	3.0	10.7	17	0.888
IPW adjusted	3.9	10.3	15.1	3.9	11.3	15.7	0.336
Subsequent CABG							
Unadjusted	0.1	1.3	3.0	0.3	1.7	3.5	0.645
PS matched	0.3	1.2	2.7	0.3	1.7	3.5	0.535
IPW adjusted	0.2	1.4	2.9	0.3	2.5	3.9	0.071
Bleeding, rate per 100 pt							
Unadjusted	0.3	1.8	3.1	0.4	2.0	4.9	0.142
PS matched	0.2	1.8	4.0	0.4	2.0	4.9	0.512
IPW adjusted	0.3	1.6	2.8	0.3	1.8	5.0	0.200

Values are %. *Covariates used are listed in the Online Appendix. †The p value compares DES and BMS at 900 days.
IPW = inverse probability weighting; PS = propensity score; other abbreviations as in Tables 1 and 2.

ing successful elective recanalization of CTO. DES were used in 80% of patients. These patients were typically younger and less likely to have peripheral vascular disease, but they were more likely to have longer stents and multivessel revascularization. Compared with BMS implantation, use of DES for revascularization of CTO was associated with a lower long-term mortality rate. Additionally, DES and BMS use at long-term follow-up had similar rates of MI, overall repeat revascularization (PCI and CABG), with a trend toward more subsequent PCI and less CABG with DES. Hospitalizations for bleeding were similar in the 2 groups. After risk adjustment, DES use for CTO revascularization was associated with a reduced incidence of death at long-term-follow up, but had similar rates of MI, subsequent revascularization, and hospitalization for bleeding.

These findings add substantially to the available data on patients undergoing total occlusion recanalization with DES compared with BMS. Although some of the patients may have had a subacute occlusion, most of these stable elective outpatients undergoing CTO PCI do not represent patients randomized in the OAT (Occluded Artery Trial), who were enrolled with an occlusion identified between 3 and 30 days after MI (19). Regarding elective CTO revascularization, a small prospective randomized trial in 200 CTO patients (20) and analysis of a subgroup in the SCANDSTENT (Stenting Coronary Arteries in Non-Stress/Benestent Disease) trial (21) found a reduced rate of binary restenosis and a need for target vessel revascularization in patients treated with sirolimus-eluting stents versus BMS. Data from these studies was recently combined in a systematic review that included 17 published studies of DES use in patients with total occlusions, including 8 case series studies without controls and 7 nonrandomized observational comparisons (22). Although this review of nearly 1,500 patients found DES use in the case of CTO was associated with reduced angiographic restenosis, limited data with regard to the long-term safety and clinical outcomes do not allow correlation with the current study's findings.

Safety and effectiveness of DES and BMS in older patients with total occlusions. The findings from this study suggest that the use of DES in elderly patients with CTO revascularization is associated with a lower mortality. It is possible that there was selection bias, with DES-treated patients

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representing lower risk patients than the BMS-treated patients. However, multiple important baseline characteristics that predict outcomes were well balanced in the propensity score-matched cohort and adjusted for in the analysis. Possible mechanisms of the protective effect observed with the selection for DES versus BMS include more prolonged dual antiplatelet therapy, a lower burden of ischemia, and improved ventricular function. Studies evaluating recanalization of CTO have shown that patients with areas of viable myocardium improve their ventricular function with CTO revascularization (23). Finally, the potential benefits of more complete revascularization, as evidenced by the use of more stents and higher rates of multivessel PCI at the index procedure in the DES-treated patients may contribute to these proposed protective mechanisms.

Of note, the findings from this large observational study of elderly patients are qualitatively consistent with findings from the individual trials and meta-analysis of studies comparing DES with BMS (13,24). These other studies estimated a trend toward a reduction in both mortality and subsequent MI. The elderly patients in this analysis with higher baseline risk, higher coronary disease burden, and long-term follow-up may allow detection of smaller degrees of incremental benefit with DES over BMS, compared with the randomized trials aimed at evaluating restenosis. Conservatively, these data support that DES use for CTO PCI is at least as safe and effective as BMS use.

Repeat revascularization procedures. In this large observational study, subsequent revascularization procedures occurred at similar rates in patients treated with both DES and BMS for total coronary occlusions. These data may in part be reconciled with prior data on repeat revascularization with DES when the types of subsequent revascularization are reviewed. Evaluation of the subsequent revascularization mode shows that, although not statistically significant, patients receiving DES, compared to BMS-treated patients, had higher absolute rates of subsequent PCI and lower absolute rates of CABG. In fact, these small absolute differences were present starting at 30 days and continued at 30 months. After adjusting for baseline characteristics and applying propensity score matching, these trends hold with regard to risk of subsequent revascularization.

These findings likely underscore a treatment strategy for patients with CTO where DES implantation was associated with a higher likelihood of multivessel PCI at index procedure and subsequent PCI within 30 days, compared with BMS-treated patients where the decision to attempt complete percutaneous revascularization may not have been made. In fact, within this dataset, the subsequent site of revascularization (such as target lesion revascularization) cannot be identified and may represent staged revascularization of other coronary stenosis. The lack of a significant difference in subsequent revascularization in this observational study may be in part also explained by the significant difference in observed mortality, the potential for planned subsequent revascularization in DES patients getting CTO PCI, and the potential for incomplete adjustment for operator selection of lower restenosis risk patients for BMS and higher restenosis risk patients for DES. Nevertheless, the findings of similar revascularization rates with both DES and BMS are discordant from randomized trials and may represent bias around case selection. Despite these potential biases, combined with the observed mortality and MI outcomes, the revascularization findings for DES use are reassuring.

Although a longer duration of dual antiplatelet therapy is typically prescribed with DES, we observed lower unadjusted bleeding rates with selection for DES rather than BMS in this study. This may reflect unaccounted-for factors in matching stent type to estimated patient bleeding risk by physicians. Supporting this idea, the propensity score-matched and IPW rates for bleeding were not significantly different for DES versus BMS.

Strengths and limitations. As with all observational studies, there are several important points to consider when interpreting the results of this study. First, we must consider the data source. The CathPCI Registry represents over 1,000 U.S. hospitals and, therefore, a significant portion of PCI nationally. Patients over 65 years of age compose more than 50% of patients undergoing PCI. This is a real-world cohort of consecutive older patients with CTO undergoing elective revascularization; as such, many of these patients would have been excluded from the pivotal trials, due to the lesion complexity and/or associated comorbidities. As with all studies from the NCDR, there is the potential for case selection bias, as well as operator and institutional variation. The second important consideration is the duration of follow-up and data collected. Because the follow-up information was linked to the Medicare administrative data files, we were able to obtain long-term incidence of death, MI, revascularization, and bleeding associated with hospitalization. Yet because the registry data are linked with administrative data, it is not possible to determine target vessel revascularization or stent thrombosis through ICD-9 coding. However, all additional revascularization procedures (PCI or CABG), MI, and death are captured—arguably, these additional procedures are a more important patient-centered outcome.

Although important determinants of both angiographic and clinical outcomes were collected (i.e., baseline comorbidities and procedural characteristics, such as the number of stents, stent length, and vessels intervened per patient), data on other important factors (i.e., medication during follow-up and anatomic factors, such as vessel caliber and lesion length) were not captured. Additionally, duration of CTO was not known, although this is considered a stronger determinant on elective PCI success, and as mentioned previously, all patients with recent acute coronary syndrome emergent indications were excluded. The inability to capture all potential determinants of

outcomes could bias the observation toward no significant difference between DES and BMS.

Finally, as in all observational studies, there remains the possibility of unmeasured confounders that could influence the use of a DES instead of a BMS for patients with CTO. This study used a large number of variables in the multivariable adjustment and replicated the results using 2 different statistical approaches.

Conclusions

In a large national consecutive cohort study of Medicare beneficiaries undergoing elective PCI for CTO, 80% of patients received DES. In a propensity score-matched cohort, these older patients who received DES had significantly lower mortality rates throughout 30 months of follow-up than did those who received BMS. There was no significant difference in long-term rates of MI, repeat revascularization, or bleeding requiring hospitalization. These data add significantly to available data on DES in elective CTO revascularization, providing evidence of safety and efficacy in routine practice in this large, high-risk group of elderly patients.

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Reprint requests and correspondence: Dr. Manesh R. Patel, Duke University Medical Center, Duke Clinical Research Institute, 2400 Pratt Street, Durham, North Carolina 27710. E-mail: manesh.patel@duke.edu.

REFERENCES

1. Serruys PW, Morice MC, Kappetein AP, et al., for the SYNTAX Investigators. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;360:961–72.
2. Stone GW, Kandzari DE, Mehran R, et al. Percutaneous recanalization of chronically occluded coronary arteries: a consensus document: part I. Circulation 2005;112:2364–72.
3. 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.
4. 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.
5. Spaulding C, Daemen J, Boersma E, Cutlip DE, Serruys PW. A pooled analysis of data comparing sirolimus-eluting stents with bare-metal stents. N Engl J Med 2007;356:989–97.
6. Suttorp MJ, Laarman GJ, Rahel BM, et al. Primary Stenting of Totally Occluded Native Coronary Arteries II (PRISON II): a randomized comparison of bare metal stent implantation with sirolimus-eluting stent implantation for the treatment of total coronary occlusions. Circulation 2006;114:921–8.
7. Weintraub WS, McKay CR, Riner RN, et al., for the American College of Cardiology Database Committee. The American College of Cardiology National Database: progress and challenges. J Am Coll Cardiol 1997;29:459–65.
8. Brindis RG, Fitzgerald S, Anderson HV, Shaw RE, Weintraub WS, Williams JF. The American College of Cardiology—National Cardiovascular Data Registry (ACC-NCDR): building a national clinical data repository. J Am Coll Cardiol 2001;37:2240–5.
9. Anderson HV, Shaw RE, Brindis RG, et al. A contemporary overview of percutaneous coronary interventions: the American College of Cardiology–National Cardiovascular Data Registry (ACC-NCDR). J Am Coll Cardiol 2002;39:1096–103.
10. National Cardiovascular Data Registry. Available at: http://www.ncdr.com. Accessed August 2012.
11. Weiner M, Stump TE, Callahan CM, Lewis JN, McDonald CJ. A practical method of linking data from Medicare claims and a comprehensive electronic medical records system. Int J Med Inform 2003;71:57–69.
12. Hammill BG, Hernandez AF, Peterson ED, Fonarow GC, Schulman KA, Curtis LH. Linking inpatient clinical registry data to Medicare claims data using indirect identifiers. Am Heart J 2009;157:995–1000.
13. Douglas PS, Brennan JM, Anstrom KJ, et al. Clinical effectiveness of coronary stents in elderly persons: results from 262,700 Medicare patients in the American College of Cardiology—National Cardiovascular Data Registry. J Am Coll Cardiol 2009;53:1629–41.
14. Bang H, Tsiatis AA. Median regression with censored cost data. Biometrics 2002;58:643–9.
15. Gray R. Class of K-sample tests for comparing the cumulative incidence of a competing risk. Ann Statis 1988;16:1141–54.
16. Hullsiek KH, Louis TA. Propensity score modeling strategies for the causal analysis of observational data. Biostatistics 2002;3:179–93.
17. Parsons L. Group OR. Reducing bias in a propensity score matched-pair sample using greedy matching techniques. Paper presented at: SAS Users Group International Conference 26; 2001; April 22–25 Long Beach, California. Available at: http://www2.sas.com/proceedings/sugi26/p214-26.pdf. Accessed September 4, 2012.
18. Cole SR, Hernán MA. Adjusted survival curves with inverse probability weights. Comput Methods Programs Biomed 2004;75:45–9.
19. Hochman JS, Lamas GA, Buller CE, et al. Coronary intervention for persistent occlusion after myocardial infarction. N Engl J Med 2006;355:2395–407.
20. Suttorp MJ, Laarman GJ, for the PRISON III Study Investigators. A randomized comparison of sirolimus-eluting stent implantation with zotarolimus-eluting stent implantation for the treatment of total coronary occlusions: rationale and design of the PRImary Stenting of Occluded Native coronary arteries III (PRISON III) study. Am Heart J 2007;154:432–5.
21. Kelbaek H, Helqvist S, Thuesen L, et al., for the SCANDSTENT Investigators. Sirolimus versus bare metal stent implantation in patients with total coronary occlusions: subgroup analysis of the Stenting Coronary Arteries in Non-Stress/Benestent Disease (SCANDSTENT) trial. Am Heart J 2006;152:882–6.
22. Saeed B, Kandzari DE, Agostoni P, et al. Use of drug-eluting stents for chronic total occlusions: a systematic review and meta-analysis. Catheter Cardiovasc Interv 2011;77:315–32.
23. Baks T, van Geuns RJ, Duncker DJ, et al. Prediction of left ventricular function after drug-eluting stent implantation for chronic total coronary occlusions. J Am Coll Cardiol 2006;47:721–5.
24. Kirtane AJ, Gupta A, Iyengar S, et al. Safety and efficacy of drug-eluting and bare metal stents: comprehensive meta-analysis of randomized trials and observational studies. Circulation 2009;119:3198–206.

Key Words: bare-metal stents ■ drug-eluting stents ■ total coronary occlusion.

APPENDIX

For additional data and a supplemental figure, please see the online version of this paper.