CORONARY ARTERY DISEASE

Editor's Choice

Comparative Effectiveness of Drug-Eluting Stents on Long-Term Outcomes in Elderly Patients Treated for In-Stent Restenosis: A Report from the National Cardiovascular Data Registry

Michael A. Kutcher,1* MD, J. Matthew Brennan,2 MD,MPH, Sunil V. Rao,2 MD, David Dai,2 PhD,MS, Kevin J. Anstrom,2 PhD, Nowwar Mustafa,3 MD, Art Sedrakayan,4 MD, Michael E. Booth,2 MBA, Pamela S. Douglas,2 MD, and John C. Messenger,5 MD

Objective: We assessed the long-term outcomes of elderly patients who had in-stent restenosis (ISR) treated with drug-eluting stents (DES) compared with other treatment strategies. Background: Elderly patients with ISR represent a vulnerable group of which little is known regarding the safety and efficacy of repeat percutaneous coronary intervention (PCI). Methods: We analyzed patients ≥65 years of age who underwent PCI for ISR in the National Cardiovascular Data Registry from 2004 to 2008. Death, myocardial infarction (MI), revascularization, stroke, and bleeding were assessed for up to 30 months by a linkage with Medicare rehospitalization claims. Results: Of 43,679 linked patients, 30,012 were treated with DES, 8,277 with balloon angioplasty (BA), and 4,917 with bare metal stents (BMS). Compared with BMS, DES use was associated with a lower propensity score-matched (PM) risk of death (hazard ratio [HR] 0.72; 95% confidence interval [CI] 0.66–0.80, P < 0.001), MI (HR 0.81; 95% CI 0.70–0.93, P = 0.003), and revascularization (HR 0.90; 95% CI 0.82–1.00, P = 0.055). Compared with BA, DES use was associated with a lower PM risk of death (HR 0.82; 95% CI 0.76–0.89, P < 0.001) and revascularization (HR 0.86; 95% CI 0.80–0.93, P < 0.001), but no statistically significant difference across other endpoints. There were no significant differences in long-term outcomes for BA compared with BMS. Conclusions: There was lower mortality and reduced risk for MI, revascularization, and stroke, but a similar rate of bleed-

1Wake Forest School of Medicine, Winston-Salem, North Carolina
2Duke Clinical Research Institute, Durham, North Carolina
3Christiana Care Health System, Newark, Delaware
4Weill Cornell Medical College, New York
5University of Colorado School of Medicine, Aurora, Colorado

Conflict of interest: M.A. Kutcher: Research grant support from Abbott Vascular (Fellowship Grant Support); P.S. Douglas: no disclosures to report; S. Rao: TBD; J.M. Brennan: no disclosures to report; D. Dai: no disclosures to report; K.J. Anstrom: research and salary support from Alexion, AstraZeneca, Bristol Myers Squibb, Lilly, Inno-coll Pharmaceuticals, Medtronic, Pfizer, and Proctor & Gamble (modest); data safety monitoring boards: Pfizer and Vertex (modest); consulting services: Pacific Therapeutics, Bristol Myers Squibb, and AstraZeneca (modest); N. Mustafa: TBD; A. Sedrakayan: TBD; M.E. Booth: no disclosures to report; J.C. Messenger: serving as the Site PI for Resolute Study and EDUCATE study: Medtronic, Inc. (modest).

Grant sponsor: Agency for Healthcare Research and Quality (AHRQ), United States Department of Health and Human Services, Rockville, MD; Grant numbers: 24-EHC-1 (as part of the Cardiovascular Consortium); HHSAA290-2005-0032—TO4-WA2 (as part of the Developing Evidence to Inform Decisions about Effectiveness (DEcIDE) program); Grant sponsor: National Cardiovascular Data Registry, American College of Cardiology, Washington, DC.

*Correspondence to: Michael A. Kutcher, MD; Wake Forest School of Medicine; Medical Center Boulevard, Winston-Salem, NC 27157.
E-mail: mkutcher@wakehealth.edu

Received 21 February 2013; Revision accepted 27 June 2013
DOI: 10.1002/ccd.25108
Published online 3 July 2013 in Wiley Online Library (wileyonlinelibrary.com).

© 2013 Wiley Periodicals, Inc.
INTRODUCTION

The development of balloon expandable intracoronary stents in the early 1990s resulted in a 25–35% reduction of angiographic restenosis rates after percutaneous coronary intervention (PCI), primarily through the elimination of elastic recoil and arterial remodeling within the coronary artery [1]. In-stent restenosis (ISR) after bare metal stents (BMS) was found to be predominantly due to intimal hyperproliferation through the stent struts [2]. In the early 2000s, the use of drug-eluting stents (DES) further reduced the angiographic restenosis rate to below 10% by a mechanism of suppressing the intimal hyperproliferative response [3,4].

During the past two decades, multiple strategies have been considered for the treatment of ISR within a previously implanted BMS (BMS-ISR). However, BA [5], rotational atherectomy [6], excimer laser [7], and additional BMS implantation did not result in durable long-term benefit. A breakthrough occurred when studies demonstrated that vascular brachytherapy (VBT) reduced the reactive hyperproliferative response of BMS-ISR [8,9]. Subsequently, a number of randomized multicenter trials verified the safety and effectiveness of DES over VBT for the treatment of BMS-ISR [10,11]. As a result, DES implantation has emerged as the most widely used treatment for BMS-ISR [12].

With the widespread use of DES for the treatment of de novo lesions, significant safety concerns have been reported that are related to late stent thrombosis with DES as initial therapy [13,14]. In addition, there are now evolving issues regarding the most effective treatment for ISR when it occurs within a previously implanted DES (DES-ISR). Stent thrombosis may be magnified if DES is used for BMS-ISR or DES-ISR. The elderly ISR population is particularly vulnerable because of the possibilities of excessive bleeding with protracted dual antiplatelet therapy (DAPT), an increased in-stent thrombosis risk, and questions regarding the mortality and morbidity benefit of repeat PCI with DES. There is a lack of contemporary data regarding the safety and effectiveness of various ISR treatment strategies in an elderly patient cohort. As a result, we undertook a comparative effectiveness analysis of the long-term outcomes of patients ≥65 years of age who had ISR treated with DES versus other device strategies.

METHODS

Study Population

The National Cardiovascular Data Registry® (NCDR) CathPCI Registry® is a voluntary registry sponsored by the American College of Cardiology (ACC) and the Society for Cardiovascular Angiography and Interventions (SCAI). The CathPCI Registry collects patient and hospital characteristics, clinical presentations, treatments, and in-hospital outcomes for PCI procedures from over 1,000 sites across the United States [15,16]. There are rigorous data quality programs, transmission specifications, and standardized data element definitions that can be found at http://www.ncdr.com.

We analyzed all CathPCI Registry version 3.0 patients who underwent PCI from January 1, 2004, to December 31, 2008. A de novo lesion was defined as a lesion that had not been previously treated in the current (or any prior) hospitalization. ISR was defined as a lesion that had been previously treated with a stent (either DES or BMS). We excluded lesions that were previously treated with other nonstent devices or BA. The primary device treatment strategy for baseline ISR was divided into DES, BMS, BA (included balloon dilation and cutting balloon), atherectomy (included rotational and laser atherectomy), and VBT. The ISR-PCI population was further divided into patients <65 years and patients ≥65 years. The Duke University Medical Center Institutional Review Board granted a waiver of informed consent and authorization for this study.

Follow-up Information

The CathPCI Registry only captures in-hospital events. Therefore, to assess long-term outcomes, the ISR ≥65 age group was longitudinally linked with subsequent Medicare fee-for-service readmission claims by using techniques described in previous publications [17,18]. The PCI procedure codes (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM], 00.66, 36.0x, 37.22, 37.23, and 88.5x, except 88.59) were used to identify index procedures in the Medicare files which were then linked to CathPCI Registry data using indirect identifiers (non-unique fields that when used in combination may identify unique hospitalizations).
Linking rules used a hierarchy of evidence approach such that rules with the greatest specificity were applied first. Once a match was achieved for a patient, no further rules were applied. The linking rules contained combinations of information denoting the index PCI procedure site, patient date of birth or age, admission, discharge date, and sex. If a single CathPCI Registry record matched with multiple Medicare records using the same rules, then no linking occurred, and the patient was excluded from the analysis of treatment outcomes. Patients were also excluded if their index PCI procedure did not occur during a period of fee-for-service enrollment, or if they underwent an index PCI procedure did not occur during a period of rehospitalization. Patients were also excluded if their Medicare rehospitalization claims link.

Clinical Endpoints

Both in-hospital and postdischarge outcomes were evaluated in patients ≥65 years of age. In-hospital adverse events were identified directly from the CathPCI Registry data and included death; emergency or emergent salvage coronary artery bypass graft (CABG) surgery; and several general, bleeding, and vascular complications. General complications included: Periprocedural myocardial infarction (MI), cardiogenic shock, congestive heart failure, stroke, tamponade, thrombocytopenia, contrast reaction, and renal failure. Bleeding complications consisted of: Bleeding at percutaneous entry; and retroperitoneal, gastrointestinal, genitourinary, or unknown bleeding. Vascular complications included: access site occlusion, peripheral embolization, dissection, pseudoaneurysm, pseudoaneurysm requiring treatment, and arteriovenous fistula.

Long-term outcomes were identified from Medicare fee-for-service claims files. The primary outcomes in the longitudinal analysis were: Death, any MI, revascularization, major bleeding, and stroke. MI was further subdivided into ST-segment elevation MI (STEMI) and non–ST-segment elevation MI (NSTEMI). Revascularization was subdivided into those who underwent PCI or CABG. Patient mortality was identified from the Medicare denominator file, whereas other endpoints were determined using the following primary hospital ICD-9-CM diagnosis codes: Any MI (410.X1) (further subdivided into NSTEMI [410.7] and STEMI [410.0-410.6, 410.8-9]) and revascularization (further subdivided into PCI [36.00, 36.06, 36.07, 36.09] or CABG [36.10-19]). In addition, the following ICD-9-CM codes were assessed as measures of safety: Bleeding (430.432, 578.X, 719.1X, 423.0, 599.7, 626.2, 626.6, 626.8, 627.0, 627.1, 786.3, 784.7, or 459.0) and stroke (430.X, 431.X, 432.X, 434.X). Information regarding the specific duration of DAPT was not available in the Medicare rehospitalization claims link.

Statistical Analysis

Baseline in-hospital characteristics for the elderly ISR Medicare-linked population were categorized by device types (DES, BMS, BA) and summarized as counts and percentages for categorical variables and means with standard deviations for continuous variables. Differences between groups were compared using χ² tests for categorical variables and the Wilcoxon rank sum or Kruskal–Wallis test for continuous variables. Statistical significance was defined as P < 0.05, with no correction for multiple comparisons. SAS statistical software (version 9.2, SAS Institute, Cary, NC) was used for all calculations.

Unadjusted estimates of the event rates for clinical endpoints at 30, 360, and 900 days postintervention were based on inverse probability-weighted (IPW) estimates [19]. The cumulative incidence rates for time-to-event clinical outcomes were estimated by using the Gray-Fine method [20]. Unadjusted estimates of hazard ratio (HR) comparing DES vs. BMS were calculated using a Cox model with type of stent as the only covariate.

For adjusted analyses, three different propensity score models were created, one for comparing DES vs. BMS, one for DES vs. BA, and one for BMS vs. BA [21]. Propensity scores represent the estimated probabilities of patients receiving one device type versus another, in this case conditioned upon 99 observed covariates. The propensity score logistic regression models had c-indexes of 0.755 for DES vs. BMS, 0.763 for DES vs. BA, and 0.741 for BMS vs. BA. Three propensity score-matched (PM) cohorts were created using the Greedy 5–1 Digit Matching Algorithm based on each pair of device types [22]. After PM, the distribution of estimated propensity scores for patients with one type of device closely matched those for patients with another type of device as evidenced by the 5-number summaries (min, 25th, 50th, 75th, max) describing the curves for patients receiving each type of device: DES vs. BMS with DES (10.1%, 67.7%, 81.3%, 88.9%, 98.9%) and BMS (10.1%, 67.6%, 81.3%, 88.9%, 98.9%); DES vs. BA with DES (6.9%, 59.2%, 70.5%, 80.3%, 100.0%) and BA (7.1%, 59.2%, 70.5%, 80.3%, 100.0%); BMS vs. BA with BMS (4.6%, 27.9%, 40.1%, 52.4%, 98.6%) and BA (4.6%, 27.9%, 40.3%, 52.7%, 98.0%). Adjusted event rates and HRs comparing each pair of device types were calculated among the paired patients who had similar propensity scores. As a secondary
approach, IPW methods were used to calculate adjusted HRs [23].

RESULTS

Study Population

Figure 1 shows the study population that was analyzed. From January 1, 2004, to December 31, 2008, there were 1,485,203 patients at 967 sites who had PCI procedures reported to the CathPCI Registry. Of these, 145,485 (9.8%) at 957 sites had PCI for ISR and 69,071 patients at 939 sites were ≥65 years of age. Of this elderly cohort, 67% were then successfully matched to Medicare readmission billing data. The resulting study population consisted of 43,679 ISR treated patients at 903 sites. In this cohort, the etiology of the ISR was 57% DES-ISR and 43% BMS-ISR.

Fig. 1. Study population. Flow diagram depicts the study population of patients treated with percutaneous coronary intervention for ISR and criteria for selection of the resulting Medicare-linked study cohort. ACC-NCDR, American College of Cardiology-National Cardiovascular Data Registry; CMS, Centers for Medicare & Medicaid Services; DN-PCI, PCI for de novo lesions; FFS, fee-for-service; ISR-PCI, percutaneous coronary intervention for in-stent restenosis. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
Analyses revealed few interactions between the strategies for the treatment of DES-ISR and BMS-ISR either in unadjusted events or following IPW. The only interactions were weak and related to MI. As a result, we concentrated our analysis of the association of PCI strategies, in-hospital outcomes, and long-term follow-up.
outcomes to the overall issue of ISR—regardless of the type of previously implanted stent.

**ISR Medicare-Linked Cohort**

Clinical characteristics based on device treatment. Table I lists the clinical characteristics of the 43,679 ISR-PCI elderly patients who were successfully linked with the longitudinal Medicare database according to the device used: DES, BMS, or BA. DES (30,012 patients) were the most common mode of treatment for ISR, followed by BA (8,277 patients) and BMS (4,917 patients). The exact dose of aspirin and the intended duration of DAPT after discharge were not recorded in the NCDR database. Patients treated with “other” or uncategorized devices ($n = 473$), VBT ($n = 8$), or atherectomy ($n = 24$) were excluded from in-hospital and long-term outcomes analysis, because of the prohibitively small sample size associated with these procedures. In diabetic patients, there was relatively equal use of DES, BMS, and BA. A DES was used more often in the clinical presentation of stable angina (19.2% DES vs. 10.9% BMS vs. 14.4% BA, $P < 0.001$). The unadjusted incidence of periprocedural MI was lowest in the BA group (1.0% DES vs. 3.5% BMS vs. 2.3% BA, $P < 0.001$).

Long-term outcomes based on device treatment: Unadjusted event rates. By 30 months after treatment for ISR, unadjusted adverse events in the entire Medicare-linked group was substantial, with an incidence of 17.3% death, 12.0% MI, 32.6% repeat revascularization, 3.4% bleeding, and 3.0% stroke.

Figure 2 shows unadjusted cumulative incidence rates in the Medicare-linked ISR-PCI elderly cohort and portrays the primary and secondary endpoints based on device use (DES, BMS, or BA). Over time, patients who received DES had lower unadjusted mortality compared with BA and BMS (Fig. 2A). The unadjusted rate of readmission for any MI (Fig. 2B) was significantly lower in the DES and BA groups compared with BMS. When MI was differentiated into STEMI (Fig. 2C) and NSTEMI (Fig. 2D) the unadjusted patterns were similar over time. The unadjusted incidence of readmission for repeat revascularization (Fig. 2E) was similar in DES, BMS, and BA. When subdivided into forms of revascularization, there was no unadjusted difference between the three treatment modalities for repeat PCI (Fig. 2F), yet the unadjusted rate of readmission for CABG was significantly lower among patients treated with DES compared with either BMS or BA (Fig. 2G).

With respect to safety, the unadjusted rate of admission for bleeding (Fig. 2H) was similar in all three treatment groups. The unadjusted incidence of stroke...
(Fig. 2I) was lower in the DES- and BA-treated group, compared with the BMS group.

**Hazard Ratios: unadjusted and adjusted.** Forest plots with resulting endpoints of death, any MI (subdivided into STEMI and NSTEMI), revascularization (subdivided into PCI and CABG), bleeding, and stroke are shown in Fig. 3. Compared with BMS, the use of DES for the treatment of ISR was associated with a significant reduction in both the unadjusted and the PM-adjusted 30-month incidence of: Death (PM HR 0.72; 95% CI 0.66–0.80, \( P < 0.001 \)), any MI (PM HR 0.81; 95% CI 0.70–0.93, \( P = 0.003 \)), and stroke (PM HR 0.74; 95% CI 0.55–0.99, \( P = 0.045 \)). There was a trend towards the reduction of revascularization (PM HR 0.90; 95% CI 0.82–1.00, \( P = 0.055 \)) with DES treatment. The IPW analyses were in concurrence with these findings. There was no increase in STEMI in the DES treatment group. In addition, DES use was associated with a significantly lower risk for bleeding in unadjusted and IPW adjustment (IPW HR 0.81; 95% CI 0.67–0.97, \( P = 0.020 \)), but a nonsignificant lower risk in the PM adjustment (PM HR 0.94; 95% CI 0.73–1.23, \( P = 0.672 \)).

Compared with BA treatment for ISR, DES was associated with a significantly lower 30-month risk for death (PM HR 0.82; 95% CI 0.76–0.89, \( P < 0.001 \)), but not in the IPW-adjusted analysis (IPW HR 1.00; 95% CI 0.94–1.07, \( P = 0.968 \)). A PM analysis demonstrated a significant reduction of readmission for revascularization in patients treated with DES for ISR compared with treatment with BA (PM HR 0.86; 95% CI 0.80–0.96, \( P < 0.001 \)). The risk of MI, bleeding, and stroke were similar between DES and BA treatments. Compared with BA, BMS treatment for ISR did not result in statistically significant differences in any of the endpoints.

**DISCUSSION**

This is the largest contemporary report on the DES treatment of ISR compared with other PCI strategies and the subsequent short- and long-term outcomes in elderly patients \( \geq 65 \) years of age. There are four main findings from these analyses. First, the use of DES for the treatment of ISR was associated with a reduced 30-month risk of adverse outcomes compared with either BMS or BA. Second, no increase in the risk of STEMI was noted among DES patients by 30 months. Third, the risk of readmission for bleeding and stroke in the DES-treated group, compared with the BMS-treated group, was not increased. Finally, compared with...
BMS, BA treatment for ISR was not associated with significant differences in long-term outcomes.

The initial randomized clinical trials with DES in de novo lesions did not demonstrate a mortality and MI benefit with DES over BMS [3,4]; however, these trials included stable elective patients with uncomplicated single-vessel stenoses. The improved mortality and morbidity outcomes for DES treatment of ISR in our study are consistent with Kirtane’s meta-analysis of observational registries that demonstrated a reduced mortality and MI rate with DES use [14]. These registries, as in ours, had a more contemporary mix of “real world” DES and BMS use in unstable, MI, and complex anatomy patients.

One of the compelling findings of our study is the poor overall outcome of elderly ISR patients with mortality rates ranging from 14.8 to 26% at 900 days depending on the treatment modality. Even with DES for ISR, revascularization rates were 33% at 900 days. Therefore, elderly patients with ISR constitute a high-risk population in which the most effective treatment strategy may have a real impact on long-term outcomes.

The effectiveness of DES for BMS-ISR was affirmed by two randomized studies—the Intracoronary Stenting or Angioplasty for Restenosis Reduction–Drug-Eluting Stents for in-Stent Restenosis (ISAR-DESIRE) study [24] and the Restenosis In Intrastent: Balloon Angioplasty Versus Selective Sirolimus-Eluting Stenting (RIBS-II) study [25]—both of which reported reduced angiographic restenosis and target lesion revascularization with DES compared with BA.

One of the compelling findings of our study is the poor overall outcome of elderly ISR patients with mortality rates ranging from 14.8 to 26% at 900 days depending on the treatment modality. Even with DES for ISR, revascularization rates were 33% at 900 days. Therefore, elderly patients with ISR constitute a high-risk population in which the most effective treatment strategy may have a real impact on long-term outcomes.

The effectiveness of DES for BMS-ISR was affirmed by two randomized studies—the Intracoronary Stenting or Angioplasty for Restenosis Reduction–Drug-Eluting Stents for in-Stent Restenosis (ISAR-DESIRE) study [24] and the Restenosis In Intrastent: Balloon Angioplasty Versus Selective Sirolimus-Eluting Stenting (RIBS-II) study [25]—both of which reported reduced angiographic restenosis and target lesion revascularization with DES compared with BA. Our study has demonstrated a similar finding in elderly patients treated with DES versus BA for ISR.
With regard to existing ISR treatment literature, our study is unique in that it is focused on the effect of DES compared with various other PCI options on long-term outcomes in patients ≥65 years old. In comparison, Marroquin et al. [26] reported on 6,551 PCI patients from the National Heart, Lung, and Blood Institute’s Dynamic Registry. The mean patient age was 63 years. “Off-label” use occurred in 2,110 patients treated with BMS and 1,312 patients treated with DES. Of these, “restenotic lesion” was the indication in 11.6 and 16.0%, respectively. In this restenotic group, when DES was compared with BMS, the 1-year incidence of adjusted death or MI (HR 0.80; 95% CI 0.41–1.59) and revascularization (HR 0.75; 95% CI 0.47–1.18) indicated a favorable trend, but no superiority for DES. Nevertheless, it is unclear whether all these restenotic lesions were true ISR and not due to other previous nonstent PCI procedures. These findings are complimentary to ours in that DES use in restenotic lesions was not found to be detrimental.

Singh et al. [27] reported on long-term outcomes in the treatment of BMS-ISR from the Cleveland Clinic Registry. Over an 8-year time frame, 706 patients were identified with BMS-ISR. Of these, 362 were subsequently treated with DES and 344 with BMS. BA was not a treatment strategy evaluated in this study. DES use was associated with an adjusted lower primary composite endpoint of death or MI, and target lesion revascularization compared with BMS (21 vs. 45%) (HR 0.63; 95% CI 0.42–0.95, \( P = 0.03 \)). The individual secondary endpoint of death (8 vs. 24%, \( P = 0.005 \)) favored DES, but MI (3 vs. 8%, \( P = 0.31 \)) and target lesion revascularization (13 vs. 20%, \( P = 0.23 \)) failed to reach statistical significance. The authors’ conclusion was similar to our findings: DES use was associated with lower death and a composite endpoint compared with BMS for the treatment of ISR. Although this was not an exclusive study of Medicare patients, the average age of the groups was 64 ± 11 and 63 ± 12 years, respectively.

Our present study shows that DES use, over BMS and BA, was the predominant mode of treatment for ISR in elderly patients. Atherectomy and VBT were rarely used. Additionally, the use of BMS compared with BA for the treatment of ISR did not improve 30-month outcomes. As a result, BA is a reasonable option for ISR patients in whom BMS or DES implantation and commitment to protracted DAPT is questionable.

Although the long-term safety of DES use in ISR may be magnified in the elderly, the known risks of late and very late stent thrombosis of 1.3–1.4% in de novo lesions [13] did not translate into an increase in mortality and morbidity in our study; rather, the reverse was found. Likewise, the potential increased risk of bleeding with DAPT in the elderly was not reflected by a higher incidence of bleeding or stroke in ISR patients treated with DES treatment compared with BMS or BA in our study. However, the absence of data regarding the duration of DAPT may affect the strength of these findings. Overall and in perspective, these favorable long-term outcomes for DES therapy must be tempered by the realization that a thoughtful assessment of the risk/benefit ratio of device selection is still important in elderly ISR patients.

**Study Limitations**

Our study had several limitations. First, despite some variation of IPW and PM adjustments within groups, outcomes were concurrent in the large majority of analyses. These variations are a reflection of the analysis populations, whereby PM adjustment matches a subgroup of the overall study population for their propensity to receive a treatment strategy. On the other hand, IPW uses the entire study population and creates a reweighted population for both treatment groups. We decided to report both to provide the most information that could be generalized to this long-term outcomes cohort.

Second, important specific ISR lesion characteristics (such as focal or diffuse patterns) that affect the treatment strategy (DES, BMS, BA, or other modalities) were not collected in this version of the CathPCI Registry. In addition, there are intangible clinical variables in an elderly patient population that may enter into the physician’s decision process for device choice in ISR. There may still be an effect of residual treatment bias, in spite of our statistical risk adjustment techniques.

Finally, patients and hospitals who participate in the CathPCI Registry and are successfully linked to Medicare readmission coding data may not be representative of PCI treatment strategy patterns and outcomes for all elderly ISR patients across the United States. Nevertheless, the Medicare claims data linkage algorithm has been well-validated [17,18], and together with standards of statistical risk adjustment, has been the source of major peer-reviewed papers of comparative effectiveness [28]. Regardless, the data link provides a “real-world view” of the personal and economic impact that various cardiovascular treatment strategies may have on elderly patients.

**CONCLUSIONS**

In this large national contemporary registry study of elderly patients longitudinally linked to the Medicare Catheterization and Cardiovascular Interventions DOI 10.1002/ccd. Published on behalf of The Society for Cardiovascular Angiography and Interventions (SCAI).
database, the use of DES for ISR was associated with similar bleeding results, but lower mortality and a reduced risk for MI, revascularization, and stroke, compared with other device treatment strategies. Overall, our results indicate that DES use is a comparatively effective treatment strategy for properly selected elderly patients with ISR.

ACKNOWLEDGMENTS
The authors thank Tammy Davis of Wake Forest School of Medicine for transcribing the original paper and Erin LoFrese, MS, of Duke Clinical Research Institute, for organizing and editing the final manuscript. Neither Ms. Davis nor Ms. LoFrese received compensation for their assistance, apart from their employment at the institutions where the study was conducted.

REFERENCES

Catheterization and Cardiovascular Interventions DOI 10.1002/ccd. Published on behalf of The Society for Cardiovascular Angiography and Interventions (SCAI).


