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Comparison of long-term safety and efficacy outcomes after drug-eluting and bare-metal stent use across racial groups: Insights from NHLBI Dynamic Registry ☆

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ABSTRACT

Background: Long-term data on outcomes after percutaneous coronary intervention (PCI) with drug-eluting stent (DES) and bare-metal stent (BMS) across racial groups are limited, and minorities are under-represented in existing clinical trials. Whether DES has better long-term clinical outcomes compared to BMS across racial groups remains to be established. Accordingly, we assessed whether longer-term clinical outcomes are better with DES compared to BMS across racial groups.

Methods: Using the multicenter National Heart, Lung, and Blood Institute (NHLBI)-sponsored Dynamic Registry, 2-year safety (death, MI) and efficacy (repeat revascularization) outcomes of 3326 patients who underwent PCI with DES versus BMS were evaluated.

Results: With propensity-score adjusted analysis, the use of DES, compared to BMS, was associated with a lower risk for death or MI at 2 years for both blacks (adjusted Hazard Ratio (aHR) = 0.41, 95% CI 0.25–0.69, $p < 0.001$) and whites (aHR = 0.67, 95% CI 0.51–0.90, $p = 0.007$). DES use was associated with a significant 24% lower risk of repeat revascularization in whites (aHR = 0.76, 95% CI 0.60–0.97, $p = 0.03$) and with nominal 34% lower risk in blacks (aHR = 0.66, 95% CI 0.39–1.13, $p = 0.13$).

Conclusion: The use of DES in PCI was associated with better long-term safety outcomes across racial groups. Compared to BMS, DES was more effective in reducing repeat revascularization in whites and blacks, but this benefit was attenuated after statistical adjustment in blacks. These findings indicate that DES is superior to BMS in all patients regardless of race. Further studies are needed to determine long-term outcomes across racial groups with newer generation stents.

1. Introduction

Drug eluting stents (DESs) are superior to bare metal stents (BMSs) in reducing incidence of in-stent restenosis and the need for repeat revascularization, but are not associated with decreased incidence of death or myocardial infarction (MI), in randomized clinical trials [1–4]. Analyses of data from real-world patients enrolled in registries suggest that DES use, compared with BMS, is not only associated with lower rates of repeat revascularization, but also, lower rates of death and MI [5]. These benefits appear to be driven primarily by a reduction in the incidence of in-stent restenosis and the need for repeat revascularization [5]. Despite the marked efficacy demonstrated by DES in reducing the need for repeat revascularization [5], some concerns have emerged regarding the long-term safety of DES [6–9] with some studies indicating that DES use is associated with increased incidence of stent thrombosis and MI, especially among blacks [8,9]. Whether DES has better long-term clinical outcomes compared with BMS in blacks and whites remains to be established.

Blacks have more comorbid conditions and present at a younger age for percutaneous coronary intervention (PCI), compared with their white counterparts [10]. Although in-hospital outcomes are similar in blacks and whites, higher 1-year mortality has been observed in blacks [10–12]. Data on minority populations are limited because of under-representation of minorities in the existing randomized clinical trials including those evaluating PCI outcomes [1–4,6]. Therefore, little is known about the safety of DES, in relation to BMS, among minority populations, particularly blacks. Accordingly, the purpose of this study is to assess whether longer-term clinical outcomes are better with DES

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compared to BMS across racial groups using the National Heart, Lung, and Blood Institute (NHLBI) Dynamic Registry.

2. Methods

2.1. NHLBI Registry design

The NHLBI Dynamic Registry has been previously described in detail [13,14]. In brief, the Dynamic Registry, coordinated at the University of Pittsburgh, involves multi-center recruitment of consecutive patients undergoing percutaneous coronary interventions (PCI) at 27 clinical centers in North America during pre-specified time intervals or "waves". Each clinical center received approval from its institutional review board. Five recruitment waves of approximately 2000 patients were enrolled and followed over a 10-year period (wave 1: 1997 to 1998, n = 2524 patients; wave 2: 1999, n = 2105 patients; wave 3: 2001 to 2002, n = 2047 patients; wave 4: 2004, n = 2112 patients; and wave 5: 2006, n = 2176 patients). Only BMSs were available during the recruitment period for waves 1, 2 and 3, and DESs were introduced prior to the start of wave 4.

Data on baseline demographic, clinical and angiographic characteristics and procedural characteristics during the index PCI, as well as the occurrence of death, myocardial infarction, and the need for coronary artery bypass grafting (CABG) were collected. In-hospital and 24-month follow-up data were obtained by research coordinators using standardized report forms. Coordinators periodically evaluated the vital status of patients who were lost to follow-up using the Social Security Administration's Death Master File (www.Ntis.gov/products/ssa-dmf.asp). If patients underwent subsequent repeat revascularization (either PCI or CABG), vessel-specific and lesion-specific data were collected whenever possible to determine target-vessel revascularization.

2.2. Study population

The present study cohort was divided into two racial groups in accordance with the Congressional Office of Management and Budget, and based on patient's self-description of their race as black or African American, and as white or Caucasian. Multiple racial/ethnic groups were not allowed and patients reporting a race other than black or white were excluded for this analysis. We further subdivided these two groups of patients into those that received BMS and those that received DES. Given that this analysis evaluated outcomes beyond one year, the patients enrolled in recruitment waves 1 and 3 were excluded due to the shorter maximum follow-up. To reduce a potential treatment bias, only data from centers with at least 5% black population were included in this analysis. Finally, only patients receiving at least one stent were included.

2.3. Endpoints

The end points were death from any cause, MI, and repeat revascularization. Safety endpoints were death and MI, and efficacy endpoint was repeat revascularization. MI was diagnosed on the basis of evidence of at least two of the following: typical chest pain lasting more than 20 min and not relieved by nitroglycerine; serial electrocardiograms showing changes from baseline or serially in ST and T waves, Q-waves, or both in more than two contiguous leads; a rise in the creatine kinase (CK) level to more than twice the upper limit of the normal range with an increase in CK-MB of more than 5% of the total value; and an elevation in the troponin level to more than twice the upper limit of the normal range. Repeat revascularization was defined as the combined end point of repeat PCI or CABG during the follow-up period. Repeat PCI included revascularization of target lesions and target vessels but did not included staged procedures. Only definite stent thrombosis, defined as angiographically confirmed cases, is reported in this study. Stent thrombosis events were captured only in waves 4 and 5, and all were independently adjudicated. Stent thrombosis events that occurred in stents placed after the index procedure were not included in this analysis.

2.4. Statistical analysis

For each race category, patient characteristics pertaining to the index PCI, including demographic characteristics, medical history, cardiac presentation, peri-procedural medications, procedural characteristics, and in-hospital outcomes were compared between stent types and race using the Student's t-tests or Wilcoxon nonparametric tests for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Similar methods were used for lesion-level analyses. Two year cumulative incidence rates of individual clinical outcomes and composite outcomes were estimated by the Kaplan–Meier method and tested by the log-rank statistic. Patients who did not experience the outcome of interest were censored at the last known date of contact or at 2-years if contact extended beyond 2 years. To complement these analyses, stratified analyses and formal test for interaction were performed to evaluate whether the association between stent type and clinical outcomes varied by race.

Multivariable Cox proportional-hazards regression modeling was used to estimate the independent effect of stent type (DES vs. BMS) in both black and white patients. A propensity score approach was used to balance factors associated with the nonrandom assignment of stent type. Logistic regression was used initially to identify the variables to include in each propensity score (one for blacks and one for whites). The models were conservative, such that it included variables with a p-value <0.20. A probability score was created for each study participant using parameter estimates for the variables in the model. All statistical analyses were performed with the use of SAS software, version 9.1 and a two-sided p value of 0.05 or less was considered to indicate statistical significance.

3. Results

3.1. Cohort characteristics

A total of 3,326 patients (718 blacks (21.6%) and 2608 whites (78.4%)) received stents. Among blacks, 543 (75.6%) were treated with DES and 175 (24.4%) were treated with BMS, while the whites consisted of 1946 (74.6%) treated with DES and 662 (25.4%) treated with BMS. Table 1 lists baseline characteristics. For both blacks and whites, there were no significant differences in age, or prevalence of prior MI, cerebrovascular and peripheral vascular disease between those treated with DES and BMS, but black and white patients who were treated with DES compared to those treated with BMS were more likely to have severe non-cardiac comorbid conditions, renal disease, hypertension, hypercholesterolemia and a higher mean body mass index (Table 1). White patients who received DES, compared to BMS, were more likely to have diabetes, >50% stenosis in left main, left anterior descending and circumflex artery, and more likely to have disease amenable to revascularization by CABG. While blacks treated with DES, compared to BMS, were more likely to present with a total occlusion and disease amenable to revascularization by PCI (Table 2).

3.2. Procedural and lesion characteristics

For both blacks and whites, DES-treated patients were more likely to have calcified lesions, less likely to present with unstable angina, and to receive procedural antithrombotic therapy compared to BMS-treated patients. Among the black patients, there was greater use of glycoprotein IIb/IIIa inhibitors in the DES-treated patients, although there was no significant difference in the urgency of the procedure between DES and BMS groups. Among white patients, DES-treated patients had longer lesion length and higher proportion of ACC/AHA type C lesions (Table 3).