JACC: CARDIOVASCULAR INTERVENTIONS VOL. 3, NO. 7, 2010
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ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC. DOI: 10.1016/j.jcin.2010.04.012

Outcomes After Implantation of the TAXUS Paclitaxel-Eluting Stent in Saphenous Vein Graft Lesions

Results From the ARRIVE (TAXUS Peri-Approval Registry: A Multicenter Safety Surveillance) Program

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Objectives The aim of this study was to examine the incidence of clinical events after implantation of the TAXUS Express (Boston Scientific Corporation, Natick, Massachusetts) paclitaxel-eluting stent in saphenous vein graft (SVG) lesions in an unselected patient population.

Background Saphenous vein grafts have 1-year occlusion rates of 12% to 20%, with >50% failure by 7 to 10 years. Many diseased SVGs are treated by percutaneous coronary intervention to avoid higher-risk reoperation, but bare-metal stents have 35% to 40% historical SVG restenosis rates by 18 months. Reported outcomes of drug-eluting stents in SVG lesions are limited and mainly retrospective.

Methods The ARRIVE (TAXUS Peri-Approval Registry: A Multicenter Safety Surveillance) program compiled data on 7,492 patients receiving ≥1 TAXUS Express (Boston Scientific) stent, including 474 patients with SVG. All cardiac events were monitored with independent adjudication of end points. Patients enrolled at procedure start with no mandated inclusion/exclusion criteria.

Results The ARRIVE SVG patient 2-year follow-up was 96% complete (457 of 474). The SVG patients had significantly more baseline comorbidities/complex disease than simple-use patients (n = 2,698) undergoing native coronary intervention or other expanded-use patients (n = 4,320 without SVG patients). They had higher 2-year rates of mortality (10.9% vs. 4.2%, $p < 0.001$), myocardial infarction (5.3% vs. 2.2%, $p < 0.001$), and Academic Research Consortium definite/probable stent thrombosis (4.7% vs. 1.4%, $p < 0.001$) than the simple-use group. They also had higher 2-year adverse event rates, including significantly more mortality (10.9% vs. 7.5%, $p = 0.008$) than other expanded-use patients.

Conclusions The ARRIVE SVG patients have significantly different baseline risk and higher clinical risk through 2 years than simple-use and other expanded-use patients. Nonetheless, compared with historical SVG revascularization rates, treatment with paclitaxel-eluting stent seems to offer a reasonable therapeutic option in this high-risk group. (TAXUS ARRIVE: TAXUS Peri-Approval Registry: A Multicenter Safety Surveillance Program; NCT00569491) and (TAXUS ARRIVE 2: A Multicenter Safety Surveillance Program; NCT00569751) (J Am Coll Cardiol Intv 2010;3:742–50) © 2010 by the American College of Cardiology Foundation

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Manuscript received October 29, 2009; revised manuscript received March 23, 2010, accepted April 17, 2010.

Saphenous vein grafts (SVG) historically have had occlusion rates of approximately 12% to 20% after 1 year, progressing to over 50% by 7 to 10 years (1–4). Recently, a large randomized controlled trial (RCT) reported per-patient angiographic vein graft failure rates of >40% by 18 months (5). Given the higher risk of adverse outcomes associated with repeat bypass surgery (6), percutaneous coronary intervention (PCI) is generally the preferred revascularization option for patients with recurrent graft-related disease. In the U.S., 6% to 10% of all PCI are performed in SVGs (7). Patients undergoing PCI of SVG lesions with or without bare-metal stents (BMS) also have a high risk for adverse clinical events due to restenosis or thrombus at the treatment site and/or disease progression elsewhere in the SVG (6,8–12). Implantation of drug-eluting stents (DES) has improved short- and mid-term SVG clinical outcomes compared with BMS in some studies (13–29), but much of the available data are retrospective. Two small prospective RCTs have reported significantly lower angiographic restenosis with DES compared with BMS in SVGs during a median follow-up of 18 to 32 months (30–32).

In the absence of large RCTs of SVG stenting, registries can provide insight into the clinical outcomes of such patients. The ARRIVE (TAXUS Peri-Approval Registry: A Multicenter Safety Surveillance) Program captured usage patterns and outcomes in 7,492 patients, including 474 patients who underwent SVG stenting (33,34). With data from the ARRIVE program, we evaluated 2-year clinical outcomes after SVG DES implantation, compared them with outcomes in patients receiving the same DES in noncomplex or complex native coronary lesions, and examined outcomes in the SVG subgroup in relation to other published studies.

Methods

Study design, data collection, and follow-up. The TAXUS ARRIVE Program, which has been described previously, included 2 prospective, multicenter U.S. safety surveillance registries (ARRIVE 1 [50 sites, February to May 2004] and ARRIVE 2 [53 sites, October 2004 to October 2005]) (33,34). The program was designed to enroll consecutive patients treated with the slow-release TAXUS Express (Boston Scientific Corporation, Natick, Massachusetts) paclitaxel-eluting stent (PES). No specific inclusion/exclusion criteria were mandated. Patients who gave informed consent for participation under a protocol approved by the local institutional review board in conformity with the Declaration of Helsinki and U.S. Food and Drug Administration guidelines were enrolled at the time of procedure initiation. Follow-up angiography was performed at operator discretion. Dual antiplatelet therapy (DAPT) with aspirin and clopidogrel or ticlopidine was begun before or immediately after the procedure. Aspirin was continued indefinitely and thienopyridine was recommended for 6 months per the TAXUS Express (Boston Scientific Corporation) stent Directions For Use. At 1 year, 67.7% of ARRIVE patients (4,687 of 6,927) were taking DAPT with 53.1% (3,487 of 6,569) at 2 years (35). The SVG patients were somewhat higher at 74.2% (322 of 434) and 66.6% (269 of 404), respectively. Both studies are registered (see clinical trial registry data after abstract; identifiers NCT00569491 and NCT00569751).

An independent clinical events committee with no financial conflicts of interest with the sponsor determined the relationship of reported cardiac events to the study device; an event was deemed related to the TAXUS stent if it occurred at the stented segment or if the relationship to the stent could not be excluded on the basis of existing information (33). Data were source verified for death, major cardiac events (cardiac death, myocardial infarction [MI], target vessel revascularization [TVR], target lesion revascularization [TLR] [defined as "TAXUS-stent-related" TVR]), and stent thrombosis (ST) along with an additional 10% to 20%/site random sampling of patients. Adjudication of ST per the Academic Research Consortium (ARC) definite/probable definition (36) was performed by an independent committee at the Harvard Clinical Research Institute.

Abbreviations and Acronyms

BMS = bare-metal stent(s)
DAPT = dual antiplatelet therapy
DES = drug-eluting stent(s)
MI = myocardial infarction
PCI = percutaneous coronary intervention
PES = paclitaxel-eluting stent(s)
RCT = randomized controlled trial
SES = sirolimus-eluting stent
ST = stent thrombosis
SVG = saphenous vein graft
TLR = target lesion revascularization
TVR = target vessel revascularization

Statistical analysis. For baseline variables, simple proportions were used with 2-sided p values from a Student *t* test for continuous variables (summarized as mean ± 1 SD) and chi-square test for discrete variables (presented as frequencies and group percentages). Statistical analyses of events were carried out on the basis of the clinical events committee assessment of relation to the TAXUS stent. The Kaplan-Meier product method (log-rank p value) was used for time-to-event analyses. Backward Cox proportional hazards regression was used to assess 41 variables (Appendix) to identify predictors of major events; the threshold to remain in the model was $p = 0.10$. All analyses were performed with SAS System Software version 8.0 or higher (SAS Institute, Cary, North Carolina); $p < 0.05$ was considered statistically significant.

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Results

Patient and procedural characteristics. Of 7,492 total ARRIVE patients, 474 (6.3%) underwent stenting of an SVG lesion (578 lesions). Most ARRIVE cases (n = 4,794) were considered expanded-use on the basis of patient and/or lesion characteristics outside the simple-use subgroup (n = 2,698) who would have met the criteria for inclusion in the TAXUS IV pivotal trial (37). As shown in Table 1, SVG patients had significantly more baseline comorbidities and complex disease than the simple-use subgroup as well as the cohort of other expanded-use, non-SVG cases (n = 4,320). Patients who underwent SVG stenting were mostly men and had a high prevalence of diabetes, prior MI, and prior PCI. Table 2 shows procedural data for the SVG subgroup. Primary stenting was performed in approximately one-half of SVG lesions, and an embolic protection device was used in 29% of SVG patients at the discretion of the physician.

Clinical outcomes. Among ARRIVE SVG patients, clinical follow-up was available in 98% (465 of 474) at 1 year and 96% (457 of 474) at 2 years. Clinical outcomes through 2 years (Kaplan-Meier analysis) in the SVG, the simple-use, and the other expanded-use (minus SVG) cohorts are shown in Table 3 and Figure 1. Rates for mortality, all MI, and ST were significantly higher in the SVG subgroup than in simple-use patients, although Q-wave MI was not. Mortality was also significantly higher for the SVG cohort than the subgroup of other expanded-use patients. From year 1 to year 2, mortality increased among SVG patients (5.1% and 5.8%, respectively), whereas MI was higher in year 1 (3.5% and 1.8%), and ST was equal (2.4% and 2.3%). By comparison, in the simple-use subgroup, year 1 rates were higher for mortality (2.3% and 1.9%), MI (1.4% and 0.8%), and ST (0.9% and 0.5%). The expanded-use (minus SVG) cohort also had higher event rates in year 1 for mortality (4.1% and 3.4%), MI (2.5% and 1.2%), and ST (2.2% and 1.0%). In the SVG cohort, early (0 to 30 days) ST was 1.3% (6 of 474), and late (31 days to 1 year) ST was 1.1% (5 of 467), as reported previously (35). Among the 21 ARRIVE SVG patients suffering an ST event, 16 underwent subsequent revascularization within 30 days, all of which were TLR. Early and late ST were 0.4% and 0.5%, respectively, in the simple-use subgroup (35) and 1.4% and 0.8%, respectively, in the expanded-use minus SVG cohort.

In patients with SVG stenting, the 2-year rate of target vessel failure (defined as cardiac death, MI, and TVR) was significantly higher than in the simple-use cohort (19.9% vs. 9.6%, respectively, $p < 0.001$) or the subgroup of other expanded-use patients (19.9% vs. 14.8%, $p = 0.005$). In the

Table 1. Comparison of Baseline Patient and Lesion Characteristics in ARRIVE Vein Graft, Simple Use, and Other Expanded Use (Minus Vein Graft) Cohorts

Variable	Vein Graft (n = 474 Patients) (n = 578 Lesions)	Simple Use* (n = 2,698 Patients) (n = 3,112 Lesions)	Other Expanded Use (Minus Vein Graft)* (n = 4,320 Patients) (n = 6,874 Lesions)	p Value Vein Graft vs. Simple Use	p Value Vein Graft vs. Other Expanded Use (Minus Vein Graft)
Patient characteristics					
Age (yrs)	68.0 ± 10.4 (474)	63.0 ± 11.5 (2,698)	64.6 ± 11.9 (4,320)	<0.001	<0.001
Male	80.8% (383)	65.9% (1,777)	66.7% (2,883)	<0.001	<0.001
Hypertension	79.7% (378)	75.4% (2,034)	75.9% (3,279)	0.04	0.06
Hyperlipidemia	88.6% (420)	74.4% (2,007)	75.2% (3,250)	<0.001	<0.001
Diabetes mellitus†	40.3% (191)	29.8% (805)	31.8% (1,372)	<0.001	<0.001
Oral medications	29.5% (140)	21.8% (589)	22.9% (989)	<0.001	0.001
Insulin	15.0% (71)	8.9% (241)	10.5% (452)	<0.001	0.003
Smoking at baseline	12.4% (59)	24.2% (652)	24.4% (1,053)	<0.001	<0.001
Prior MI	48.9% (232)	26.9% (725)	40.9% (1,765)	<0.001	<0.001
Prior PCI	48.1% (228)	34.5% (930)	36.3% (1,567)	<0.001	<0.001
Prior stroke	10.3% (49)	5.0% (135)	6.6% (283)	<0.001	0.002
Lesion characteristics					
RVD (mm)	3.3 ± 0.5 (578)	3.0 ± 0.4 (3,110)	3.0 ± 0.5 (6,873)	<0.001	<0.001
Lesion length (mm)	16.7 ± 12.6 (575)	13.7 ± 5.8 (3,103)	16.4 ± 10.0 (6,848)	<0.001	0.48
B2/C lesion	58.3% (337)	33.3% (1,035)	57.2% (3,927/6,870)	<0.001	0.59
Diameter stenosis (%)	86.9 ± 10.1 (578)	84.4 ± 10.4 (3,111)	85.7 ± 11.2 (6,871)	<0.001	0.01
Moderate/severe calcification (%)	7.3% (42)	0.0% (0)	27.1% (1,863)	<0.001	<0.001
Restenotic lesions	11.6% (67)	0.0% (0)	6.9% (475)	<0.001	<0.001

Data are % (n) or mean ± SD (n); p values are chi-square test (binary) or *t* test (continuous). *Simple-use cases, with or without diabetes, excluded 1 or more of the following: acute myocardial infarction (MI); bifurcation, cardiogenic shock, chronic total occlusion, prior brachytherapy, vein graft stenting, in-stent restenosis, large vessel (reference vessel diameter [RVD] >3.75 mm), left main disease/stenting, long lesion (>28 mm), moderate/severe calcification, multivessel stenting (mean of 2.1 vessels/patient), ostial lesion, renal disease (serum creatinine >3.0 mg/dl or dialysis), severe tortuosity, small vessel (RVD <2.5 mm). Expanded-use cases are those not described as simple-use. †Includes patients treated with diet/exercise plus those treated with oral medications and/or insulin.

ARRIVE = TAXUS Peri-Approval Registry: A Multicenter Safety Surveillance Program; PCI = percutaneous coronary intervention.

Table 2. ARRIVE Vein Graft Stenting Procedural Characteristics

Variable	ARRIVE Vein Graft Stenting (474 Patients; 524 Vessels; 578 Lesions)
Clinical procedural success*	95.3% (462)
Technical success†	99.0% (483)
Implant success‡	94.4% (458)
Pre-dilation	48.3% (279)
Recipient vessel for graft§	
LAD/diagonal	26.3% (152/578)
Circumflex/OM	38.1% (220/578)
RCA/PDA	35.5% (205/578)
Vessels treated/patient	
1	89.7% (425)
2	10.1% (48)
≥3	0.2% (1)
Lesions treated/patient	
1	81.0% (384)
2	16.5% (78)
≥3	2.5% (12)
Stents/vessel	1.4 ± 0.7 (522) (1.0, 6.0)
Stents/lesion	1.2 ± 0.6 (576) (1.0, 6.0)
Total stent length/lesion (mm)	24.0 ± 16.7 (576) (8.0, 180.0)
Stents/patient	1.5 ± 0.9 (473) (1.0, 7.0)
1	67.1% (318)
2	21.9% (104)
≥3	10.8% (51)
Stent length/patient (mm)	29.3 ± 21.0 (473) (8.0, 180.0)
Embolic protection device	28.9% (137)
Pre-stenting TIMI flow grade (per lesion)	
0	3.1% (18)
1	3.5% (20)
2	19.7% (114)
3	73.7% (426)
Post-stenting TIMI flow grade (per lesion)	
0	0.2% (1)
1	0.0% (0)
2	1.2% (7)
3	98.6% (569)
Post-dilation (per lesion)	37.9% (219)
Post-stent balloon pressure (atm)	15.9 ± 4.0 (218) (3.0, 25.0)
Slow flow/no flow after PCI	6.6% (38)
Post-procedure %DS	1.3 ± 6.6 (576) (0.0, 100.0)
Procedural medications‖	
sGPIIb/IIIa inhibitor	44.3% (210)
Bivalirudin	37.3% (177)
Aspirin	71.3% (338)
Clopidogrel	81.0% (384)
DAPT	67.7% (321)

Data are presented as % (n) or mean ± SD (n) (minimum, maximum). *Clinical procedural success was defined as mean lesion diameter stenosis <30%, a Thrombolysis In Myocardial Infarction (TIMI) flow grade of 3 as visually assessed by the physician, and no in-hospital clinical events committee-adjudicated events (n = 485). †Technical success was defined as a successful delivery or deployment of the study stent to the target lesion without device malfunction (n = 488). ‡Implant success was defined as the percentage of implant procedures exhibiting both procedural and technical success (n = 485). §Left main in 1 patient (0.2%). ‖1 patient received ticlopidine (0.2%).

DAPT = dual antiplatelet therapy (aspirin plus clopidogrel/ticlopidine); DS = diameter stenosis; LAD = left anterior descending artery; OM = obtuse marginal; PDA = posterior descending artery; RCA = right coronary artery; other abbreviations as in Table 1.

Table 3. Death and MI in ARRIVE Vein Graft, Simple-Use, and Other Expanded-Use (Minus Vein Graft) Cohorts

	Vein Graft (n = 474 Patients)		Simple Use* (n = 2,698 Patients)		Other Expanded Use (Minus Vein Graft)* (n = 4,320 Patients)		p Value Vein Graft vs. Simple-Use	p Value Vein Graft vs. Other Expanded-Use (Minus Vein Graft)
Clinical Event*	1 yr	2 yrs	1 yr	2 yrs	1 yr	2 yrs		
Death	5.1 (24)	10.9 (50)	2.3 (60)	4.2 (108)	4.1 (173)	7.5 (303)	<0.001	0.008
Cardiac	3.5 (16)	7.1 (32)	1.3 (33)	2.1 (54)	2.6 (110)	4.3 (174)	<0.001	0.008
MI	3.5 (16)	5.3 (24)	1.4 (36)	2.2 (56)	2.5 (103)	3.7 (149)	<0.001	0.081
Q-wave MI	0.7 (3)	1.4 (6)	0.5 (12)	0.7 (19)	0.7 (31)	1.1 (45)	0.19	0.67

Data are from Kaplan-Meier analysis and are expressed as % (n); p values are log-rank (0 to 2 years). *Simple use and expanded use are defined in Table 1.
MI = myocardial infarction; other abbreviations as in Table 1.

SVG cohort, target vessel failure was higher in the first year (11.9%) than during the second year (8.0%), reflecting higher first-year rates for graft-related TVR (8.6% compared with 5.4% in year 2) (Fig. 1). Although much of the observed graft-related TVR was driven by in-stent restenosis (5.7% in year 1, 4.5% in year 2), progressive disease in the SVG outside the stent is a well-known failure mode for SVG intervention, and non-TLR TVR accounted for 34% of TVR in year 1 and 17% of TVR in year 2. In the overall ARRIVE population, SVG stenting was an independent predictor (1.5- to 2-fold increased risk) for death, cardiac death, MI, TLR, and ST through 2 years (Table 4). The increased risk for TLR was driven solely by a 2-fold increased risk in year 2. The increased risk for ST was driven exclusively by a 3-fold increased risk for very late ST (>1 year).

Discussion

The ARRIVE registries gathered data on 7,492 patients treated in routine practice with the TAXUS Express (Boston Scientific Corporation) PES, including 474 patients who underwent SVG stenting (33,34). These SVG patients had significantly more comorbidities and a higher risk of clinical events through 2-year follow-up than the subgroup of simple-use patients (n = 2,698) who would have been eligible for the TAXUS IV pivotal trial (37). They also had similar or greater comorbidities and higher adverse event rates than the cohort of other (non-SVG) expanded-use patients (n = 4,320). However, repeat revascularization after PES implantation in ARRIVE SVG patients (14.0% TVR and 10.2% TLR through 2 years) was still lower than the historical 35% to 40% failure rate of BMS in SVG at 18

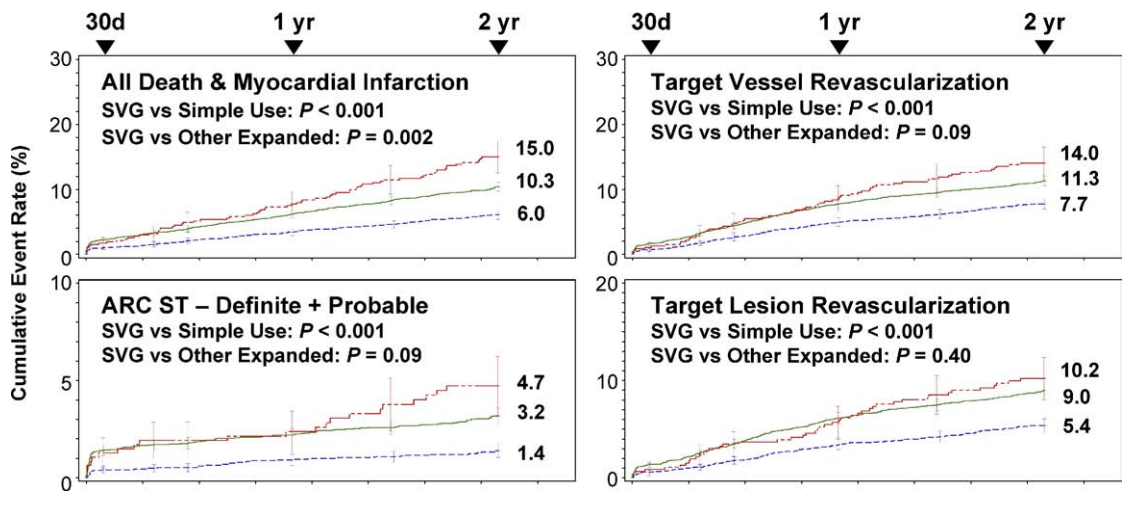

Figure 1. Death/MI, ST, and Revascularization Through 2 Years in the ARRIVE Vein Graft, Simple Use, and Other Expanded-Use (Minus Vein Graft) Subgroups

Cohorts were ARRIVE vein graft (n = 474) **(red line)**, ARRIVE simple use (n = 2,698) **(blue line)**, and ARRIVE other expanded use (minus vein graft, n = 4,320) **(green line)**. Simple use and expanded use cohorts are defined in Table 1. Graft-related revascularization is shown for the saphenous vein graft (SVG) cohort. Target lesion revascularization was defined as "TAXUS-stent-related" target vessel revascularization, given the absence of a central angiographic core laboratory. Stent thrombosis (ST) is per Academic Research Consortium (ARC) definite/probable definitions (36). The p values (log-rank) are for the comparison between vein graft and simple use cohorts and between vein graft and other expanded use (minus vein graft) cohorts; error bars are ± 1.5 SEM. MI = myocardial infarction.

Table 4. Vein Graft Stenting as an Independent Risk Factor for Adverse Events in ARRIVE

Event Type (n = 7,492 ARRIVE Patients)	Hazard Ratio (95% CI)
Death (0–2 yrs, n = 461)	1.43 (1.05–1.96)
Cardiac death (0–2 yrs, n = 260)	1.61 (1.09–2.37)
MI (0–2 yrs, n = 229)	1.86 (1.18–2.94)
TVR (0–2 yrs, n = 715)	1.60 (1.23–2.10)
TVR (0–1 yr, n = 492)	1.50 (1.07–2.11)
TVR (1–2 yrs, n = 223)	1.68 (1.12–2.53)
TLR (0–2 yrs, n = 545)	1.76 (1.30–2.39)
TLR (0–1 yr, n = 373)	NS*
TLR (1–2 yrs, n = 172)	1.77 (1.13–2.79)
ST (0–2 yrs, n = 184)	2.03 (1.27–3.23)
Early ST (0–30 days, n = 77)	NS*
Late ST (31 days–1 yr, n = 51)	NS*
Very Late ST (1–2 yrs, n = 56)	2.90 (1.44–5.83)

*$p > 0.05$.
ST = stent thrombosis; TLR = target lesion revascularization (TAXUS stent-related target vessel revascularization [TVR]).

months (4,14). The ARRIVE revascularization outcomes were similar to what was observed with PES in the multicenter prospective SOS (Stenting Of Saphenous vein grafts) RCT at 2 years where TVR was significantly lower with TAXUS than with BMS (16% vs. 35%, respectively) (32).

Long-term data have shown a reduction in TLR with DES compared with BMS with no significant difference in death or MI in the inherently lower-risk patients/native coronary lesions generally studied in RCTs (38). The first prospective trial of DES in SVGs, the RRISC (Reduction of Restenosis In Saphenous vein grafts with CYPHER sirolimus-eluting stent) trial (n = 75), also reported a lower 6-month rate of ischemia-driven TVR for sirolimus-eluting stent (SES) compared with BMS (5.3% vs. 27.0%, respectively, p = 0.012) as well as reduced neointimal hyperplasia volume (30,39). However, after a median of 32 months, the incidence of TVR was similar in the 2 study groups due to late catch-up in the SES group (34% for SES vs. 38% for BMS, p = 0.74) (31). Outcomes at 2 years in ARRIVE SVG patients (14.0% TVR) are similar to that of PES patients in SOS (16% TVR), suggesting that "real-world" PES use in SVG lesions might have a lower revascularization rate than BMS and potentially SES, at least through 2 years (32,40). The ongoing BASKETSAVAGE study (Clinical Trials Identifier, NCT00595647) will compare TAXUS with BMS in SVG when used in conjunction with a glycoprotein IIb/IIIa inhibitor and a distal filter system and should provide additional randomized trial data regarding SVG stenting.

Reported revascularization rates among SVG patients receiving DES in observational studies have been varied. One single center study reported a 19% TVR rate at 1 year among 110 consecutive SVG patients (41). In another single-center registry, TVR was 13% at 1 year, with disease progression in the nonstented segment accounting for one-third of revascularizations (42). Through 2 years in the STENT (Strategic Transcatheter Evaluation of New Therapies) registry, TVR with DES was 18.2%, similar to that in the ARRIVE program, with a lower event rate and propensity adjusted hazard ratio compared with BMS (7). Reports from nonrandomized comparisons of DES and BMS in SVG lesions of various ages have also communicated diverse results (14–29,43,44). Many are retrospective, and some are limited by short follow-up. Approximately one-half have shown some significant revascularization benefit with DES; others have suggested no benefit at all (45).

Late outcomes (median follow-up of 32 months) in the RRISC trial have raised concerns about a significant albeit not fully understood mortality excess in SVG patients receiving SES (31). Higher mortality was not observed, however, in the multicenter 350-patient case-control study comparing SES with a variety of BMS in clinical use during the 2000s (16). Through 2 years in the SOS trial, there were numerically more deaths overall with PES versus BMS (5 vs. 2, respectively), but the BMS group had more cardiac deaths (2 vs. 1). Annual mortality among ARRIVE SVG patients was approximately 5.5%; although higher than in simple-use patients, this rate was comparable to results from 2,119 patients in the Duke Cardiovascular Disease Database where annual mortality after SVG stenting with BMS (median follow-up of 4.8 years) ranged from 5.7% to 8.6% (46). Among SVG patients receiving DES in the STENT registry, mortality was 4.6% at 9 months and 8.2% at 2 years (7). In a recently reported observational study, SVG patient mortality through 4 years was not significantly different between DES and BMS (22.5% vs. 27.0%, respectively, p = 0.65) (28). The data overall suggest that, although DES might not increase mortality relative to BMS, they also do not prevent the high annual mortality rate seen in patients after SVG stenting with BMS. Among ARRIVE SVG patients, medically treated diabetes was a significant predictor of 2-year cardiac death (hazard ratio: 2.11, 95% confidence interval: 1.02 to 4.36, p = 0.044). Many late events after SVG stenting are likely to reflect background disease activity outside the stented segment, as has been reported for lower-risk patients participating in RCTs (47,48).

Early ST was higher in the ARRIVE SVG subgroup compared with the simple-use cohort (38), and through 2 years, ARRIVE SVG patients had a significantly higher ST incidence (Fig. 1). Among the 21 ARRIVE SVG patients suffering an ST event, however, all 16 revascularizations performed were TLR. Stent thrombosis could be related to in-stent restenosis but might also result from SVG disease progression in nonstented segments. In the overall ARRIVE population, first-year ST reflected mostly DAPT compliance along with anatomic and clinical factors known to increase the risk of BMS ST, whereas ST in the second year seemed

more related to biological markers (35). Extended DAPT use might help reduce the high incidence of late ST, but this remains to be proven.

Moderate, nonischemic SVG lesions have been associated with both midterm and late cardiac events after coronary artery bypass grafting (49–51). Prophylactic DES stenting of such lesions might provide preventive treatment against SVG atherosclerosis progression. In a recent report, at 1-year follow-up the use of PES stenting of moderate nonsignificant lesions in old SVGs compared with medical therapy alone was associated with a lower rate of disease progression as assessed by intravascular ultrasound and a trend toward a lower cumulative incidence of major adverse cardiac events related to the target SVG (3% vs. 19%, respectively, $p = 0.09$) (52).

Study limitations. The main limitation of the current study is its observational nature and the lack of an appropriate control group. However, clinical outcomes in ARRIVE patients receiving a PES in a vein graft were similar to those of the PES arm of the SOS trial. To be in the ARRIVE registry, a patient had to receive a TAXUS Express stent, and this operator choice might have been influenced by the angiographic appearance of the lesion and the clinical characteristics of the patient. The incidence of MI might be underestimated, because systematic measurement of cardiac biomarkers was not mandated by the study protocol. The comparatively low (29%) use of embolic protection in this series is consistent with the low penetration of this group of technologies, despite numerous trials showing reduction in adverse events when embolic protection is used during SVG intervention (53). The angiographic data were based on visual assessment at each site and were not evaluated by an independent core laboratory. The MI rates reported in the article represent clinical MI, but the rates of peri-procedural MI were not collected.

Conclusions

The ARRIVE patients undergoing SVG stenting have more baseline comorbidities and higher risk for adverse events compared with patients undergoing simple native coronary artery stenting and even those undergoing complex (non-SVG) stenting. Although the 2-year repeat revascularization rates in SVG patients are higher than in simple-use patients, they are lower than historical revascularization rates for BMS in SVGs. Outcomes in the ARRIVE SVG group are similar to that of the PES arm in the SOS trial and suggest that use of the TAXUS Express stent might have a lower repeat revascularization rate than when BMS are used to treat focal SVG disease. These results provide further support for a large, prospective, multicenter RCT of DES in SVG lesions (45,54).

Acknowledgments

This article is dedicated to the memory of Dr. Donald S. Baim, MD. The authors thank Yun Lu, MS, and Aijun Song, MS (Boston Scientific Corporation) for assistance with statistical analyses.

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Key Words: coronary artery bypass graft surgery ■ paclitaxel-eluting stent ■ percutaneous coronary intervention ■ saphenous vein graft.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 3, NO. 7, 2010
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Appendix
Baseline Characteristic Variables Used in Predictor Modeling

Acute MI
Age >70 yrs
Bifurcation
Brachytherapy, prior
CABG, previous
Cardiogenic shock
Chronic total occlusion
Congestive heart failure (site reported as NYHA functional class ≥III)
Diabetes, insulin treated
Diabetes, not requiring insulin
Gender, male
Hypercholesterolemia (patient was reported as having this condition and may or may not have been receiving medication for it)
Hypertension (patient was reported as having this condition and may or may not have been receiving medication for it)
In-stent restenosis
IVUS post deployment
IVUS pre-deployment
LAD as target vessel
Left main disease
Left main stenting
Lesion >28 mm
Lesion calcification (moderate and severe)
Lesion type B2/C
MI, previous
Multiple overlapping stents
Multiple stents per patient
Multivessel disease
Multivessel stenting
Ostial lesion
PCI, previous
Post-procedure dilation
Pre-procedure dilation
Pre-procedure TIMI flow grade 0
Renal disease (Site reported as serum creatinine >3.0 mg/dl or patient on dialysis)
RVD <3 mm
Smoking at baseline
Stent inflation pressure >14 atm
Stroke, previous
Thienopyridine <12 months
Thienopyridine <6 months
Tortuosity, severe
Vein graft

Hazard ratios were assessed with the Cox proportional hazards regression model; backward selection was used; the threshold to stay in the model was set at 0.10.

CABG = coronary artery bypass graft; IVUS = intravascular ultrasound; LAD = left anterior descending artery; MI = myocardial infarction; PCI = percutaneous coronary intervention; RVD = reference vessel diameter; TIMI = Thrombolysis In Myocardial Infarction.