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Pathology of Drug-Eluting Versus Bare Metal Stents in Saphenous Vein Bypass Graft Lesions

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Abstract

Objectives—The purpose of this study was to assess the pathologic responses of atherosclerotic saphenous vein bypass grafts (SVBGs) to drug eluting stents (DES) versus bare metal stents (BMS).

Background—Repeat bypass surgery is typically associated with a high rate of morbidity and mortality. Percutaneous coronary interventions have emerged as the preferred treatment, however, only limited data are available on SVBGs pathologic responses to DES and BMS.

Methods—Formalin-fixed SVBG of >2 years duration (n=31) were collected to histologically characterize advanced atherosclerotic lesions in native SVBG. In a separate group, SVBGs treated with DES (n=9) and BMS (n=9) for >30 days duration were assessed for morphologic and morphometric changes.

Results—Necrotic core lesions were identified in 25% of SVBG sections and plaque rupture with luminal thrombosis was observed in 6.3% of histologic sections [32% (10 of 31) vein grafts examined]. Morphometry of DES demonstrated reduction in neointimal thickening versus BMS (0.13 mm [IQR 0.06 to 0.16 mm] vs. 0.30 mm [IQR 0.20 to 0.48 mm], p=0.004). DES lesions also showed greater delayed healing characterized by increased peri-strut fibrin deposition, higher percentage of uncovered struts, and less endothelialization compared to BMS. Stent fractures (DES 56% vs. BMS 11%, p=0.045) and late stent thrombosis (DES 44% vs. BMS 0%, p=0.023) were more common in DES vs. BMS.

Conclusions—Advanced SVBG atherosclerotic lesions are characterized by large hemorrhagic necrotic cores. Stenting of such lesions is associated with delayed vascular healing and late thrombosis particularly following DES implantation, which may help explain the higher rates of cardiovascular events observed in SVBG stenting as compared to native coronary arteries.
Keywords

drug-eluting stent; bare metal stent; saphenous vein bypass graft; pathology

Introduction

Saphenous vein bypass grafts (SVBGs) remain the most frequently used conduits for coronary artery bypass graft (CABG) surgery. These grafts are susceptible to the rapid development of atherosclerotic lesions, and repeat revascularization procedures are common after 5 years (1,2). Since repeat CABG surgery is associated with increased morbidity and mortality compared with the index bypass procedure, percutaneous coronary intervention (PCI) has emerged as the preferred treatment for atherosclerotic SVBG failure (3–6). Bare metal stent (BMS) implantation in SVBG was shown to reduce clinical events as compared to balloon angioplasty (7,8). However, results of BMS implantation in SVBGs are less favorable than those in native coronary arteries, with restenosis rates exceeding 30%, and are associated with a high rate of major cardiovascular events (9).

Reduced restenosis rates associated with sirolimus (SES, Cypher, Cordis Johnson & Johnson, Miami, FL) and paclitaxel (PES, Taxus, Boston Scientific Corporation, Boston, MA) drug eluting stents in native coronary arteries has resulted in the frequent use of DES in atherosclerotic SVBGs (10,11). Within 1-year post-procedure, DES implantation in SVBG result in a reduction in target lesion revascularization (TLR) rates compared to BMS (DES 4% vs. BMS 11%, p=0.22) (12); however, the long-term effectiveness benefit of DES vs. BMS has been inconsistent (13). In a randomized controlled trial of SVBG revascularization, DES had a lower incidence of target vessel revascularization (TVR) at 6 months (DES 4.3% vs. BMS 24.5%, p=0.005), but TVR rates were not significantly different at ≥2 years (DES 36% vs. BMS 41%, p=0.64) (14–16).

Preclinical and human autopsy studies have shown that DES implanted in native coronary arteries are associated with delayed arterial healing as compared with BMS (17). However, pathological studies of atherosclerotic SVBGs treated with DES versus BMS are lacking, and it is noteworthy that the atherosclerotic process is highly accelerated and has some morphologic differences compared to native coronary disease. The objectives of this study were: (1) to perform a detailed pathologic assessment of advanced SVBG atherosclerotic plaques and (2) to determine the vascular healing profile of SVBGs implanted with SES or PES of >30 days implant duration to gain insights into the safety and effectiveness of DES implantation.

Materials and Methods

SVBG atherosclerotic plaque assessment

Formalin-fixed human hearts from patients treated with CABG surgery at least 2 years antemortem were selected from our CVPath database. SVBGs were excised in their entirety and serially sectioned transversely at 3 mm intervals and embedded in paraffin. Each 5 μm section was stained with Hematoxylin and Eosin (H&E) and Movat pentachrome stains.

The SVBG cross-sections were categorized as non-atherosclerotic (i.e., only fibrointimal hyperplasia present (FIT)) or atherosclerotic. Atherosclerotic SVBG lesions were further categorized as: (1) intimal xanthoma (IX) or fatty streak lesions (foam cell accumulation lacking a fibrous cap or lipid core); (2) fibroatheroma lesions (FA, plaques with well-defined necrotic cores with or without focal accumulations of foam cells); (3) hemorrhagic necrotic core lesions (HNC) with intact fibrous caps; and plaque rupture (PR) with a
disrupted cap and an overlying thrombus. Morphometric analysis was utilized to measure area within the internal elastic lamina, lumen, total plaque area and total necrotic core area and to calculate area stenosis and the percent of the plaque occupied by a necrotic core \( (18,19) \).

**Stented saphenous bypass grafts**

From our registry of >600 human coronary artery stents submitted for consultation, SVBGs stented with DES implanted of >30 days antemortem were identified. Clinical histories and cardiac catheterization reports were reviewed when available. The control group consisted of SVBGs treated with BMS with matched stent lengths and implant durations.

Stented segments of SVBGs were fixed in 10% buffered formalin, dissected off the heart, radiographed, and processed for plastic embedding. Stented vein grafts were sawed consecutively from the proximal to distal ends of the stents at 2 to 3 mm intervals. The sections were cut at 6 μm and stained with H&E and Movat pentachrome stains.

Acute luminal thrombus was defined as a platelet-rich thrombus that occupied >30% of the cross-sectional area of the lumen, and restenosis was defined as >75% in-stent cross-sectional area luminal narrowing by neointima. Pre-mortem luminal thrombus was distinguished from post-mortem thrombus based on histological appearance as premortem thrombus is composed of platelet aggregation with or without white cells and a propagated thrombus is composed of interspersed layer of fibrin and red cells, whereas a post-mortem thrombus lacks the layered appearance. Late stent thrombosis (LST), consistent with the clinical definition, was defined as thrombosis within a stent implanted >30 days antemortem \( (20) \). The cause of death was determined after complete autopsy and was categorized as stent-related, non-stent related cardiac, and non-cardiac \( (21) \).

Computer-guided morphometric measurements and histological characterization of the stented segments including fibrin, inflammation, strut coverage, strut malapposition, necrotic core strut penetration, neoatherosclerosis has been previously defined \( (17,21–23) \).

**Statistical Analysis**

Continuous variables with normal distribution were expressed as mean ± SD. Discrete variables and continuous variables with non-normal distribution were expressed as median and interquartile range (IQR). Comparisons of continuous variables with normal distribution were tested by ANOVA. A Wilcoxon rank-sum test was used to compare non-normally distributed parameters or discrete variables, and the Pearson chi square test was used for categorical variables. Normality of distribution was tested with the Wilk-Shapiro test. A value of \( p<0.05 \) was considered statistically significant.

**Results**

**SVBG atherosclerotic plaque assessment**

A total of 589 histologic cross-sections from 31 SVBGs (non-stent treated) from sixteen patients were prepared and examined. There were 7 cardiac deaths (4 sudden cardiac death) and 9 non-cardiac deaths. CABG surgery had been performed 8.5±5.9 years antemortem (range 2–22 years). Grossly, older vein grafts (>5 years) showed atherosclerotic change (yellow, with cheesy material and hemorrhage) where as those implanted for 2 to 5 years usually showed intimal thickening with or without foam cell infiltration and absence of necrotic core. As shown in Table 1, incidence of fibrointimal thickening was observed in the majority of lesions (90.3%). Intimal xanthoma and fibroatheroma with necrotic core were observed in 74.2% and 64.5% of the 31 SVBG, respectively. Seventeen of the 31 lesions

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(54.8%) demonstrated hemorrhagic necrotic core, with only 10 lesions (32.3%) showing plaque rupture.

To further characterize these histologic changes, histologic cross-section from all 31SVBG (n=589 sections) were categorized. The results demonstrated that the majority of sections (56.5%) showed FIT with the remaining cross-sections (43.5%) demonstrating atherosclerotic changes. Intimal xanthoma was identified in 18.8% of the total SVBG sections, followed by lesser incidences of necrotic core (11.9%), hemorrhagic necrotic cores (7.5%), and plaque rupture and luminal thrombus (6.3%) (Table 1 and Figure 1). Ruptured plaque was primarily composed of a disrupted fibrous cap with lipid-laden macrophages close to underlying necrotic core and within the fibrous cap. The necrotic core was usually large with numerous cholesterol clefts and hemorrhage, with occasional presence of focal calcification, usually close to the vein wall (Fig. 1 supplement). The cap was more discontinuous than what is seen in native coronary artery disease. The necrotic core always showed a base of neointimal layer composed of smooth muscle cells and collagenous matrix. The fibrous caps of plaque ruptures were significantly thinner compared to SVBGs with plaque hemorrhage (82±42 μm vs. 214±162μm, respectively, p=0.002). The mean longitudinal length of plaque ruptures (estimated by the number of contiguous SVBG cross-sections demonstrating rupture) was 6.6±7.2 mm (range 3.0 mm–30mm).

At the aortic anastomosis, 67% of sites showed only fibrointimal proliferation and 33% had atherosclerotic plaque (with or without lipid core formation). At the distal anastomosis of SVBG to the native coronary artery, only 4% demonstrated atherosclerotic plaque and 96% showed fibrointimal thickening.

**Stented SVBGs**

Eighteen stented SVBGs, including 9 DES from 7 patients and 9 BMS from 8 patients were analyzed with a mean patient age of 71±10 years and 67±6 years, respectively. The DES stents consisted of 6 PES and 3 SES. Implanted BMS were 5 Multi-Link (Abbott Vascular, Santa Clara, CA), 2 AVE (Medtronic, Minneapolis, MN), one BxVelocity (Cordis Corp. Johnson & Johnson, Warren, NJ), and one Palmaz-Schatz (PS) (Johnson & Johnson, Warren, NJ). The duration of stent implantation and stent length was greater in DES versus BMS, but differences did not reach statistical significance (Table 2).

Postmortem radiographs demonstrated fractures in 5 (3 SES, and 2 PES) of the 9 DES and in 1 of 9 BMS (Bx Velocity). Stent fractures ranged from grade II (multiple breaks with preserved alignment) to grade IV (multiple breaks with transection but without gap) (24). Most of the fractures in the Cypher stents and in the Bx Velocity BMS (which has the identical platform as the Cypher) were located in the flexible N-shaped, undulating longitudinal intersinusoidal-ring linker segments, whereas in Taxus stents, fractures were observed in the straight longitudinal intercrown linker.

**Morphometric Analysis of Stented Lesions**

Lumen, stent, and plaque area measurements were comparable between the BMS and DES groups. Mean neointimal thickness [0.30 mm (IQR 0.20 to 0.48 mm) vs. 0.13 mm (IQR 0.06 to 0.16 mm, p=0.004), neointimal area (4.90±2.20 mm² vs. 2.00±0.87 mm² p=0.002) and percent area stenosis (47.9±20.5% vs. 30.1±12.4%, p=0.041) were significantly greater in BMS than in DES, respectively.

**Histological Observations**

A total of 216 sections of stented SVBGs were examined with 12±3 stent struts per section for a total of 785 struts. The underlying lesion characteristic of the stented vein grafts ranged

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from FIT, FA with a necrotic core, and FA with hemorrhagic necrotic core (HNC) with similar distributions between DES and BMS cases (Table 2). In DES, fibrin was observed at later time points and was observed more frequently around stent struts as compared to BMS and was interspersed with inflammatory cells and or surrounded by smooth muscle cells and proteoglycan/collagen matrix (Table 3). The percent of struts associated with inflammatory cells (eosinophils, lymphocytes, and foreign-body giant cells) were similar between the DES and BMS. Luminal neutrophil and eosinophil foci were numerically greater in DES vs. BMS, but the differences were not statistically significant (Table 3). Disruption of lipid core by stent struts was observed in all stented SVBG atherosclerotic lesions (BMS and DES) in which an underling fibroatheroma was present except in one lesion where a thick fibrous cap of >700 μm was seen. The frequency of stent strut penetration into pre-existing lipid core was similar between stent groups. Uncovered struts were more common in DES compared to BMS and endothelialization of DES SVBGs was significantly less frequent compared to BMS (Table 3). For stents implanted > 360 days, uncovered struts were more frequently observed in samples with strut necrotic core penetration, with greater frequency in DES as compared to BMS, whereas stents without strut necrotic core penetration irrespective of stent type, were more likely to be covered (supplement tables 1 and 2).

Evidence of accelerated in-stent atherosclerotic change within the neointima was present with equal frequently in BMS (3 out of 9 lesions) and DES (4 out of 9 lesions) and was observed at 360 days post-implant (Fig. 4). Malapposition of stent struts was only observed in DES SVBGs (2 out of 9 lesions, both PES). The percent of struts associated with calcification was similar between BMS and DES (Table 3).

**Discussion**

The present study demonstrated that flow limiting SVBG plaques are characterized by fibroatheroma with large necrotic cores and are frequently accompanied by plaque hemorrhage and a disrupted fibrous cap. In the treatment of diseased SVBG, DES reduced neointimal thickness as compared to BMS, but this benefit was associated with delayed healing characterized by persistent fibrin deposition, uncovered stent struts, and incomplete endothelialization. Focal stent strut penetration into lipid core was common and independent of BMS or DES stent type and resulted in long term (≥360 days) uncovered struts with greater frequency in DES as compared to BMS. Late stent thrombosis was seen more frequently in SVBG DES (4 of 9 lesions) vs. BMS (0 of 9 lesions), which was almost exclusively seen in vein grafts with underlying large hemorrhagic necrotic cores. Taken together, these findings suggest long term increase in delayed healing of DES stents implanted in SVBG is related to the severity of the underlying disease and uncovered struts which result in late stent thrombosis.

**Vein graft disease**

Compared to native coronary arteries, SVBGs undergo more rapid atherosclerotic lesion development. Reported rates of vein bypass graft occlusion is 8% early after the operation, 13% at 1 year, 20% at 5 years, 41% at 10 years and 45% at more than 11.5 years (4,25). Our laboratory and others have shown that within the first year following SVBG implantation, the vein wall is thickened by the neointimal growth, which has been postulated to occur because from veins being exposed to arterial pressure that is 10-fold higher than venous pressure. This hemodynamic load leads to increased levels of intracellular adhesion molecule-1 (ICAM-1), vascular adhesion molecule-1 (VCAM-1) and monocyte chemotactic protein-1 (MCP-1) (26). In animal models, the magnitude of shear stress across the endothelial surface of vein grafts has been shown to be inversely proportional to neointimal growth, suggesting that the difference in flow rates between arterial and venous beds plays an important role in the progression of vein graft disease (27).
Over time, the SVBG neointima is infiltrated by macrophages, with varying degrees of apoptosis and necrotic core formation (28). Compared to native coronary artery disease, SVBG atherosclerotic lesions are more often concentric and diffuse, with a less well-defined fibrous cap, which is more vulnerable to rupture and thrombosis (29). The present study demonstrates a high frequency of plaque rupture (32%, 10 of 31 SVBG) of a thin fibrous cap in lesions containing large hemorrhagic necrotic cores. It is likely that implantation of stents in SVBGs with thin fibrous caps and a large hemorrhagic necrotic core is an important factor in the healing of DES and BMS.

**Delayed vein graft healing after drug eluting stents**

The impact of DES on saphenous vein graft healing is poorly understood. From human native coronary arterial autopsy studies, DES have been shown to effectively suppress smooth muscle cell proliferation, followed by prolonged fibrin deposition and incomplete endothelialization in non-complex lesions observed up to 12 months post-DES implantation. In contrast, endothelialization is nearly complete by three to four months post-BMS placement (30). In the present study, the frequency of uncovered stent struts and fibrin deposition was significantly higher in SVBGs stented with DES compared to BMS, which is similar to observations in native coronary arteries (17).

In comparing the histopathology of DES in SVBG (in the presence of a necrotic core) to native coronary arteries, there was a similar incidence of strut penetration of necrotic core and the number of uncovered struts (22). However, greater incidence of fibrin was observed in SVBG stented with DES as compared to native arteries in patients presenting with acute coronary syndrome (ACS). Also, there was greater delayed healing in SVBG than in native coronary arteries likely because of greater delay in endothelialization of vein graft disease. Because the number of cases with DES in SVBG was far too few, it is difficult to compare patients presenting with acute myocardial infarction (AMI) in SVBG versus native coronaries. However, we suspect that there would be greater delayed healing in vein grafts and early neoatherosclerotic change than in native coronary disease.

The data also demonstrates the adverse effects of stent strut within necrotic core on stent healing. In DES samples implanted for ≥360 days with necrotic core penetration, greater incidence of uncovered struts was observed in comparison to DES without strut necrotic core penetration, were nearly all struts were completely covered. As presence of uncovered struts highly correlates with endothelialization, neointimal coverage of stent struts could be used as a surrogate marker for endothelialization. Undoubtedly these results correlate directly to the underlying disease in SVBG, as strut necrotic core penetration was only observed in grafts with large hemorrhagic necrotic cores. This pattern was observed both for BMS and DES with incidence of necrotic core penetration being similar, nevertheless, the number of uncovered struts was much greater in DES as compared to BMS (supplement tables 1 and 2).

Atherosclerotic change was observed following stenting of SVBG in DES as well as BMS and this change occurred as early as 360 days. These findings are similar to those previous reported by Depre et al., (31) and dissimilar to those of van Beusekom (32). These differences are most likely related to over interpretation of atherosclerotic change by van Beusekom et al. at early time points (3 to 7 months) and likely represented native vein graft atherosclerotic disease, as suggested by the authors in their discussion. On the other hand, in the study by Depre et al., atherosclerotic change was observed in 3 of the 12 stent grafts (25%) and the duration of stent implant was 15, 24, and 24 months, which is similar to our data showing that the earliest atherosclerotic change occurred beyond 12 months.
Clinical implications

The present study demonstrates that DES use for patients with SVBG disease is associated with greater incidence of uncovered struts, persistence of fibrin, and less endothelialization. Because healing is delayed for long periods of time (>1 year), the safety and efficacy of using DES cannot be determined by relatively short-term studies. Recently Lee et al. published a meta-analysis of 19 studies (2 randomized trials and 17 registries) with follow-up data ranging from 6 to 48 months (33). Although most studies with relatively short-term follow up (<2 years) demonstrated a benefit in DES vs. BMS (9 out of 13 studies), longer term (>2 years) studies were less consistent with only 3 of 6 studies showing advantages for DES implantation. In the only randomized study (RISCC trial) to date, there was a significant reduction of target lesion revascularization (TLR) in the DES group at 6-months versus BMS (5% vs. 22%, p=0.047), but this benefit was lost at 3 year follow-up (24% vs. 30%, p=0.55) (14,15). Similarly, Gioia et al. demonstrated a marginal benefit in major adverse cardiac event (MACE) rates for DES at 1 year (10% vs. 16%, p=0.15); however, MACE free survival were comparable between DES and BMS at 2 years (19% vs. 18%, p=0.9)(34). These data suggest that late in-stent neoointimal growth “catch-up” occurs beyond >2 years in SVBGs treated with DES. Catch-up has been shown in native coronary arteries; rates of target vessel revascularization increase for both PES (Taxus) and SES (Cypher) increase from 1 to 5 years post-stent implantation (35). In pathologic studies of human post-mortem stented coronary arteries, our laboratory demonstrated a significant increase in neoointimal thickness beyond 18 months in SES and PES (36). In the current study because of small number of specimens examined it is not possible to show late catch-up in SVBG. Prospective randomized long-term studies will be needed to further define the risk benefit profile of DES implantation in SVBGs.

Study Limitations

Because this is an autopsy study, the results may not adequately reflect the vascular responses of living patients who receive DES and BMS for treatment of SVBGs. Moreover, the small number of patients in this study and incomplete clinical data in some subjects did not permit an assessment of the contribution of deployment strategies that may have contributed to the pathological findings.

Conclusions

The pathologic characteristics of flow limiting SVBG plaques are characterized by fibroatheroma with large necrotic cores and are frequently accompanied by plaque hemorrhage and or a disrupted fibrous rupture. Stenting of these lesions, regardless of stent type, often results in strut penetration of the necrotic core. For DES, penetration of struts into necrotic core contributes to increased delayed healing, likely because of longer duration of drug retention resulting in greater number of uncovered struts which may contribute to late thrombotic events. Treatment strategies that reduce the lipid core burden within SVBGs warrant investigation to improve outcomes post-DES implantation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

SVBG  saphenous vein bypass grafts
BMS  bare metal stents
DES  drug eluting stents
CABG  coronary artery bypass graft
FA  fibroatheromas
FIT  fibrointimal proliferation
HNC  hemorrhagic necrotic core
TVR  target vessel revascularization
TLR  target lesion revascularization
PR  plaque rupture
IX  intimal xanthoma
LST  late stent thrombosis
IQR  interquartile range
MACE  major adverse cardiac events
PES  paclitaxel-eluting stents
SES  sirolimus-eluting stents

References


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Figure 1. Progression of atherosclerotic disease in saphenous vein grafts

(A) Within the first year, arterialization and fibroininitmal thickening of the vein graft is observed. (B) This is followed by foam cell accumulation within the neointima. (C) Between the first and third year, formation of a lipid core is observed. (D) After four to five years, hemorrhage into the lipid core and moderate to severe lumen narrowing is observed. (E) At five to ten years, plaque rupture of a large necrotic core accompanied with hemorrhage often leads to luminal thrombus. (F) At the coronary anastomosis, fibroininitmal growth is commonly observed whereas atherosclerosis is uncommon.
Figure 2. Histological evidence of delayed healing and necrotic core strut penetration in drug eluting stented saphenous vein grafts

(A) A 84-year-old women received two overlapping paclitaxel eluting Taxus stent implanted 2 years antemortem demonstrates stent strut penetration into the lipid-rich necrotic core (NC) region. The fibrous cap (green arrow) is shown to have been disrupted by the stent struts (*-stent strut). (B) In the overlapping region, struts are uncovered but are surrounded by a thin layer of thrombus (Thr) primarily composed of fibrin. (C) In the distal region, struts are surrounded by a thin layer of thrombus.
Figure 3. Stent strut penetration of lipid-rich necrotic core lesions
(A) A 79-year-old woman received a bare metal Multi-Link Vision stent 2 years antemortem demonstrates multiple stent struts (*) penetrating into the lipid-rich necrotic core (NC). A thin layer of neointima (green arrow) is observed over the necrotic core. (B) In the distal region, all struts are shown to be covered by neointima with focal areas of calcification (black arrow).
Figure 4. Atherosclerotic change in saphenous vein grafts following stenting
(A–B) A paclitaxel eluting Taxus stent implanted five months antemortem in an 84-year-old
women demonstrates foamy macrophages within the neointimal layer (*-stent strut). (C–D)
A bare metal Multi-Link Vision stent implanted 3 years antemortem in a 66-year-old man
shows foamy macrophages within the neointimal layer.
Table 1

Lesion morphology, stenosis, and lipid core size of SVBG (> 2 years).

<table>
<thead>
<tr>
<th>Changes in SVBG</th>
<th>Incidence per lesion (%)</th>
<th>Number of sections (%)</th>
<th>IEL Area (mm²)</th>
<th>Stenosis (%)</th>
<th>Lipid Core Area (mm²)</th>
<th>% Lipid Core</th>
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<tbody>
<tr>
<td>Fibrointimal thickening (FIT)</td>
<td>28 (90.3)</td>
<td>333 (56.5)</td>
<td>10.97±2.28</td>
<td>34±15</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Intimal Xantoma (IX)</td>
<td>23 (74.2)</td>
<td>111 (18.8)</td>
<td>12.36±3.02</td>
<td>37±9</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Fibroatheroma with Necrotic Core (FA)</td>
<td>20 (64.5)</td>
<td>70 (11.9)</td>
<td>14.08±2.59</td>
<td>46±17</td>
<td>1.5±1.9</td>
<td>18±19</td>
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<tr>
<td>Hemorrhagic Necrotic Core (HNC)</td>
<td>17 (54.8)</td>
<td>44 (7.5)</td>
<td>14.62±2.72</td>
<td>52±19</td>
<td>2.8±3.3</td>
<td>28±31</td>
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<tr>
<td>Plaque Rupture (PR)</td>
<td>10 (32.3)</td>
<td>31 (6.3)</td>
<td>15.35±3.56</td>
<td>75±24</td>
<td>9.3±7.9</td>
<td>57±51</td>
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Table 2

Patient and Lesion Characteristics of DES and BMS treated SVBG (>30 days).

<table>
<thead>
<tr>
<th></th>
<th>DES (n=9)</th>
<th>BMS (n=9)</th>
<th>p</th>
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<tr>
<td>Age, y</td>
<td>71±10</td>
<td>67±6</td>
<td>0.34</td>
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<td>Male gender, n (%)</td>
<td>6 (66)</td>
<td>7 (78)</td>
<td>0.62</td>
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<tr>
<td>SVBG duration (years)*</td>
<td>8.0 (6.5–10.0)</td>
<td>9.0 (7.0–12.0)</td>
<td>0.53</td>
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<td>Stent duration (days)*</td>
<td>360 (110–720)</td>
<td>360 (360–900)</td>
<td>0.39</td>
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<tr>
<td>Underlying SVBG disease, n (%)</td>
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<td></td>
</tr>
<tr>
<td>FIT</td>
<td>4 (44)</td>
<td>5 (56)</td>
<td>0.57</td>
</tr>
<tr>
<td>FA</td>
<td>1 (11)</td>
<td>0 (0)</td>
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<tr>
<td>FA with HNC</td>
<td>4 (44)</td>
<td>4 (44)</td>
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<tr>
<td>Cypher/Taxus, n</td>
<td>3/6</td>
<td>-</td>
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<tr>
<td>Stents, n</td>
<td>2 (1–2)</td>
<td>1 (1–1)</td>
<td>0.13</td>
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<tr>
<td>Stent length, mm*</td>
<td>20.0 (14.0–47.5)</td>
<td>13.0 (11.0–26.5)</td>
<td>0.12</td>
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<tr>
<td>Stent fracture, n (%)</td>
<td>5 (56)</td>
<td>1 (11)</td>
<td>0.045</td>
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<td>Thrombosis, n (%)</td>
<td>4 (44)</td>
<td>0 (0)</td>
<td>0.023</td>
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<tr>
<td>Restenosis, n (%)</td>
<td>0 (0)</td>
<td>3 (33)</td>
<td>0.058</td>
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<td>Malapposition, n (%)</td>
<td>2 (22)</td>
<td>0 (0)</td>
<td>0.13</td>
</tr>
<tr>
<td>Strut NC penetration, n (%)</td>
<td>4 (44)</td>
<td>4 (44)</td>
<td>0.49</td>
</tr>
<tr>
<td>Cause of death, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent related</td>
<td>4 (44)</td>
<td>3 (33)</td>
<td>0.38</td>
</tr>
<tr>
<td>Non stent related cardiac</td>
<td>4 (44)</td>
<td>4 (44)</td>
<td></td>
</tr>
<tr>
<td>Non cardiac</td>
<td>1 (11)</td>
<td>2 (22)</td>
<td></td>
</tr>
</tbody>
</table>

* Expressed as median (IQR)

DES = drug eluting stent(s); BMS = bare metal stent(s); SVBG = saphenous vein graft(s); FIT = Fibrointimal thickening; FA = Fibroatheroma with necrotic core; HNC = Hemorrhagic necrotic core.
**Table 3**

Pathologic and morphometric comparison of drug eluting (DES) and bare metal (BMS) stented SVBG.

<table>
<thead>
<tr>
<th></th>
<th>DES (n=9)</th>
<th>BMS (n=9)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumen area, mm$^2$</td>
<td>5.57±3.20</td>
<td>6.33±3.85</td>
<td>0.65</td>
</tr>
<tr>
<td>Stent area, mm$^2$*</td>
<td>6.7 (5.4–9.4)</td>
<td>11.1 (6.0–15.5)</td>
<td>0.15</td>
</tr>
<tr>
<td>Outer vein area, mm$^2$</td>
<td>15.23±6.63</td>
<td>19.13±9.42</td>
<td>0.32</td>
</tr>
<tr>
<td>NC area†, mm$^2$*</td>
<td>2.7 (1.3–4.0)</td>
<td>2.5 (1.0–4.0)</td>
<td>0.95</td>
</tr>
<tr>
<td>Plaque area, mm$^2$</td>
<td>7.67±3.29</td>
<td>7.91±4.97</td>
<td>0.91</td>
</tr>
<tr>
<td>Neointimal area, mm$^2$ (mean)</td>
<td>2.00±0.87</td>
<td>4.90±2.20</td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>Stenosis, % (mean)</td>
<td>30.05±12.44</td>
<td>47.86±20.54</td>
<td>0.041</td>
</tr>
<tr>
<td>Struts with inflammation, %*</td>
<td>20.0 (11.9–54.0)</td>
<td>16.1 (10.1–27.8)</td>
<td>0.72</td>
</tr>
<tr>
<td>Struts with calcification, %*</td>
<td>6.7 (0–38.0)</td>
<td>17.6 (0–30.5)</td>
<td>0.96</td>
</tr>
<tr>
<td>Struts penetrating NC†, %*</td>
<td>9.8 (1.7–19.1)</td>
<td>13.0 (4.1–30.5)</td>
<td>0.25</td>
</tr>
<tr>
<td>Mean no. of neutrophils/eosinophils*</td>
<td>21.6 (6.3–43.0)</td>
<td>7.0 (4.0–34.5)</td>
<td>0.34</td>
</tr>
<tr>
<td>Neointimal thickness, mm$^2$ (mean)</td>
<td>0.13 (0.06–0.16)</td>
<td>0.30 (0.20–0.48)</td>
<td><strong>0.004</strong></td>
</tr>
<tr>
<td>Struts with fibrin, %*</td>
<td>81.2 (58.3–92.8)</td>
<td>50.0 (30.5–63.9)</td>
<td><strong>0.019</strong></td>
</tr>
<tr>
<td>Uncovered struts, %*</td>
<td>19.6 (3.3–55.2)</td>
<td>5.1 (0.0–7.3)</td>
<td><strong>0.043</strong></td>
</tr>
<tr>
<td>Endothelialization, %*</td>
<td>70.0 (60.6–92.5)</td>
<td>98.3 (89.2–100)</td>
<td><strong>0.028</strong></td>
</tr>
</tbody>
</table>

* Expressed as median (IQR)

† Only performed in lesions with necrotic core

DES = drug eluting stent(s); BMS = bare metal stent(s); NC = necrotic core.