Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 51, No. 21, 2008
ISSN 0735-1097/08/$34.00
doi:10.1016/j.jacc.2008.01.057

Drug-Eluting Compared With Bare-Metal Coronary Stents Among Elderly Patients

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Objectives We sought to determine whether drug-eluting stents (DES) were associated with improved clinical outcomes compared with bare-metal stents (BMS) among a nationally representative, nonexperimental elderly patient cohort.

Background Randomized controlled clinical trials comparing DES and BMS for treatment of coronary artery disease indicate that although the use of DES reduces rates of coronary restenosis after percutaneous coronary intervention, it does not reduce the rates of mortality or acute myocardial infarction (AMI). Nevertheless, clinical outcomes of DES in nonexperimental, routine clinical practice are uncertain.

Methods We assembled a retrospective cohort of elderly Medicare beneficiaries (n = 76,525) who received DES within 9 months after Food and Drug Administration approval of the sirolimus-eluting stent (April 2003 to December 2003). Using propensity score methods, we assembled 2 matched control cohorts who received BMS from July 2002 to March 2003 (historical controls) or from April 2003 to December 2003 (contemporary controls). Patient enrollment and claims records were obtained through December 2005 to ascertain mortality, hospitalization for AMI, and subsequent coronary revascularization.

Results Receipt of a DES was associated with a significant survival benefit, with an adjusted mortality hazard ratio of 0.83 (95% confidence interval 0.81 to 0.86) compared with contemporary controls, and a hazard ratio of 0.79 (95% confidence interval 0.77 to 0.81) compared with historical controls (control group heterogeneity: $p < 0.001$). Patients with DES had significantly lower adjusted rates of revascularization procedures within the first 2 years after PCI and lower hospitalization rates for subsequent AMI.

Conclusions In contrast to clinical trial results, DES receipt was associated with fewer subsequent revascularization procedures, lower rates of hospitalization for AMI, and improved survival among elderly Medicare beneficiaries. (J Am Coll Cardiol 2008;51:2017–24) © 2008 by the American College of Cardiology Foundation

The first drug-eluting (coronary) stents (DES) used in routine clinical practice in the U.S.—sirolimus-eluting stents—received initial Food and Drug Administration (FDA) approval in April 2003 (1). Adoption of this new technology, augmented by the approval of the paclitaxel-eluting stent in March 2004, was rapid and widespread, such that the majority of percutaneous coronary intervention (PCI) procedures in the U.S. now use 1 of the 2 FDA-approved DES (2,3), and the annual market for DES in the U.S. alone has reached $5.3 billion (4). Despite the rapid diffusion and widespread acceptance of this new technology, the clinical effectiveness of DES compared with the less-expensive bare-metal (coronary) stents (BMS) remains uncertain, particularly when coronary stents are used in routine, nonexperimental clinical settings.

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The authors of numerous randomized controlled clinical trials have consistently demonstrated that the use of DES reduces the rate of target lesion revascularization (i.e., the need to perform a repeat interventional procedure on a coronary stenosis that had recurred at the site of the initial stenting) compared with BMS, but DES do not reduce subsequent rates of major adverse clinical events or mortality (5–7). More recently, reports from clinical registries and clinical trial consortiums with longer-term follow-up data have suggested the possibility of a higher rate of late

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Manuscript received November 16, 2007; revised manuscript received January 4, 2008, accepted January 8, 2008.

JACC Vol. 51, No. 21, 2008
May 27, 2008:2017–24

Abbreviations and Acronyms

AMI = acute myocardial infarction
BMS = bare-metal stent(s)
DES = drug-eluting stent(s)
FDA = Food and Drug Administration
PCI = percutaneous coronary intervention

stent failures—in particular, stent thrombosis—for patients receiving DES, which might further diminish the relative benefit of DES (8–10). Extrapolating clinical trial results to nonexperimental settings has been further complicated by the diverse clinical indications for which DES are currently used. It has been estimated that approximately 60% of drug-eluting stent use in the U.S. has been "off label," that is, used in patients with clinical conditions that do not precisely fit the FDA-approved clinical criteria that was based on entry criteria for the clinical trials (11). It is therefore uncertain whether the clinical outcomes observed in experimental settings for DES are representative of those obtained in routine clinical practice. Therefore, the goals of this research were to measure the clinical outcomes of DES compared with BMS among a nationally representative cohort of elderly patients receiving PCI in nonexperimental settings.

Methods

Setting. The population for the study comprised Medicare beneficiaries ages 66 and older covered under fee-for-service Medicare. Medicare Part A (hospital) coverage is almost universal for Americans older than the age of 65 years, and more than 90% of elderly Americans are enrolled in fee-for-service Medicare; thus, this population is nearly ideal for investigations of national trends in health care. From among these Medicare beneficiaries (i.e., approximately 45 million persons), we identified patients with hospital claims indicating receipt of a DES between April 24, 2003 (the FDA approval date for DES), through December 2003, or receipt of a BMS from July 1, 2002, through December 31, 2003.

Patients with procedure codes indicating receipt of both stent types during the same hospitalization were excluded. We also excluded any patients who had prior Medicare claims indicating they had undergone PCI or coronary bypass surgery within the 6-month period before the "index" PCI that qualified the patient for inclusion in our study. Patients were only allowed to enter the cohort once—at their earliest PCI within the designated time windows. We only included patients ages 66 years and older, because many 65-year-old patients would not be expected to have had at least 6 months of previous Medicare coverage during which time information on prior procedures and comorbidities would have been recorded.

Comparison groups. For all qualifying DES and BMS recipients, we obtained data on age, race, and gender from the Medicare enrollment database. Information on clinical comorbidities and other cardiac diagnoses (e.g., acute myocardial infarction or acute coronary syndromes) was obtained from the hospitalization claim at the time of PCI (i.e., the index admission), as well as all other inpatient claims during the 6 months before the index hospitalization. We also determined whether each patient's index hospitalization had been classified as elective, urgent, or emergent. Information on the patient's PCI hospital, including geographic location and academic status (indicated by membership in the American Association of Medical College's Council of Teaching Hospitals and Health Systems), was obtained by linking each patient's hospital identifier to annual Hospital Cost Report Information System report data that are submitted annually to the Centers for Medicare and Medicaid Services by all hospitals participating in the Medicare program. The volume of Medicare admissions per calendar year for each admitting hospital was calculated using all Medicare acute-care hospitalization claims from 2002 to 2004.

All DES and BMS recipients were then combined in a single dataset, and a multivariate propensity score for receipt of DES was calculated for each patient using a multivariable logistic regression model with receipt of DES (vs. BMS) being the dependent variable, and the demographic, clinical, and hospital factors listed previously included in the model as independent variables (12). The propensity score is a well-validated statistical method designed to balance a large number of potential confounders equally across 2 observational cohorts of patients, without the traditional requirement of exactly matching patients 1-to-1 on each individual confounder (12,13).

We then matched each DES recipient to a BMS control patient by using a propensity score-matching optimization algorithm that selected an optimal match for each DES recipient among BMS patients with similar propensity scores (within 0.25 times the standard deviation of the propensity score logit) and having a minimum Mahalanobis distance calculated from key covariates (in this case, the covariates were age, diabetes, congestive heart failure, acute myocardial infarction, PCI at a high-volume center, and PCI at an academic center) (13). Because the pool of potential BMS controls receiving stents in the time period before FDA approval of the DES (April 2003), may have systematically differed in unobservable ways from the pool of potential BMS controls available after the FDA approval date, we matched DES patients separately to "contemporary" BMS controls, that is, BMS patients receiving stents during the same time interval (April to December, 2003) during which the DES patients received stents, as well as to "historical" controls, that is, BMS patients receiving stents during the 9 months immediately before the FDA approval of DES (July 2002 to March 2003). All subsequent analyses of clinical outcomes were made in parallel between these 2 pairs of matched DES-BMS cohorts.

Ascertaining clinical outcomes. Using the Medicare Denominator File, which is linked to the Social Security Administration's Death Master File and thus is a reliable indicator of mortality (14), we determined whether and when patients had died during the time interval from receipt