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Safety and Efficacy of Drug-Eluting Stents in Older Patients With Chronic Kidney Disease

A Report From the Linked CathPCI Registry–CMS Claims Database

Thomas T. Tsai, MD, MSc,*† John C. Messenger, MD,† J. Matthew Brennan, MD,‡ Uptal D. Patel, MD,‡ David Dai, PhD,‡ Robert N. Piana, MD,§ Kevin J. Anstrom, PhD,‡ Eric L. Eisenstein, DBA,‡ Rachel S. Dokholyan, MPH,‡ Eric D. Peterson, MD, MPH,‡ Pamela S. Douglas, MD‡

Denver and Aurora, Colorado; Durham, North Carolina; and Nashville, Tennessee

Objectives The purpose of this study was to determine the safety and efficacy of drug-eluting stents (DES) compared with bare-metal stents (BMS) in older patients with chronic kidney disease (CKD).

Background DES may be associated with late death and myocardial infarction (MI) secondary to stent thrombosis. However, data on outcomes in older patients with CKD are limited.

Methods We estimated the glomerular filtration rate (GFR) of 283,593 patients 65 years of age and older who underwent stent implantation between 2004 and 2007. In propensity-matched cohorts grouped by GFR, the association between DES and BMS and the risk of death, MI, revascularization, and major bleeding was examined.

Results A total of 121,446 patients (42.8%) had CKD (GFR <60 ml/min/1.73 m^2). The 30-month mortality rate for patients on long-term dialysis was 52.0%. In propensity-matched pairs, placement of a DES compared with a BMS in patients with normal renal function was associated with significant reductions in 30-month revascularization (hazard ratio [HR]: 0.91; 95% confidence interval [CI]: 0.86 to 0.95), MI (HR: 0.77; 95% CI: 0.71 to 0.83), and death (HR: 0.73; 95% CI: 0.69 to 0.77), but no difference in bleeding (HR: 0.89; 95% CI: 0.79 to 1.00). Lower MI and mortality rates were also observed after DES compared with BMS implantation in all CKD subgroups with the exception of MI in the long-term dialysis group. Decreased rates of revascularization did not extend to any subgroup of patients with CKD.

Conclusions The safety of DES compared with BMS is observed in all patients regardless of renal function and is associated with reduced rates of MI and death in some subsets of patients with CKD. (J Am Coll Cardiol 2011;58:1859–69) © 2011 by the American College of Cardiology Foundation Open access under CC BY-NC-ND license.

Patients with chronic kidney disease (CKD) make up an increasing percentage of the population undergoing percutaneous coronary intervention (PCI). This trend is largely a result of the growing number of patients with CKD, estimated to exceed 19 million patients in the United States, and the high prevalence of coronary artery disease in these patients (1–3). However, their representation in randomized trials of PCI therapies has been historically low because of concerns about an increase in major in-hospital adverse events, short- and long-term mortality, and lower procedural success rates compared with patients with normal renal function (4–6).

The drug-eluting stent (DES) has emerged as the stent of choice in CKD patients in response to the high restenosis rates of 13% to 35% seen with bare-metal stents (BMS) in these patients (7–11). Although DES have been shown to lower restenosis and revascularization rates in patients enrolled in the randomized, controlled trials (RCTs) (12–14), >50% of DES are being placed in patient and anatomic subsets that were not included in the large pivotal RCTs

From the *Denver VA Medical Center, Denver, Colorado; †University of Colorado, Aurora, Colorado; ‡Duke Clinical Research Institute, Duke University Medical Center, Durham, North Carolina; and the §Vanderbilt University Medical Center, Nashville, Tennessee. This project was funded under contract no. HHSA29020050032I Task Order No. 4 from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services as part of the Developing Evidence to Inform Decisions about Effectiveness (DEcIDE) program. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services. Dr. Eisenstein has received grant support from Medtronic Cardiovascular and Eli Lilly & Co. Dr. Peterson has received research support from Bristol-Myers Squibb/Sanofi, Merck, Lilly, and Johnson & Johnson. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Abbreviations and Acronyms

BMS = bare-metal stent(s)
CI = confidence interval
CKD = chronic kidney disease
DES = drug-eluting stent(s)
GFR = glomerular filtration rate
HR = hazard ratio
IPW = inverse probability–weighted
MI = myocardial infarction
NCDR = National Cardiovascular Data Registry
PCI = percutaneous coronary intervention
RCT = randomized controlled trial

(15–17). Whether these devices are safe and effective in older patients with baseline CKD or patients on long-term dialysis has not been well studied, and the recent concerns regarding increased rates of late stent thrombosis in patients with CKD after implantation of DES may offset any potential benefit of decreased revascularization (18–20).

The contemporary prevalence of CKD in older patients undergoing PCI and the relative safety and efficacy of DES compared with those of BMS in this population is unknown. Using data from the linked American College of Cardiology National Cardiovascular Data Registry (NCDR) and the Center for Medicare Services national claims databases, we evaluated the outcomes of patients with increasing severity of CKD including patients on dialysis and in these subgroups and examined the association between DES and BMS and the risks of death, myocardial infarction (MI), revascularization, and major bleeding.

Methods

Study population. The NCDR CathPCI registry, cosponsored by the American College of Cardiology and the Society for Cardiovascular Angiography and Interventions, was previously described (21,22). The registry catalogs data on patient and hospital characteristics, clinical presentation, treatments, and outcomes for PCI procedures from more than 1,000 sites across the United States. Data are entered into NCDR-certified software at participating institutions and exported in a standard format to the American College of Cardiology. There is a standard dataset with written definitions, uniform data entry and transmission requirements, and data quality checks. The variables were prospectively defined by a committee of the American College of Cardiology and are available online (23).

This study included all Medicare-eligible patients 65 years of age and older undergoing PCI who were enrolled in the CathPCI registry between January 1, 2004, and December 31, 2007. Only patients enrolled using version 3.0 of the data forms (contains data on baseline creatinine) were included. Patients receiving more than 1 stent type (i.e., both BMS and DES) or missing creatinine values who were not on dialysis were excluded from the analysis (Fig. 1). Patients were classified into 5 groups according to the estimated glomerular filtration rate (GFR) using the 4-component MDRD (Modification of Diet in Renal Disease study) equation incorporating age, race, sex, and serum creatinine (24). The most recent creatinine level before the day of the procedure was collected on the case report forms. Patients were classified as having normal renal function (GFR $\geq$60 ml/min/1.73 m^2), mild CKD (GFR 45 to 59 ml/min/1.73 m^2), moderate CKD (GFR 30 to 44 ml/min/1.73 m^2), severe CKD (GFR $<$30 ml/min/1.73 m^2), and long-term dialysis (as indicated by the case report form). The Duke University Medical Center Institutional Review Board granted a waiver of the informed consent and authorization for this study.

Follow-up information. The CathPCI registry only covers pre-hospital testing and in-hospital outcomes, so we used the Medicare 100% inpatient fee-for-service claims file for longitudinal patient follow-up. The CathPCI Registry-CMS Claims Database linking rules were previously described (25).

Clinical endpoints. We evaluated 4 primary clinical endpoints: death, MI, repeat revascularization, and follow-up bleeding (26,27). Death was defined both during the index PCI procedure (using American College of Cardiology NCDR information) and post-discharge (using the Medicare denominator file). Other clinical endpoints were defined post-discharge only with the Medicare claims file as the primary diagnosis for the hospital admission. The ICD-9 CM diagnosis codes used to identify events were MI (410.X1) (26,27), major bleeding (430 through 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 revascularizations (ICD-9 CM procedure codes PCI: 36.00, 36.06, 36.07, 36.09; and coronary artery bypass graft surgery: 36.10–19). Only revascularizations occurring after discharge from the index hospital stay were included in the revascularization analysis.

Statistical analysis. Differences between groups were compared using chi-square tests for categorical variables and the Wilcoxon rank sum or Kruskal-Wallis test for continuous variables. Event rates were calculated based on Kaplan-Meier censoring estimates. Kaplan-Meier event curves, stratified by CKD subgroup, were generated and presented as cumulative incidence curves. To evaluate the independent effect of CKD severity on outcomes, we used a Cox proportional hazards model adjusted with variables from the NCDR PCI mortality model (28,29). Patients with normal renal function were used as the referent group in all comparisons.

Propensity scores were developed for the receipt of DES within each CKD subgroup such that the receipt of a DES is the dependent variable conditioned on 102 observed covariates. We then matched each DES recipient to a BMS control within each CKD subgroup by using the estimated logit of the propensity score using a