Long-term histological and immunohistochemical findings in human venous aorto-coronary bypass grafts

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A B S T R A C T

The aim of the present study was to analyse the long-term histology and immunohistochemistry of the plaque composition and cellular infiltration of SVGs (saphenous vein grafts) containing metallic stents. Percutaneous interventions in SVGs have a worse long-term clinical outcome compared with stenting of coronary arteries. Whether the pathological features of old degenerated SVGs condition the efficacy of drug-eluting stents is also unknown. Histology and immunohistochemistry of seven SVGs in the coronary circulation containing 12 metallic stents implanted 5 to 61 months before retrieval were analysed in patients undergoing a second aorto-coronary bypass surgery at a mean time of 11 ± 6 years. The pathology of the old SVGs showed an important thrombotic and necrotic composition of the plaque, with plaque protrusion through the stent wires and a fragile media layer that could easily be damaged by stent placement with subsequent neointimal proliferation; indeed, stents with medial fracture had significantly greater mean neointimal thickness than those without (1.37 ± 0.68 compared with 0.81 ± 0.47 mm²; P < 0.02). Neointimal inflammatory cell density correlated with increased neointimal thickness in patent vessels (r² = 0.43, P < 0.001). Immunostaining showed the total absence of ERs (oestrogen receptors), a poor cellular proliferative state as indicated by the presence of the Ki-67 marker, and persistent inflammation close to the stent wires as revealed by KP-1 and ACE (angiotensin-converting enzyme) immunostaining in most inflammatory cells in contact with the metal. These pathological findings may contribute to the more severe progression of disease and worse clinical outcome observed after conventional stented angioplasty of SVGs and might also interfere with the efficacy of drug-eluting stents in this specific atherosclerotic milieu.

INTRODUCTION

The implantation of endovascular stents in SVGs (saphenous vein grafts) used as bypass conduits to revascularize the native coronary circulation is common practice in interventional cardiology. The percutaneous treatment of narrowed veins offers an excellent alternative to a second operation that, in many cases, can be avoided or at least delayed. Indeed, repeat bypass surgery is generally burdened by technical difficulties, older age and a higher rate of graft occlusion [1]. Recent advances in stent technology and antiplatelet therapy, and the development of aspiration and protective devices to avoid distal embolization during the procedure,

Key words: angioplasty, atherosclerosis, pathology, saphenous vein graft, stent.

Abbreviations: ACE, angiotensin-converting enzyme; DES, drug-eluting stents; ER, oestrogen receptor; HPF, high-power fields; SMC, smooth muscle cell; SVG, saphenous vein graft.

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have improved the safety and short-to-mid-term results of transcatheter treatment of SVGs [2]. Nevertheless, progressive atherosclerotic degeneration of the venous conduit and the high rate of restenosis observed after stented angioplasty in this setting reduce the long-term efficacy of this approach, which is burdened by a 40% rate of vessel failure compared with 15–20% in native coronary arteries [3].

The pathological analysis of SVGs treated with coronary stents is performed on surgical or autopsy specimens which are not easily available. Indeed, studies in this field are scarce and the description of pathological changes in stented grafts available from previous reports is limited to relatively short periods. Previous studies performed in human venous bypass grafts have described the morphological characteristics of restenosis after implantation of two different stent types [4–6]; another two studies have analysed the composition of in-stent restenotic plaques retrieved by means of directional atherectomy [7,8].

In the present study, we have analysed a series of SVGs, 11 ± 6 years old (range, 5–18 years), containing metallic stents that had been in place for as long as 5 years (range, 5–61 months). The histology and immunohistochemistry of the plaque composition and the cellular infiltration around the metallic stents are described.

The present study is focused on the description of the salient features observed in this specific and rare histopathological setting. Such information may be of help in evaluating possible differences in efficacy between DES (drug-eluting stents) and conventional metallic stents implanted in degenerated SVGs.

**MATERIALS AND METHODS**

**Patients**

The pathology of seven SVGs containing 12 coronary stents retrieved from six patients (see Table 1) have been determined. All patients gave their informed consent to the analysis of the surgical specimens and angiographic images, and the approval of the Ethical Committee of the institution where the material was analysed (Ospedale Maggiore di Novara, Novara, Italy) was obtained.

All patients were treated with balloon dilation and/or stent implantation because of recurrence of angina secondary to the stenosis of one graft. At a mean time of 11 ± 6 years, the patients were re-operated on because of recurrent angina secondary to the angiographic documentation of a total occlusion of the graft in three cases, and to stent restenosis and/or progression of the disease in other grafts in the remaining patients. At the time of the repeat surgical intervention, the stented grafts were harvested, rinsed with saline and fixed in 9% neutral-buffered formalin. The proximal edge of the graft was marked with a suture stitch to identify the anatomical orientation and to allow comparison with the angiographic images.

**Pathological examination**

Using the suture stitch as a landmark, localization of the stents within the SVGs was assessed by a radiographic examination which allowed the precise identification of each stent length, the detection of overlapped or underexpanded segments and a comparison with the last digital angiographic image of the graft before surgical retrieval. The SVG segments were placed into processing vials and dehydrated via a graded series of alcohols. Samples were then infiltrated with methylmethacrylate plastic and placed in air tight vials in a 39°C water bath for polymerization. Afterwards, blocks were cut at 2–3-mm intervals along the stented and non-stented vein segments. Plastic sections (4–6-µm thick) were then cut, adhered to glass slides and allowed to dry. The plastic was then removed, and the sections selected for analysis (approx. 100 per segment) were rehydrated and stained. In segments selected for immunohistochemistry, the stent wires were carefully removed under a dissecting microscope, taking care not to alter the macroscopic wall structure before paraffin embedding. Plastic and paraffin sections were stained with haematoxylin/eosin and Movat pentachrome. The SVG segments with different degrees of lumen stenoses were selected for analysis, i.e. total occlusion, severe stenosis, moderate stenosis or mild stenosis of the vein corresponding to a diameter stenosis of 100%, <100≥50%, <50≥30% or <30% respectively, and cross-sectional area stenosis of 100%, >75%, 75–50% and <50% respectively. The following area measurements were made on each section: stent area, underlying plaque, lipid cores, calcified cores, vessel lumen and in-stent neointima. Fibrocellular tissue was graded as paucicellular or fibrotic [<30 spindled cells in HPF (high-power fields)], moderately cellular (30–100 spindled cells in HPF) and hypercellular (>100 spindled cells in HPF). Sections were magnified further (×200) and four fields containing stent struts (at 12, 3, 6 and 9 o’clock) were selected for analysis of neointimal details (neointimal thickness [in mm] and area [in mm²]), and neovessel and inflammatory cell density around the stent struts (in cells/mm²), which were classified as being slight (1–10 inflammatory cells/struts), moderate (11–20 cells/struts) or severe (>20 cells/struts)]. The stent strut penetration was categorized as being associated with the fibrous plaque (or an intact fibrous cap or intact media), medial injury or lipid core, or atheroma penetration [9].

**Immunohistochemistry**

Immunostaining for the detection of SMCs (smooth muscle cells), macrophages and cells containing ACE (angiotensin-converting enzyme), the proliferation marker Ki-67 and ERs (oestrogen receptors) were
performed in selected samples of non-stented and stented segments of all veins using techniques described previously [10]. Cellular ACE activity was investigated because ACE has been observed in the atherosclerotic plaque as a mediator of inflammation and in the process of wound healing after percutaneous injury of the vessel wall, and to identify endothelial cells [11,12]. Oestrogenic activity was investigated because of the protective mechanisms exerted by oestrogens in the vascular wall [13–15]. The total vessel area of positively stained segments for each immunological reaction was quantified by computer-aided planimetry of each specimen using an acquisition program (Image Pro Plus software, version 4.0; Media Cybernetics) in order to determine the percentage of the tissue surface containing different cell types.

### Statistical analysis
Continuous data are expressed as means ± S.D., and discrete variables are given as absolute values and percentages. A two-tailed Student’s t test was used for comparison of parametric variables, and a χ² test or exact test was used for comparison of discrete variables. A linear regression analysis was used to correlate the number of inflammatory cells around the stent struts and neointimal thickness. A $P$ value < 5% was considered significant.

### RESULTS

#### Histology
Clinical characteristics of the patients, procedural details of stent implantation, timing and the reason for surgical re-intervention are shown in Table 1.

The angiographic examination obtained before repeat bypass surgery showed three totally occluded SVGs (each one containing one, two and three stents respectively, and variable degrees of neointimal growth within the stents). In the remaining cases, a mild stenosis within the stent was observed in three stents in three different patients and a moderate-to-severe stenosis in another three stents implanted in three different patients. Segments of SVG with mild, moderate and severe stenosis not covered by the stents were also observed. Stents with medial fracture were associated with a significantly greater mean neointimal thickness compared with those not having medial fracture (1.37 ± 0.68 compared with 0.81 ± 0.47 mm² respectively; $P < 0.02$). In one case, the stent struts of two sequential stents were partially apposed to a large aneurysm, leaving a space between the struts and the SVG wall filled with thrombus and atheroma (Figures 1a and 1b). The degree of stent wall indentation, the luminal SVG percentage diameter stenosis and area narrowing, as well as the main histological characteristics, are shown in Table 2.
classification of the lesions as proposed by Virmani et al. [16].

**Stented SVG segments**

In totally occluded SVG, red thrombus was observed in all cases as well as a large amount of organized thrombus containing neovessels (Figure 2). The presence of neovessels has been described in native coronary arteries with total occlusion [17]. In two out of the three totally occluded cases, a stenosis of the graft was present proximally to the stented segment and, in one case, the stenotic plaque was in the mid-portion of the underexpanded stent, two mechanisms related previously to SVG stent occlusion [6]. Histology of the underlying stenotic lesions showed the predominance of SMCs that extended from the metallic wires towards the vessel lumen within an extensive extracellular proteoglycan/collagen matrix (Figure 2). The lumen side of the stent had a slight-to-moderate degree of inflammation (i.e. >1 to <20 cells adjacent to each stent strut), and giants cells were observed frequently. The vessel wall had a thin smooth muscular layer of the vein media (average, 900 ± 300 µm) and of the collagenous adventitia (average, 650 ± 400 µm). When the stent struts caused laceration or rupture of the vein medial wall, a thickened adventitia (>1 mm) was observed in correspondence with a thickened neointima towards the luminal side. Large calcium deposits (range, 2–8.7 mm²) were observed in all cases, always surrounded by inflammatory infiltrate of histiocytes and lymphocytes.

In patent stents, plaques causing different degrees of luminal stenoses were characterized by a similar histological pattern, mainly composed of SMCs and extracellular matrix. A moderate-to-severe infiltration of inflammatory cells (10–20 or >20 cells/strut) was observed when the stent strut was adjacent to the injured media or a lipid core rather than a fibrous plaque, confirming in the veins a mechanism described previously in native coronary arteries [9]. Furthermore, when the stent struts were in contact with an underlying plaque mainly composed of a necrotic core, no healing was present (Figure 3a) and plaque and thrombus protruding into the vein lumen were observed (Figure 3b). Different degrees of inflammation around the stent struts correlated with neointimal thickness in patent vessels; indeed, by linear regression analysis, a significant correlation was found between the areas occupied by inflammatory cells and the intimal thickness around the stent struts of plaques analysed in patent conduits ($r^2 = 0.43$, $P < 0.001$).

The degree of penetration in the vessel wall was not different for self-expanding or balloon-expanding stents. This may correspond to aggressive post-stent high-pressure balloon dilation or to the injury caused by the self-expanding stent type, which exerts a permanent radial force on the vessel wall. An interesting pathological feature of plaques causing only a small narrowing of the vein lumen is the presence of a circular layer of calcium around the stent. In these cases, organized thrombus was rarely observed and neointimal growth was only mild (Figure 4).

**Non-stented SVG segments**

Vein plaques were fibrous with calcified areas and chronic inflammatory infiltrates. Stenoses causing
Table 2  Summary of main histological findings

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Angiographic results narrowing</th>
<th>Depth of injury</th>
<th>Type of lesion</th>
<th>Main histological observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>%DS = 100</td>
<td>100%</td>
<td>Media*</td>
<td>Atherosclerotic plaque with rupture</td>
</tr>
<tr>
<td>2</td>
<td>%DS = 15</td>
<td>24%</td>
<td>Fibrous plaque</td>
<td>Fibrocalcific plaque</td>
</tr>
<tr>
<td></td>
<td>Acute total occlusion recanalized with emergency PTCA</td>
<td></td>
<td></td>
<td>UP: inflammation around the stent wires, giant cells.</td>
</tr>
<tr>
<td></td>
<td>Fibrous plaque/atheromatous plaque</td>
<td></td>
<td>Thin fibrous cap with necrotic core and haemorrhage</td>
<td>UP: large aneurysm containing organized thrombus, macrophages and cholesterol debris. Calcium and severe inflammation in atrophic media.</td>
</tr>
<tr>
<td>3</td>
<td>%DS = 38</td>
<td>60%</td>
<td>Fibrous plaque/atheromatous plaque/media*</td>
<td>Plaque with rupture</td>
</tr>
<tr>
<td></td>
<td>Acute total occlusion recanalized with emergency PTCA</td>
<td></td>
<td></td>
<td>UP: inflammation around the stent wires, giant cells.</td>
</tr>
<tr>
<td></td>
<td>Fibrous plaque/atheromatous plaque/media*</td>
<td></td>
<td></td>
<td>UP: inflammation around the stent wires, giant cells.</td>
</tr>
<tr>
<td>4</td>
<td>%DS = 16</td>
<td>16%</td>
<td>Fibrous plaque</td>
<td>Fibrocalcific plaque</td>
</tr>
<tr>
<td></td>
<td>%DS = 40</td>
<td>40%</td>
<td>Fibrous plaque</td>
<td>Fibrocalcific plaque</td>
</tr>
<tr>
<td>5</td>
<td>%DS = 100</td>
<td>100%</td>
<td>Fibrous plaque</td>
<td>Pathological intimal thickening</td>
</tr>
<tr>
<td></td>
<td>%DS = 55</td>
<td>84%</td>
<td>Media-elastic lamina*</td>
<td>UP: atrophy of the media and adventitia, infrequent SMCs in a rich extracellular matrix. Inflammatory cells around the stent wires.</td>
</tr>
<tr>
<td>6</td>
<td>%DS = 28</td>
<td>43%</td>
<td>Fibrous plaque</td>
<td>Fibrocalcific plaque</td>
</tr>
<tr>
<td></td>
<td>%DS = 46</td>
<td>72%</td>
<td>Fibrous plaque/media*</td>
<td>UP: SMCs and chronic inflammatory cells.</td>
</tr>
</tbody>
</table>

%DS, percentage diameter stenosis; PTCA, percutaneous transluminal coronary angioplasty; NI, neointima; UP, underlying plaque. Classification of the lesion was according to the scheme proposed by Virmani et al. [16]. *Disrupted media.
lumen narrowing of SVGs were mainly composed of organized thrombus with neovessels. Histiocytes and, less frequently, lymphocytes were observed beneath the endothelial layer that covered the intima. In the lumen of the SVG, red thrombus was observed in as many as 70% of the segments analysed (Figure 5).

Restenotic or primary lesions
Primary lesions were composed mostly of moderately cellular plaques (30-100 spindled cells/HPF), whereas restenotic plaques had a trend to be predominantly paucicellular (<30 spindled cells/HPF). No significant differences in extracellular matrix formation or cell proliferation were observed between primary and restenotic SVG tissue, in contrast with findings described previously in arterial tissue [18]. The lack of a diagnostic pattern that differentiate primary from restenotic plaques in SVGs has been reported previously [5,8].

Stents in place for less than 6 months
The pathology of stents analysed within 6 months of implantation revealed moderate-to-severe inflammation of the media around the stent wires (10–20 or >20 cells/strut respectively), neointimal proliferation and SMCs; the endothelial layer was not always observed and, when present, the endothelial cells had large nuclei and polygonal cellular shape.
Histopathology of saphenous vein grafts

Figure 4 Haematoxylin/eosin-stained cross-section of a stented segment of an SVG

The section was stained with haematoxylin/eosin, and shows large circular calcification around the stent struts and mild neointimal growth at the luminal side of the stent. Magnification, × 4.

Figure 5 Movat pentachrome-stained cross-section of a non-stented segment of an SVG treated previously with balloon angioplasty

Late luminal narrowing (asterisk), thickened neointima (1), organized thrombus (2), red thrombus (3) and neovessels of the thickened adventitia (4) are evident. Magnification, × 4.

Stents in place from 6 months to 2 years

The neoendothelium had a thin layer of cells with a normal aspect covering the neointima located within the stented segments. Large calcified semi-circular areas with moderate inflammation near the calcified core and the metallic wires were observed. In some areas, macrophages included iron pigments.

Stents in place from 2 to 5 years

The histology appeared basically as described above, with more intense infiltration of lymphocytes under the endothelial layer and giant cells close to the stent struts. Calcified areas of the vessel wall were larger the older the SVG (mean calcified surface in veins > 10 years was 6.8 ± 3.4 mm² compared with 3.4 ± 3.0 mm² in veins ≤ 10 years; \( P < 0.01 \)).

Immunohistochemistry

Immunostaining for \( \alpha \)-actin identified SMCs as the cellular component of 40–80% of the media layer in all cases, and infrequent elements in the adventitia. On the lumen side, cellular components of the neointima within the stent revealed SMCs accounting for 55% of the neointimal area and a rich extracellular fibrous matrix. There were more SMCs close to the neoendothelium than close to the stent struts (53 compared with 12% respectively; \( P < 0.01 \)), but the percentage area of stained cells did not differ among the different types of tissue analysed (Table 3).

KP-1 staining was observed in areas of clusters of macrophages in all cases. In the underlying plaque, KP-1 stained macrophages situated close to the necrotic or the calcified cores and the external side of the metallic stent struts. Some inflammatory cells were also observed in the adventitia. In the neointima, KP-1-positive cells were in contact with the metallic struts (Figure 6a) and beneath the neoendothelial layers when this was present. In plaques causing severe in-stent restenosis, KP-1-positive cells were significantly more frequent than in plaques causing only mild in-stent stenosis (Table 3). In non-stented segments, KP-1-stained cells were also present close to necrotic, atheromatous or calcified cores.

ACE activity was detected mostly in cells that co-localized with KP-1 in identical sections, suggesting their inflammatory nature. These cells were most commonly observed close to the stent wires (Figure 6b) and, in some cases, close to the adventitia. A second type of ACE-positive cells that did not stain for KP-1 were identified as endothelial cells of neovessels of the plaque and cells of the neoendothelium that faced the vessel lumen. A third group of ACE-positive cells that co-localized with \( \alpha \)-actin in identical sections was observed in the media.

Table 3 Quantitative immunohistochemical analysis

<table>
<thead>
<tr>
<th>Type of SVG sample</th>
<th>α-Actin</th>
<th>KP-1</th>
<th>ACE</th>
<th>Ki-67</th>
<th>ER</th>
</tr>
</thead>
<tbody>
<tr>
<td>De novo lesion</td>
<td>58 ± 35</td>
<td>21 ± 15</td>
<td>18 ± 16</td>
<td>&lt; 1</td>
<td>-</td>
</tr>
<tr>
<td>Restenotic lesion</td>
<td>49 ± 31</td>
<td>27 ± 19</td>
<td>22 ± 19</td>
<td>&lt; 1</td>
<td>-</td>
</tr>
<tr>
<td>Severe in-stent restenotic lesion</td>
<td>51 ± 31</td>
<td>33 ± 20*</td>
<td>25 ± 24*</td>
<td>&lt; 1</td>
<td>-</td>
</tr>
<tr>
<td>Mild in-stent lesion</td>
<td>45 ± 40</td>
<td>18 ± 14</td>
<td>10 ± 7</td>
<td>&lt; 1</td>
<td>-</td>
</tr>
<tr>
<td>Stented SVG</td>
<td>54 ± 33</td>
<td>22 ± 18</td>
<td>19 ± 17†</td>
<td>&lt; 1</td>
<td>-</td>
</tr>
<tr>
<td>Non-stented SVG</td>
<td>56 ± 27</td>
<td>16 ± 12</td>
<td>9 ± 6</td>
<td>&lt; 1</td>
<td>-</td>
</tr>
</tbody>
</table>

\* \( P < 0.05 \) compared with immunostaining in mild in-stent lesion; † \( P < 0.05 \) compared with immunostaining in the non-stented SVG.
and the subendothelial layer of the neointima with a spindle-shape morphology. In plaques causing in-stent restenosis, there was significantly more ACE activity in macrophages compared with plaques of non-stented vein segments (Table 3).

Immunostaining for Ki-67 showed few positive cells, suggesting the poor proliferative state of the old veins. There was no difference in the amount of Ki-67-positive cells between restenotic or 'de novo' lesions and between plaques causing severe or mild in-stent obstructions (Table 3).

Immunostaining for ER was completely negative in all of the sections examined, irrespective of the patient’s gender and of the presence of a stent.

**DISCUSSION**

Despite the improvement in the immediate results of transcatheter treatment of diseased SVGs [2], the long-term outcomes remain suboptimal [3]. The reasons for such unfavourable results are probably related to the nature of the venous wall and the changes that follow the implantation of the vein in the systemic circulation [19]. Metallic stents may interact with the venous wall in a different manner compared with the arterial wall; the more fragile media layer and the friable atherosclerotic type of plaque of the SVG can easily be damaged by percutaneous devices inducing a subsequent exaggerated reparative response.

Our present study extends the available knowledge about the long-term effects of metallic stents in SVGs up to 5 years after implantation and the evolution of the atherosclerotic disease in the SVG wall up to 18 years.

The main findings of our present study can be summarized as follows. First, histology shows, on the one hand, that the media layer of the SVG, being thinner than that of coronary arteries, is likely to be more susceptible to the mechanical damage caused by stents and balloon pressure, and that easier media fracture follows aggressive neointimal proliferation. On the other hand, very long-term chronic inflammation close to the metallic wires is a relevant phenomenon and, similar to what has also been reported in coronary arteries, this finding correlates with a thicker neointima within the stents [9,20]. However, organized thrombus with neovessels represents the main component of the lumen-narrowing material (particularly in totally occluded conduits), whereas substantial amounts of plaque easily protrude into the SVG lumen after stent placement. The larger diameter and the lower elasticity of the vein conduit may cause a less brisk flow in the SVG that fosters platelet apposition, thrombus formation and subsequent lumen narrowing. Thus the atherosclerotic material of SVG lesions appears highly friable because it lacks excess collagen and is richer in lipids, necrotic cores and macrophages, facilitating plaque prolapse through the stent struts.

Unlike native coronary arteries, in which calcification is basically seen in the intima embedded in the collagen matrix and focally precipitated in necrotic cores, atherosclerosis of the degenerated SVG is characterized by large areas of calcification of the vessel wall itself. In particular, in segments of veins with only mild in-stent proliferation, calcium deposition may assume a circular pattern embedded in a thin muscular wall, and these annular calcified areas are more extensive the longer the time the implant is in the arterial circulation.
Secondly, immunohistochemical assays show a long-lasting presence of macrophages staining positively for KP-1 and ACE, confirming a preliminary report from our group in which ACE activity in cells close to the stent wires was observed after 6 months of stent implantation in an artery [21]. Such an observation extends the concept proposed by Komatsu et al. [22], who demonstrated ACE activity as a mediator of inflammation, but being limited to a short time after balloon arterial wall injury. This phenomenon was observed predominantly in sections of veins that received a coronary stent. The presence of ACE was not only detected in inflammatory cells; indeed, ACE immunostaining was observed in endothelial cells, as expected, but also in groups of neointimal spindle-shaped cells that also stained positively for α-actin. This finding suggests a possible role of the enzyme in the transformation of SMC-like cells from a dedifferentiated to a differentiated phenotypic state or from other types of cells such as infiltrating macrophages or fibroblasts, as has been proposed previously in native coronary arteries [10,12,22]. A predominant role for ACE in the repair process of wall damage in SVGs is supported by the 3-fold greater ACE activity observed in human SVGs compared with the internal thoracic artery of patients re-operated 20 years after a first coronary bypass surgery [23].

Immunostaining for ERs was completely negative in the samples in the present study, which is in agreement with previous observations in saphenous veins [24,25]; however, ERs may be found infrequently in veins of fertile women, but not in men or postmenopausal women [24]. The lack of anti-atherosclerotic effects of oestrogens on the structure of the vein wall may contribute another possible reason for the aggressive atherosclerotic degeneration of the veins used as bypass grafts [15].

The infrequent presence of cells staining with the proliferation marker Ki-67 highlighted the poor proliferative state of this type of tissue, and suggests that organized thrombus and migrated cells, rather than cell proliferation, could be the principal reasons of SVG lumen narrowing.

The recent availability of DES has dramatically improved the efficacy of percutaneous coronary interventions in native vessels, but very little information is available regarding the efficacy of DES implanted into old degenerated SVGs [26–28]. Furthermore, results on the histopathology of such kinds of stents implanted into old SVG is not available to date. Commercially available DES inhibit restenosis in coronary arteries, exerting mainly antiblastic and antiproliferative effects [29]; therefore, from a practical standpoint, DES may exert different levels of effectiveness (either higher or lower) in old degenerated atherosclerotic SVGs according to the predominant histopathological characteristics observed in these plaques, as described in the present study.

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