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Letters

Drug-Eluting Stent Implantation and Long-Term Survival Following Peripheral Artery Revascularization

Drug-eluting stents (DES) are important additions to the armamentarium of devices used for peripheral artery revascularization, associated with decreased rates of restenosis and target vessel revascularization (1-3). A recent meta-analysis found an association between peripheral paclitaxel-coated devices and increased long-term mortality (4). These findings have not been replicated in other data sources with extended follow-up.

Patients admitted with a principal diagnosis of peripheral artery disease (5) in the U.S. Centers for Medicare & Medicaid Services (CMS) Medicare Provider Analysis and Review files were identified using International Classification of Diseases-Ninth Revision-Clinical Modification (ICD-9-CM) codes. The study started December 1, 2012, corresponding to the approval of the first peripheral DES (Zilver PTX, Cook Medical, Bloomington, Indiana), and continued through September 30, 2015. International Classification of Diseases-Ninth Revision-Procedure Coding System (ICD-9-PCS) codes were used to identify peripheral DES (00.55) and bare-metal stent (BMS) (39.90) placement. For patients with repeated procedures, only the first procedure was included. Comorbidities were ascertained using index diagnosis codes and from all hospitalizations within 12 months of the procedure. Temporal trends of BMS and DES use were plotted over quarterly time periods. The cumulative incidence of death through December 31, 2016 was calculated using Kaplan-Meier methods, and log-rank tests were used to evaluate for differences between groups. Multivariable Cox regression was used to calculate hazard ratios (HR), adjusted for age, sex, and comorbidities (5). Subgroup analyses were performed among patients with critical limb ischemia (CLI) and acute limb ischemia (ALI). All p values <0.05 were considered significant.

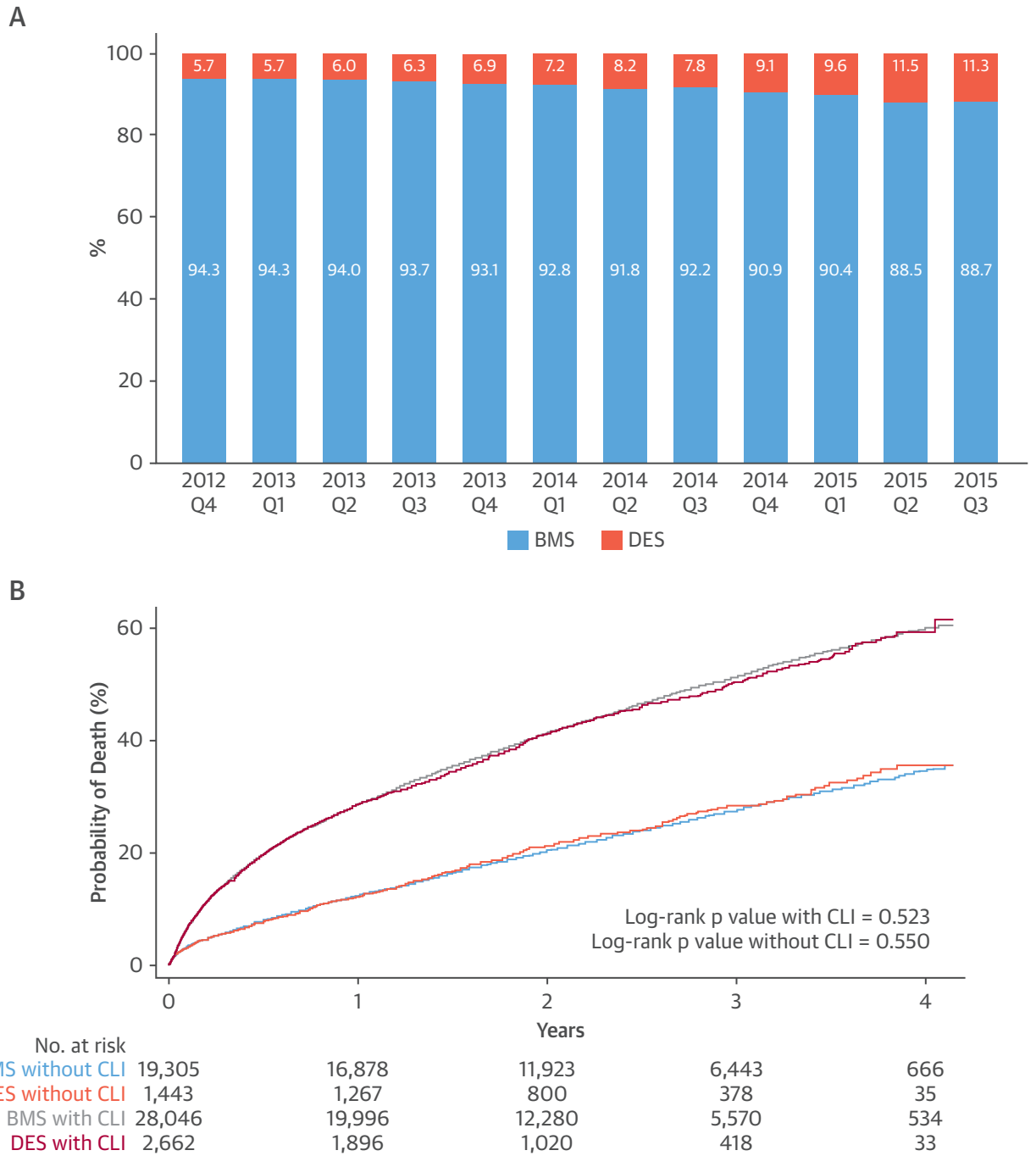
Among 51,456 patients who underwent peripheral stenting, the average age was 72.8 $\pm$ 10.5 years, 54.2% were male, 59.7% had CLI, 7.1% had ALI, and 39.3% were diabetic. Median follow-up was 2.0 years (interquartile range: 1.2 to 3.0 years; longest 4.1 years). During the study, there was a gradual uptake in peripheral DES use (**Figure 1A**). Patients treated with DES versus BMS had similar mortality through 4.1 years (51.7% for DES vs. 50.1% for BMS; log-rank $p = 0.16$), and this relationship persisted after stratification by CLI (**Figure 1B**). There was no association between stent type and mortality after multivariable adjustment (HR for DES vs. BMS: 0.98; 95% confidence interval [CI]: 0.93 to 1.03; $p = 0.53$). In addition, there was no adjusted relationship between stent type and death among patients with CLI (HR: 0.97; 95% CI: 0.92 to 1.03; $p = 0.32$) or ALI (HR: 0.99; 95% CI: 0.81 to 1.21; $p = 0.95$).

In this study of Medicare beneficiaries admitted for peripheral artery revascularization, we observed a gradual uptake of DES use and found no difference in mortality between DES and BMS through the end of follow-up. This finding remained after multivariable adjustment, and among patients with CLI or ALI.

Peripheral artery revascularization has been challenged by high rates of restenosis and need for reintervention. The first DES indicated for femoropopliteal artery revascularization, the paclitaxel-eluting Zilver PTX, was approved in November 2012 after demonstrating improved patency at 12 months compared with balloon angioplasty and BMS (3). Follow-up data through 5 years (1,2) have shown persistent efficacy over these other devices, supporting their routine use.

However, the long-term safety of these devices has not been well established, mainly due to their limited duration on the market. A recent meta-analysis of randomized trials has raised concern regarding a possible association with long-term mortality (4). In particular, this meta-analysis found that DES use corresponded with an 87% increased risk of long-term all-cause death (4). Due to the significant implications of these findings and the increasing use of peripheral DES, investigation of this relationship in other data sources is needed urgently, thus motivating this analysis.

FIGURE 1 Temporal Trends in Use of DES for PAD and Survival Stratified by CLI Diagnosis



(A) Temporal trends in use of DES for PAD and **(B)** long-term survival stratified by CLI diagnosis are shown. BMS = bare-metal stents; CLI = critical limb ischemia; DES = drug-eluting stents; PAD = peripheral artery disease; Q = quarter.

This analysis is limited by an inability to localize the lesion of interest, possible misclassification due to use of claims codes, lack of data on outpatient procedures and drug-coated balloons (no ICD-9-PCS code), the potential influence of unmeasured confounding, and the inability to determine specific causes of death. In addition, this Medicare population was older and had more comorbidities,

including CLI, compared with the Katsanos et al. (4) meta-analysis.

In summary, we found no evidence of increased long-term mortality following peripheral artery revascularization with DES compared with BMS among Medicare beneficiaries, suggesting the safety of these devices in routine practice.

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Major Adverse Events With Percutaneous Left Atrial Appendage Closure in Patients With Atrial Fibrillation

Transcatheter left atrial appendage (LAA) closure is an alternative strategy for stroke prevention in atrial fibrillation (AF) patients with contraindications for long-term anticoagulant treatment. A better characterization of clinical events after LAA closure for these patients in daily practice is still needed.

We analyzed data from all patients with AF treated with LAA closure in 8 French cardiology departments from 2012 to 2017 (NCT03279406). Industry did not support and had no role in the design, data analysis, or manuscript writing of the study. Subjects eligible for LAA closure according to European guidelines were recruited from the general population in each institution. Antithrombotic management was decided for each patient on an individual basis (1). A Cox regression model was used for multivariable analysis of outcomes.

A total of 469 consecutive AF patients received LAA closure using WATCHMAN devices (Atritech, Boston Scientific, Natick, Massachusetts) (58%) or Amplatzer cardiac plug devices (AGA, St. Jude Medical, Minneapolis, Minnesota) (42%). Mean follow-up was 11.4 months (median 7 months; interquartile range: 3 to 22 months), during which 70 major adverse events were recorded in 69 patients (**Table 1**). Among these, deaths were the most common events, most of which were noncardiovascular deaths. None of the baseline characteristics was predictive of major adverse events, neither in univariate nor in multivariable analysis.

In AF patients treated with LAA closure, we report high yearly rates of mortality (7.4%), ischemic strokes