Choice of Stent for Percutaneous Coronary Intervention of Saphenous Vein Grafts

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Background—There are limited data on comparison of contemporary drug-eluting stent (DES) platforms, previous generation DES, and bare-metal stents (BMS) for percutaneous coronary intervention in saphenous vein grafts (SVG). We aimed to assess clinical outcomes following percutaneous coronary intervention to SVG in patients receiving bare-metal stents (BMS), first-generation DES, and newer generation DES in a large unselected national data set from the BCIS (British Cardiovascular Intervention Society).

Methods and Results—Patients undergoing percutaneous coronary intervention to SVG in the United Kingdom from January 2006 to December 2013 were divided into 3 groups according to stent use: BMS, first-generation DES, and newer generation DES group. Study outcomes included in-hospital major adverse cardiovascular events, 30-day mortality, and 1-year mortality. Patients (n=15 003) underwent percutaneous coronary intervention to SVG in England and Wales during the study period. Of these, 38% received BMS, 15% received first-generation DES, and 47% received second-generation DES. The rates of in-hospital major adverse cardiovascular events were significantly lower in patients treated with second-generation DES (odds ratio, 0.51; 95% confidence interval, 0.38–0.68; $P<0.001$), but not with first-generation DES, compared with BMS-treated patients. Similarly, 30-day mortality (odds ratio, 0.43; 95% confidence interval, 0.32–0.59; $P<0.001$) and 1-year mortality (odds ratio, 0.60; 95% confidence interval, 0.51–0.71; $P<0.001$) were lower in patients treated with second-generation DES, but not with first-generation DES, compared with the patients treated with BMS.

Conclusions—Patients receiving second-generation DES for the treatment SVG disease have lower rates of in-hospital major adverse cardiovascular events, 30-day mortality, and 1-year mortality, compared with those receiving BMS. **(*Circ Cardiovasc Interv*. 2017;10:e004457. DOI: 10.1161/CIRCINTERVENTIONS.116.004457.)**

Key Words: cardiovascular diseases ■ coronary artery bypass ■ percutaneous coronary intervention ■ mortality ■ saphenous vein graft

Coronary artery bypass graft surgery with ≥1 saphenous vein grafts (SVGs) is a commonly selected mode of revascularization for patients with multivessel coronary artery disease. The long-term patency rates of SVGs, when compared with arterial conduits, remain poor despite optimal secondary prevention therapy.[1] A sizeable proportion (10%–40%) of SVGs occlude within the first year and with inexorable attrition at a rate of 2% to 5% annually, which accelerates with graft age.[2–10] Although patients can undergo redo coronary artery bypass graft surgery, there is high morbidity and mortality associated with this. Therefore, percutaneous coronary intervention (PCI) of SVGs is often a preferred revascularization modality in patients with significant SVG disease[11,12] with 5% to 10% of all PCI procedures being undertaken in SVGs.[11,13]

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WHAT IS KNOWN

- There are limited studies comparing bare-metal stents to drug-eluting stents (DES) for percutaneous coronary intervention for saphenous vein graft.
- In general, these studies suggest that DES are associated with reduced repeat revascularization but no survival benefit.
- These studies are mainly of first-generation DES, and there are now second-generation stents and more recent studies suggest that newer generation stents have lower mortality than bare-metal stents but no differences in mortality between newer and 1st generation DES.

WHAT THE STUDY ADDS

- We observe that patients receiving DES for the treatment of saphenous vein graft disease have lower rates of in-hospital major adverse cardiac events, 30-day mortality, and 1-year mortality, compared with those receiving bare-metal stents.
- The reduction in adverse outcomes is greatest with newer generation DES.
- Patients undergoing percutaneous coronary intervention for saphenous vein graft disease should be considered for treatment with DES, unless there are any contraindications such as higher risk of bleeding with dual antiplatelet therapy or requirement for a short dual antiplatelet therapy course.

For treating native coronary arteries, drug-eluting stents (DES) are preferred over the bare-metal stents (BMS) as DES have been shown to reduce repeat revascularization and major adverse cardiac events (MACE).[14] However, there are situations where a BMS can be more appropriate, for example when a short duration of dual antiplatelet therapy (DAPT) is desirable or for treating focal lesions in large diameter vessels.[14,15] As old degenerative SVGs are usually of a large calibre and these patients are frequently old and frail with multiple comorbidities, BMS may be considered an appropriate choice. Indeed, different registries have shown that from one-third to half of patients undergoing PCI of SVGs receive BMS. However, more recent data suggest a growing use of newer generation DES in treating SVG disease.[16]

Only a few studies have compared BMS and DES for PCI of SVGs and generally shown that use of DES in SVGs can reduce the need for repeat revascularization but with no survival benefit.[17–22] However, these studies have largely compared either only first-generation DES or a combination of first- and newer generation DES against BMS with limited data on contemporary DES platforms. Conversely, data from the DELAYED RRISC trial (Death and Events at Long-Term Follow-Up Analysis: Extended Duration of the Reduction of Restenosis in Saphenous Vein Grafts With Cypher Stent) reported worse outcomes for patients with first-generation sirolimus-eluting stents compared with BMS (29% versus 0%, $P<0.001$ for mortality, 58% versus 41%, $P=0.13$ for MACE during 3-year follow-up).[20] In contrast, more contemporary registry data from the Veterans Affairs CART Program (Clinical Assessment, Reporting and Tracking) suggest the use of newer generation DES is associated with lower mortality than BMS (hazard ratio [HR], 0.72; 95% confidence interval [CI], 0.57–0.89), and similar rates of myocardial infarction (MI; HR, 0.94; 95% CI, 0.71–1.24) at long-term follow-up (>2 years), but there was no difference in mortality or MI between first- and newer generation DES in this study.[16] In view of limited and divergent results in the literature, we aimed to assess stent choice and clinical outcomes after PCI to SVGs in patients receiving BMS, first-generation DES, and newer generation DES in a large unselected all-comer national data set from the BCIS (British Cardiovascular Intervention Society).

Methods

Study Design and Data Collection

The BCIS database records information on PCI procedures in United Kingdom with data collection managed by the NICOR (National Institute of Cardiovascular Outcomes Research).[23–27] This is a retrospective analysis of prospectively collected national data for all patients undergoing PCI of SVGs in the United Kingdom from January 2006 to December 2013. Using the Medical Research Information Services, we tracked participants in this database via the patient's National Health Service (NHS) number, a unique identifier for any person registered within the NHS in England and Wales, for mortality and adverse outcomes. Institutional review board approval and patient consent were not obtained because this study was an analysis routinely collected anonymized data.

Variables and Outcomes Collected

We collected data on participants' demographics (age, sex, smoking status, and family history of heart disease) and comorbidities (diabetes mellitus, hypertension, hyperlipidemia, previous MI, stroke, peripheral vascular disease, and renal disease). In addition, data were also collected on left ventricular ejection fraction, access site, use of glycoprotein IIb/IIIa inhibitor, use of thrombectomy device, cardiogenic shock, use of intra-aortic balloon pump, use of ventilatory support, and use of distal protection devices.

Patients undergoing PCI to an SVG were grouped into 3 cohorts based on stent type, that is, BMS group (including Titan-2), first-generation DES (Cypher, Taxus Liberte, Eucatax, Achieve, Sorin, Costar stents) and newer generation DES (Promus, Xience, Resolute, Biomatrix, Endeavor, Biofreedom, Nobori, and Yukon stents).

We evaluated all-cause mortality at 30-day and 1-year follow-up and major adverse cardiovascular events (MACE; defined as a composite of in-hospital mortality, in-hospital myocardial reinfarction, and target vessel revascularization).

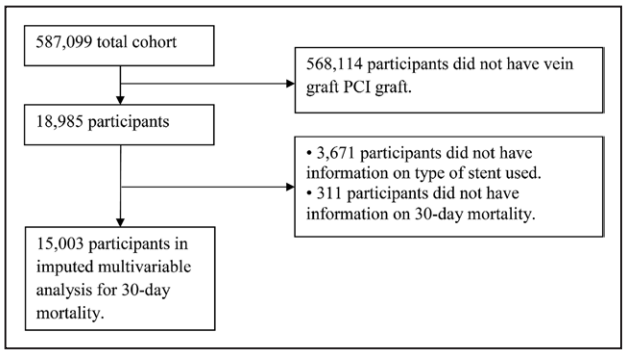

Figure 1. Flow diagram of participant inclusion. PCI indicates percutaneous coronary intervention.

Statistical Methods

We excluded patients with missing data for 30-day mortality, stent type, or age. A flow diagram graphically describes how the final cohort was derived (Figure 1). Summary statistics are presented as mean±SD for continuous data and percentage or proportions for categorical variables, according to the stent group (BMS, first-generation DES, and second-generation DES). The clinical characteristics of the 3 groups were compared using ANOVA and χ^2 tests for continuous and categorical variables, respectively. The risk of adverse outcomes was estimated with multiple logistic regressions with imputation for missing variables. Multiple imputations by chained equations was performed using mi impute chained function in Stata to generate 10 complete data sets. We also calculated the propensity score for each stent group and used it to match and estimate adjusted risk estimates in pairwise stent group comparisons (BMS versus first-generation DES, BMS versus second-generation DES, and first-generation versus second-generation DES). To achieve this, we used the teffects psmatch function in Stata to estimate the average treatment effects while accounting for baseline differences across the groups. For each group member, we calculated propensity scores using all the covariates across the 10 imputed datasets. Using the standard setting for matching, a minimum of 1 neighbor was matched for all observations. Tolerance for the overlap assumption was set to 10^{-5}. For consistency with the main analyses and an easier comparison, we transformed the differences in probability to odds ratios (ORs), after making assumptions about the baseline probability risk with BMS. Statistical analyses were performed using Stata v13 (Stata Corp, TX).

Results

Study Cohort

A total of 18 985 patients underwent PCI to at least 1 SVG in England and Wales from January 2006 to December 2013. The study cohort with complete data for stent type and 30-day mortality was 15 003 (79.0%) as 3982 patients had missing values for type of stent used (3671 patients) or 30-day mortality (311 patients; Figure 1). The characteristics of those included in the study and those excluded are shown in Table I in the Data Supplement. A total of 5685 patients (38%) received BMS and 9318 (62%) received DES. Among patients receiving DES, 2265 (24.3%) received first-generation DES and 7053 (75.7%) received second-generation DES. There was a temporal change in the use of stents (Figure 2). In 2007, 42% of patients received BMS with the remainder receiving first-generation DES. By 2013, use of first-generation DES had ceased with the ratio of newer generation DES:BMS being 78% to 22%, respectively.

Characteristics of Participants

The characteristics of patients in the 3 groups are shown in Table 1. There were significant differences in the demographic and clinical characteristics within groups, in particular, patients treated with first-generation DES being younger. Comorbidities such as diabetes mellitus, hypertension, hyperlipidemia, previous MI, and peripheral vascular disease were more prevalent in patients receiving second-generation DES. Multivessel disease was significantly different among stent types (21% versus 27% versus 14%) for second-generation DES, first-generation DES, and BMS, respectively.

Clinical Outcomes

The highest unadjusted rates of in-hospital MACE and 30-day and 1-year mortality were observed in the BMS group. We found that the in-hospital MACE rate according to stent type was 3% (n=167), 1% (n=31), and 2% (103) for BMS, first-generation DES, and second-generation DES, respectively. Mortality rates were also significantly lower for DES than for BMS at both 30 days (3% [n=171], 0.9% [n=21], and 1% [n=94]) and 365 days (9% [n=491] versus 5% [n=106] versus 6% [n=371]). The specific components of MACE according to the stent type is shown in Table II in the Data Supplement. Adjusted MACE and mortality were also significantly lower with the use of DES (Table 2). For in-hospital MACE, second-generation stent use was associated with a significant reduction in odds of MACE (OR, 0.51; 95% CI, 0.38–0.68; P<0.001) compared with BMS. The risk for adjusted 30-day mortality was significantly lower in patients with second-generation DES (OR, 0.43; 95% CI, 0.32–0.59; P<0.001) with a trend toward lower risk that was not significant for first-generation DES (OR, 0.63; 95% CI, 0.37–1.10; P=0.104) than in those with BMS. At longer follow-up of 1 year, only second-generation stents were associated with decreased mortality (OR, 0.60; 95% CI, 0.51–0.71; P<0.001) compared with BMS.

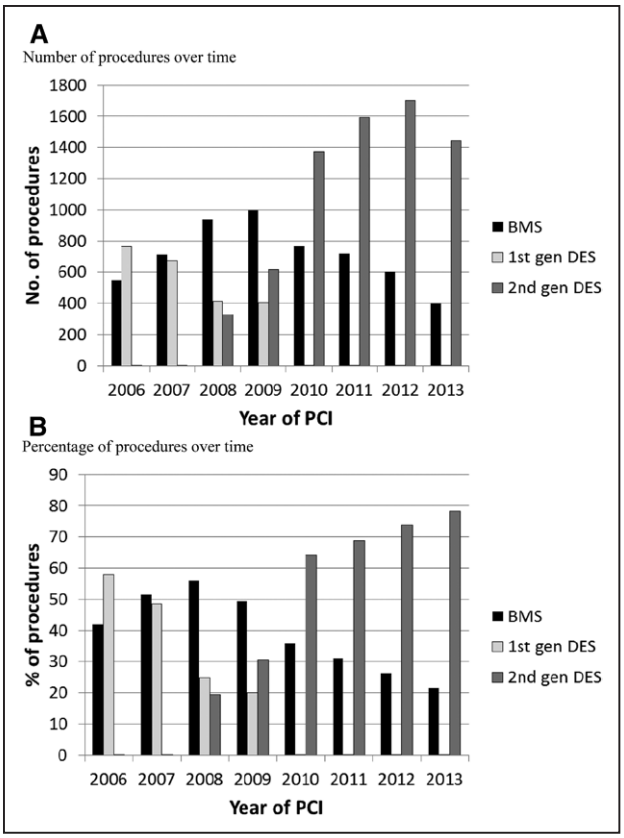

Figure 2. Changes in (**A**) number of procedures and (**B**) percentage of procedures over time. BMS indicates bare metal stents; DES, drug-eluting stent; and PCI, percutaneous coronary intervention.

Propensity Score Matching for Adverse Outcomes

The results of propensity score matching are shown in Table 3, and the matching success diagnostics is shown in Table III in the Data Supplement. For in-hospital MACE, use of both first- and second-generation DES significantly reduced events compared with BMS (Table 3). Similarly, use of

Table 1. Descriptive Statistics

Variable	BMS (n=5685)	First-Generation DES (n=2265)	Second-Generation DES (n=7053)	*P* Value		
				First-Generation DES vs BMS	Second-Generation DES vs BMS	Second- vs First-Generation DES
Age, y	70 (±10)	68 (±9)	69 (±10)	<0.001	<0.001	<0.001
Male sex, n (%)	4757 (84)	1868 (83)	5891 (84)	0.22	0.98	0.21
Smoking status, n (%)				0.053	<0.001	0.038
Never	1629 (33)	632 (34)	2332 (37)			
Ex-smoker	2643 (54)	1013 (55)	3230 (52)			
Smoker	651 (13)	204 (11)	705 (11)			
Diabetes mellitus, n (%)	1565 (29)	645 (31)	2236 (33)	0.096	<0.001	0.050
Hypertension, n (%)	3539 (64)	1351 (63)	4674 (68)	0.54	<0.001	<0.001
Hyperlipidemia, n (%)	3564 (65)	1440 (67)	4740 (69)	0.014	<0.001	0.22
Previous MI, n (%)	3250 (61)	1231 (60)	4071 (61)	0.23	0.66	0.36
Previous stroke, n (%)	373 (7)	111 (5)	467 (7)	0.012	0.94	0.009
Peripheral vascular disease, n (%)	592 (11)	198 (9)	680 (10)	0.064	0.13	0.41
Renal disease, n (%)	267 (5)	90 (4)	317 (5)	0.24	0.57	0.43
Previous PCI, n (%)	1836 (34)	903 (43)	2862 (42)	<0.001	<0.001	0.21
Left ventricular ejection fraction, n (%)				0.033	<0.001	0.017
Good	1497 (53)	640 (57)	2097 (57)			
Moderate	1004 (35)	355 (32)	1288 (35)			
Poor	342 (12)	123 (11)	316 (9)			
Family history of CAD, n (%)	2404 (52)	994 (55)	2967 (49)	0.019	0.004	<0.001
Radial access, n (%)	1402 (25)	373 (17)	2435 (35)	<0.001	<0.001	<0.001
Glycoprotein IIb/IIIa inhibitor, n (%)	1374 (25)	675 (32)	1351 (20)	<0.001	<0.001	<0.001
Bivalirudin, n (%)	95 (2)	30 (2)	167 (2)	0.37	0.013	0.010
Multivessel disease, n (%)	820 (14)	604 (27)	1511 (21)	<0.001	<0.001	<0.001
Cardiogenic shock, n (%)	125 (2)	9 (0.5)	73 (1)	<0.001	<0.001	0.010
Intra-aortic balloon pump, n (%)	134 (2)	30 (1)	77 (1)	0.008	<0.001	0.26
Thrombus aspiration, n (%)	481 (9)	68 (3)	603 (9)	<0.001	0.83	<0.001
Ventilatory support, n (%)	83 (2)	10 (0.6)	61 (1)	0.001	0.001	0.098
Embolic protection device, n (%)	875 (16)	311 (14)	1021 (15)	0.13	0.19	0.56
Diagnosis, n (%)				<0.001	<0.001	<0.001
Stable angina	2082 (38)	1122 (51)	2689 (39)			
NSTEMI	2682 (49)	980 (45)	3521 (51)			
STEMI	693 (13)	88 (4)	686 (10)			
In-hospital MACE, n (%)	167 (3)	31 (1)	103 (2)	<0.001	<0.001	0.87
Death at 30 d, n (%)	171 (3)	21 (0.9)	94 (1)	<0.001	<0.001	0.13
Death at 365 d, n (%)	491 (9)	106 (5)	371 (6)	<0.001	<0.001	0.058

BMS indicates bare-metal stent; CAD, coronary artery disease; DES, drug-eluting stent; MACE, major adverse cardiovascular events; MI, myocardial infarction; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention; and STEMI, ST-segment–elevation myocardial infarction.

first- and second-generation DES was associated with significant reductions in 30-day mortality ($P<0.001$ and $P<0.001$) when compared with BMS. For 1-year mortality, there was a reduction with use of second-generation DES ($P<0.001$) but not with first-generation DES ($P=0.373$), compared with BMS. The effects were generally small, but statistically significant because the outcomes are rare (Table 1). For example, first-generation DES was estimated 1.29% less likely to be associated with in-hospital MACE than BMS, but the baseline probability risk for BMS is 3%. The results after transforming probabilities to ORs are reported in Table IV in the Data Supplement. In the propensity score matching

Table 2. Multivariable Logistic Regression for Adverse Outcomes According to the Stent Type With Multiple Imputations

Outcomes*	Odds Ratio (95% CI)	*P* Value
In-hospital MACE (n=15 003)		
Bare-metal stent	1.00 (reference)	
First-generation DES	0.77 (0.50–1.21)	0.262
Second-generation DES	0.51 (0.38–0.68)	<0.001
Mortality at 30 d (n=15 003)		
Bare-metal stent	1.00 (reference)	
First-generation DES	0.63 (0.37–1.10)	0.104
Second-generation DES	0.43 (0.32–0.59)	<0.001
Mortality at 365 d (n=15 003)		
Bare-metal stent	1.00 (reference)	
First-generation DES	0.78 (0.61–1.01)	0.059
Second-generation DES	0.60 (0.51–0.71)	<0.001

Multivariable estimates with 10 imputations and adjusted for age, sex, smoking status, diabetes mellitus, hypertension, hyperlipidemia, previous myocardial infarction, previous stroke, peripheral vascular disease, renal disease, previous percutaneous coronary intervention, left ventricular ejection fraction, family history of coronary artery, radial access, glycoprotein IIb/IIIa inhibitor, bivalirudin, multivessel disease, cardiogenic shock, intra-aortic balloon pump, thrombus aspiration, ventilatory support, embolic protection device, and diagnosis. CI indicates confidence interval; DES, drug-eluting stent; and MACE, major adverse cardiovascular events.

analyses, we continued observing the positive associations for both first- and second-generation DES with outcomes, compared with BMS.

Discussion

Our data, derived from a large all-comer national registry of patients undergoing PCI of SVG, suggest that use of DES is associated with better outcomes when compared with BMS. There is reduction is MACE and mortality in DES-treated patients, in particular those receiving newer generation DES.

Our study overcomes the limitations of small sample size seen in the 3 randomized trial (RRISC [Reduction of Restenosis in Saphenous Vein Grafts With Cypher Sirolimus-Eluting Stent], SOS [Stenting of Saphenous Vein Grafts], and ISAR-CABG [Efficacy Study of Drug-Eluting and Bare Metal Stents in Bypass Graft Lesions]) comparing DES and BMS in SVG lesions. RRISC was a prospective, double-blind, randomized trial of patients (n=75 patients; 96 SVG lesions) treated with first-generation sirolimus-eluting Cypher (Cordis Ltd, NJ) DES (n=38 patients; 60 stents) or BMS (n=37 patients; 54 stents). The 2 groups were well balanced for baseline clinical and angiographic characteristics. At 6-month follow-up, the DES group had less in-stent restenosis (DES 11.3% versus BMS 30.6%; relative risk [RR], 0.37; 95% CI, 0.15–0.97; *P*=0.024), target lesion revascularization (DES 5.3% versus BMS 21.6%; RR, 0.24; 95% CI, 0.05–1.0; *P*=0.047), and target vessel revascularization (DES 5.3% versus BMS 27%; RR, 0.19; 95% CI, 0.05–0.83; *P*=0.012). Median neointimal volume on intravascular ultrasound was also substantially reduced in the DES group (DES 1 mm^3 versus BMS 24 mm^3; *P*<0.001). Death and MI rates were not different at 6 months.[19] A post hoc, long-term follow-up, DELAYED RRISC was subsequently conducted to report clinical events up to 3 years (median, 32 months) after the index procedure. An increase in death rate in DES patients (DES 29% versus BMS 0%; *P*<0.001) was observed although the trial was not powered for clinical outcomes. There were 11 all-cause and 7 cardiac deaths in the DES group. Stent thrombosis according to Academic Research Consortium (ARC) criteria occurred in 5 DES patients.[20] However, patients receiving DES were mandated to receive DAPT for only 2 months, which could potentially explain higher rates of stent thrombosis and mortality in the DES group. The SOS trial randomized 80 patients with 112 lesions in 88 SVGs to a BMS (39 patients; 43 grafts; 55 lesions) or first-generation paclitaxel-eluting Taxus (Boston Scientific Corp, MN) DES (41 patients; 45 grafts; 57 lesions). Binary angiographic restenosis was substantially lower in the DES group (DES 9% versus BMS 51%; RR, 0.18; 95% CI, 0.07–0.48; *P*<0.001). During a median follow-up of 1.5

Table 3. Propensity Score Matching Analysis on 10 Imputed Data Sets, Reporting ATE*

Analysis	Method	Group	Coefficient†	95% CI	*P* Value
In-hospital MACE	Propensity score matching, ATE	First-generation DES vs BMS (n=7950)	−0.0129	−0.0212 to −0.0047	0.002
		Second-generation DES vs BMS (n=12 738)	−0.0096	−0.0165 to −0.0028	0.006
30-d mortality	Propensity score matching, ATE	First-generation DES vs BMS (n=7950)	−0.0166	−0.0233 to −0.0099	<0.001
		Second-generation DES vs BMS (n=12 738)	−0.0146	−0.0218 to −0.0074	<0.001
1-y mortality	Propensity score matching, ATE	First-generation DES vs BMS (n=7950)	−0.0198	−0.0639 to 0.0244	0.373
		Second-generation DES vs BMS (n=12 738)	−0.0332	−0.0457 to −0.0207	<0.001

ATE indicates average treatment effects; BMS, bare-metal stent; CI, confidence interval; DES, drug-eluting stent; and MACE, major adverse cardiovascular event.

*To better control for the baseline differences across the groups, multiple imputation propensity score matching (mi estimate:teffects psmatch on Stata) was used to estimate the ATE. The method used all the predictors in Table 1 in 3 separate multiple imputation logistic regression models (first-generation DES vs BMS, second-generation DES vs BMS and second-generation DES vs first-generation DES), calculating propensity scores for group membership. Standard settings for the matching algorithm were used. A minimum of 1 neighbor was requested, and all observations were considered as potential matches regardless of how dissimilar their propensity scores were. Tolerance for the overlap assumptions was set to 10^{-5}. Simple logistic regression models were run (the only predictor being group membership) to obtain the ATE, and the ATE is a measure of the difference in mean outcomes between participants assigned to the treatment and participants assigned to the control. The output of the teffects psmatch on Stata are coefficients and 95% CIs rather than odds ratios.

†The coefficient is the difference in probability. Using the first row as an example, a coefficient of −0.0129 means that first-generation DES are 1.29% less likely to be associated with in-hospital MACE than with BMS.

years, the DES group had less target lesion revascularization (28% versus 5%; HR, 0.38; 95% CI, 0.15–0.74; *P*=0.003) and target vessel failure (46% versus 22%; HR, 0.65; 95% CI, 0.42–0.96; *P*=0.03), a trend toward less target vessel revascularization (31% versus 15%; HR, 0.66, 95% CI, 0.39–1.05; *P*=0.08) and MI (31% versus 15%; HR, 0.67; 95% CI, 0.40–1.08; *P*=0.10).[21] However, there was no difference in mortality (5% versus 12%; HR, 1.56; 95% CI, 0.72–4.11; *P*=0.27) at 1.5 years.[21] Extended clinical follow-up (median of 35 months) was subsequently obtained showing no difference in all-cause (HR, 2.04; *P*=0.19) or cardiac mortality (HR, 0.62; *P*=0.51).[22] However, the DES group had a lower incidence of MI (HR, 0.32; *P*=0.01), target lesion revascularization (HR, 0.20; *P*=0.004), target vessel revascularization (HR, 0.41; *P*=0.03), and target vessel failure (HR, 0.34; *P*=0.001), as well as a trend toward less definite or probable stent thrombosis (HR, 0.15; *P*=0.08).[22] The larger ISAR-CABG trial (n=610) randomized patients with diseased SVGs to DES (1 of the 3 types: permanent-polymer paclitaxel-eluting stents, permanent-polymer sirolimus-eluting stents, or biodegradable-polymer sirolimus-eluting stents) and BMS and reported a reduction in the primary end point of MACE at 1 year in the DES group (DES 15.4% versus BMS 22.1%; *P*=0.03), which was mainly driven by a near 50% relative reduction in the risk of target lesion revascularization (DES 7.2% versus BMS 13.1%; *P*=0.02), with no significant differences in mortality.[18] A meta-analysis comparing DES with BMS in SVG intervention (which also included nonrandomized studies) has reported lower mortality, MACE, target lesion revascularization, and target vessel revascularization without increased risk of MI or stent thrombosis.[28] Multiple other meta-analyses comparing DES with BMS in SVG intervention have demonstrated consistent results of improved efficacy with DES and no significant safety hazards.[29–35]

Our data provide supportive evidence that use of newer generation DES is associated with improved outcomes and survival in patients undergoing PCI in SVGs. These findings are consistent with another contemporary registry of PCI in SVGs.[16] It is possible that the difference in outcomes is because of the fact that BMS are being used in older or high-risk patients or in patients with other morbidities that are not collected in registry data sets. Nevertheless, propensity-matching analysis from the Veterans Affairs CART Program,[16] data from older patients in the Medicare-linked National Cardiovascular Data Registry CathPCI Registry[36] and our propensity-matched analysis suggest that the advantage seen with DES use may not be all because of differences in conventionally measured patient characteristics. It is therefore possible that this survival advantage with second-generation DES is a real entity. DES use reduces restenosis, need for repeat revascularization and associated adverse events. However, it is also plausible that this is not the only mechanism for improved outcomes. The newer generation DES with biocompatible and bioresorbable polymers have low rate for stent thrombosis, which is definitely lower than first-generation DES and possibly also lower than BMS. Moreover, DES use is generally associated with longer duration of dual-antiplatelet therapy, which may in turn be associated with a reduction in adverse ischemic and thrombotic events.[37] The association with a survival advantage seen with newer generation DES in the treatment of SVGs is also consistent with recently reported meta-analysis of 51 clinical trials (n=52 158 patients) showing that newer generation DES are associated with lower rates of mortality, stent thrombosis, and MI than BMS and first-generation DES for the treatment of native coronary arteries.[38] An adequately powered randomized controlled trial is warranted to confirm these findings.

There are no randomized data comparing newer versus first-generation DES for the treatment of SVG disease. In a multicenter analysis of 172 real-world patients comparing first-generation DES, SVG intervention with sirolimus- and paclitaxel-eluting stents resulted in nonsignificant differences in survival (HR, 1.28; 95% CI, 0.39–4.25; *P*=0.69) and target vessel revascularization (HR, 2.54; 95% CI, 0.84–7.72; *P*=0.09).[36] Previously, there have been limited data on use of newer generation DES for PCI to SVGs. In the SOS-Xience V study (Stenting of Saphenous Grafts With Xience V), 40 patients with SVG lesions were treated with a newer generation everolimus-eluting stent (Xience-V; Abbott Vascular Ltd, Santa Clara). Of these 40 patients, 27 underwent 12-month coronary angiography and 12 (only 1 of whom had in-stent restenosis) also had follow-up optical coherence tomography evaluation. Optical coherence tomography strut-level analysis (n=2584 struts) showed that 96% struts were covered at 12 months; however, 9% struts were mal-apposed.[37] These findings can potentially create uncertainty about the role of newer generation DES in treating SVG lesions. Our data from a large all-comer national registry and propensity-matched cohort provide further reassurance that the newer generation DES seems effective and safe for the treatment of SVG disease. Finally, although BMS have conventionally been used in older, multimorbid patients at higher risk of bleeding complications where shorter DAPT duration would be preferable, the recent LEADERS FREE trial (A Prospective Randomized Comparison of the BioFreedom Biolimus A9 Drug Coated Stent Versus the Gazelle Bare Metal Stent in Patients With High Risk of Bleeding) using a polymer and carrier-free biolimus coated BioFreedom stent (Biosensors Europe) was superior to a BMS with respect to the primary safety and efficacy end points when used with a 1-month course of DAPT[38] in patients at high risk of bleeding complications. It is therefore likely that the use of BMS in SVG will decline further.

Study Strengths and Limitations

The strengths of these data are that they represent among the largest analysis of PCI to SVG in contemporary practice, including an almost complete collection of all PCI procedures performed in England and Wales. They therefore reflect an all-comers, real-world experience that includes many high-risk patients who are often excluded from randomized controlled trials.

This study has several potential limitations. First, although mortality tracking within the United Kingdom is robust, the cause of death is not currently available, and the MACE outcomes are self-reported and are not formally adjudicated. Therefore, the analysis is subject to reporting biases, and complications may be under-reported. Second, we do not

have data for duration of DAPT. Third, our analysis report outcomes derived from grafts as the BCIS data set does not differentiate between venous and arterial grafts. Previous data derived from the National Cardiovascular Data Registry CathPCI registry suggest that arterial grafts represented 2.5% of all PCI procedures undertaken to bypass grafts in the United States; hence, it is likely that the majority of graft interventions reported here are those undertaken in saphenous vein grafts.[39] Finally, our analysis is observational, with inherent limitations of any such data analysis. Nonetheless, we used robust statistical analyses including multiple logistic regression and propensity-matching to adjust for known confounders.

Conclusions

In one of the largest analyses to date, we have observed that patients receiving DES (particularly newer generation DES) for the treatment of SVG disease have lower rates of in-hospital MACE, 30-day mortality, and 1-year mortality, compared with those receiving BMS. Patients undergoing PCI for SVG disease should therefore receive a DES, unless any contraindication or higher risk of bleeding with DAPT or requirement for a short DAPT course.

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Disclosures

None.

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Choice of Stent for Percutaneous Coronary Intervention of Saphenous Vein Grafts

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SUPPLEMENTARY MATERIAL

Supplemental Table 1: Missing data

Variable	Number of available values (%)	Number of missing values (%)
Age	14,998 (99.97%)	5 (0.03%)
Male gender	14,969 (99.8%)	34 (0.2%)
Smoker (current or ex)	13,039 (87%)	1,964 (13%)
Diabetes	14,383 (96%)	620 (4%)
Hypertension	14,539 (97%)	464 (3%)
Hyperlipidemia	14,539 (97%)	464 (3%)
Previous MI	14,041 (94%)	962 (6%)
Previous stroke	14,539 (97%)	464 (3%)
Peripheral vascular disease	14,539 (97%)	464 (3%)
Renal disease	14,785 (99%)	218 (1%)
Previous PCI	14,433 (96%)	570 (4%)
Left ventricular ejection fraction	7,662 (51%)	7,341 (49%)
Family history of CAD	12,515 (83%)	2,488 (17%)
Radial access	14,644 (98%)	359 (2%)
Glycoprotein IIb/IIIa inhibitor	14,107 (94%)	896 (6%)
Bivalirudin use	13,999 (93%)	1,004 (7%)
Multivessel disease	12,068 (80%)	2,935 (20%)
Cardiogenic shock	13,589 (91%)	1,414 (9%)
Use of intra-aortic balloon pump	14,309 (95%)	694 (5%)
Thrombus aspiration	14,414 (96%)	589 (4%)
Ventilatory support	13,288 (89%)	1,715 (11%)
Embolic protection device	14,502 (97%)	501 (3%)
Diagnosis	14,543 (97%)	460 (3%)
Year	15,003 (100%)	0 (0%)
MACE	14,470 (96%)	533 (4%)
Death at 30 days	15,003 (100%)	0 (0%)
Death at 365 days	14,268 (95%)	735 (5%)

MI=myocardial infarction, PCI=percutaneous coronary intervention, MACE=major adverse cardiovascular event.

Supplemental Table 2: Outcomes which collectively combine to produce in-hospital MACE

Variable	Bare metal stent (BMS)	1st gen. DES	2nd gen. DES	p-value		
	6,680	2,101	5,987	1st gen. DES vs BMS	2nd gen. DES vs BMS	2nd vs 1st gen. DES
Non-q wave myocardial infarction	31 (0.46%)	11 (0.52%)	23 (0.38%)	0.73	0.49	0.40
Death in-hospital	100 (1.5%)	13 (0.62%)	52 (0.87%)	0.002	0.001	0.27
Reinfarction	7 (0.10%)	2 (0.10%)	6 (0.10%)	0.91	0.94	0.95
Reintervention PCI	32 (0.48%)	5 (0.24%)	14 (0.23%)	0.14	0.022	0.97

BMS=bare metal stent, DES=drug eluting stent, gen.=generation, PCI=percutaneous coronary intervention.

Supplemental Table 3: Matching success diagnostics for propensity model

Comparison	Group	Mean (SD)	Median (IQR)
1st generation DES vs BMS	Case (1st gen DES)	0.7151 (0.2231)	0.7000 (0.5236-0.9939)
	Control (BMS)	0.7151 (0.2230)	0.7000 (0.5235-0.9940)
	Abs(Case-Control)	0.00029 (0.00110)	0.00011 (0.00004-0.00027)
2nd generation DES vs BMS	Case (2nd gen DES)	0.4563 (0.2558)	0.3400 (0.2541-0.6320)
	Control (BMS)	0.4463 (0.2557)	0.3400 (0.2542-0.6319)
	Abs(Case-Control)	0.00019 (0.00139)	0.00005 (0.00002-0.00014)

BMS=bare metal stent, DES=drug eluting stent, gen.=generation, PCI=percutaneous coronary intervention, IQR=interquartile range.

Distribution of propensity scores and residual propensity score differences between pairing for each comparison are shown and quality of matching for propensity matched imputed cohort.

Supplemental Table 4: Propensity score matching analysis on 10 imputed datasets, reporting odds ratios (transformed from the average treatment effect reported in Table 3 of the main paper)

Analysis	Method	Group	Odds ratio	95% CI		p-value
In-hospital MACE	Propensity score matching, ATE	1st gen. DES vs BMS (n=7,950)	0.56	0.29	0.84	0.002
		2nd gen. DES vs BMS (n=12,738)	0.67	0.44	0.90	0.006
30 day mortality	Propensity score matching, ATE	1st gen. DES vs BMS (n=7,950)	0.44	0.22	0.66	<0.001
		2nd gen. DES vs BMS (n=12,738)	0.51	0.27	0.75	<0.001
1 year mortality	Propensity score matching, ATE	1st gen. DES vs BMS (n=7,950)	0.76	0.27	1.31	0.373
		2nd gen. DES vs BMS (n=12,738)	0.61	0.47	0.75	<0.001

MACE=major adverse cardiovascular events, BMS=bare metal stent, DES=drug eluting stent, gen.=generation, ATE=average treatment effects.