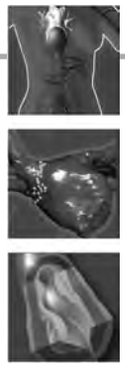

A novel approach to aortocoronary saphenous venous graft percutaneous treatment

Evaluation of: Abizaid A, Weiner B, Bailey SR, Londero H: Use of a self-expanding super-elastic all-metal endoprosthesis; to treat degenerated SVG lesions: the SESAME first in man trial. Catheterization and cardiovascular interventions. *J. Soc. Cardiac Angiogr. Interv.* 76(6), 781–786 (2010). Saphenous veins remain an important conduit in coronary artery bypass surgery. However, owing to accelerated atherosclerosis, approximately 50% of grafts are occluded by 10 years making the percutaneous treatment the preferable approach. Previously, the results of percutaneous treatment of saphenous vein grafts (SVGs) were affected by the high rates of periprocedural myocardial infarction and restenosis/occlusion. These unfavorable results were supplanted, in part, by the use of embolic protection devices (EPDs). However, less than 25% of SVG lesions have the anatomical criteria for the use of EPDs. Moreover, their use adds complexity to the procedure and requires training. This first-in-man study describes a novel nanosynthesized, membrane-covered self-expanding superelastic all-metal endoprosthesis stent (SESAME Stent™) in 20 patients undergoing percutaneous intervention of SVG (21 lesions with an average length of 8.9 mm) without EPDs. The acute success rate was 100%. No complications occurred and the incidence of major adverse cardiac events (MACE) at 30 days and 9 months was 0 and 14%, respectively. Larger trials with more complex SVG lesions are warranted to determine if the SESAME stent can improve the outcomes of SVG percutaneous treatment.

KEYWORDS: devices ▪ embolic protection ▪ percutaneous coronary intervention ▪ saphenous vein graft

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This article reviews the recent paper by Abizaid *et al.* demonstrating the first-in-man experience with a novel nanosynthesized, membrane-covered self-expanding all-metal stent (SESAME Stent™, Palmaz Scientific) in patients undergoing percutaneous coronary intervention of diseased saphenous vein graft (SVG) [1].

Nowadays, the old quote 'the challenging landscape of SVG PCI' can still be written in this introduction paragraph. However, new data on the natural history of SVG disease (SVGD) was added by new modalities images (invasive and noninvasive), by the improvement of the clinical treatment and, mainly, by the progress of percutaneous intervention technology/technique. This new data has been important in reducing the outcomes in patients and refining the treatment SVGD.

The use of SVG as a conduit in coronary artery bypass surgery (CABG) remains an important option. However, the palliative nature of vein grafts can appear early, even during the first year due to accelerated atherosclerosis characterized by SVGD. Therefore, the percutaneous treatment of SVGD represents an important subset of patients, representing overall 5–15% of all percutaneous interventions [2].

SVGD has a vascular biology that differs from the native vessels. Three pathophysiologically interlinked processes are observed in SVGD: subacute thrombosis (occurring 1 month after surgery), neointimal 'adaptative' hyperplasia that creates an atherosclerosis-prone region (1 month to 1 year after CABG) and vein atherosclerosis (usually after 3 years of CABG) [2]. Furthermore, some morphological characteristics are also different from the native vessel; vein graft lesions, for example, are mostly friable, tend to be diffuse and concentric with poorly developed or absent fibrous cap and the presence of superimposed thrombus and little evidence of calcification [2].

Angiographic studies have demonstrated an occlusion frequency of 15% during the first year, 1–2% per year between 1 and 6 years, and 4% per year after 6 years. Ultimately, by the end of 10 years after CABG, 40% of SVG are occluded and only 50% of patent vessels are free of significant stenosis [3,4].

This pathological process translates into angina recurrent during the first year, which can affect 20% of patients [5]. Moreover, acute coronary syndromes after CABG have the culprit lesion located at the SVG with more than 70%

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with superimposed thrombus. Angioscopy studies have documented thrombus in 70% of SVG lesions undergoing percutaneous treatment [6].

Consequently, additional revascularization (redo-CABG) is required in approximately 5% of patients at 5 years, 20% at 10 years and 30% at 12 years after CABG and, as compared with the first surgery, the redo-CABG carries a higher risk of morbidity and mortality making the percutaneous approach an important option for these patients [7]. On the other hand, these pathological aspects can explain part of the unfavorable outcomes of percutaneous treatment of diseased SVG, even with the use of drug-eluting stents (considered the best technology), which have yielded conflicting results [8–10].

The worse outcomes after SVG percutaneous intervention are related to the higher rates of periprocedural myocardial infarction [11] and to the historically higher rates of restenosis and to the progression of disease in other places.

A new era of acute outcomes after SVG percutaneous intervention was initiated after the efficacy of embolic protection devices (EPDs) was reported showing the reduction of 30-day major adverse cardiac events (MACE) by approximately 40% and becoming a class I device for SVG percutaneous intervention when technically feasible [12]. Apart from the well known anatomic exclusions criteria, recent reports have indicated that the current overall use of EPD from the American College of Cardiology-National Cardiovascular Data Registry is 22% [13]. Furthermore, these devices have limitations, including the effects of the particles released during the first pass of the devices and even the atherothrombotic material that remains adherent to the stent surface, which hypothetically can embolize immediately after the procedure when the EPD devices are no longer in place.

Therefore, a further improvement in the technology with new devices is warranted for SVG percutaneous intervention. This article examines the first-in-man study recently published by Abizaid *et al.* that evaluates primarily the technical feasibility, and secondly the incidence rates of MACE at 30 days and 9 months of a new membrane-covered self-expanding superelastic all-metal stent (SESAME stent) in elective patients who underwent SVG percutaneous intervention [1].

Methods

This study is a first-in-man prospective registry totaling 20 consecutive patients (21 lesions) with diseased SVG treated at two centers with the SESAME stent. The primary objective was to evaluate the technical efficacy stated as: 1) device success: successful delivery and deployment of the stent; 2) clinical success: device success without procedural events. The secondary end point was a composite of MACE at 30 days including death, myocardial infarction and target vessel revascularization within 30 days of intervention and target vessel failure at 9 months.

The inclusion criteria were evidence of myocardial ischemia as evidenced by stable or unstable angina or positive functional test study. Angiographic inclusion criteria were the following: target lesion was within a SVG that was ≥50% and ≤100% stenosed, a thrombolysis in myocardial infarction (TIMI) flow ≥2, a reference vessel diameter ≥3.5 mm and ≤5.0 mm by visual estimation, and eligible for treatment with a single 20-mm long SESAME stent.

The exclusion criteria included patients with documented Q wave or non-Q wave myocardial infarction within 24 h prior to the procedure, patients requiring angioplasty/stent treatment in more than one vessel (or concomitant treatment of native vessel), SVG younger than 6 months and the presence of left ventricular ejection fraction <30%.

The clinical 30-day follow-up was available for all patients (100%). One patient was lost to follow-up and others had the angiography at 12 months, with 90% of the initial cohort (19 lesions) remaining for the 9 month clinical and angiographic follow-up.

Results

The sampled population (20 patients/21 lesions) included 72% male with a mean age of 67.1 ± 7.9 years of age and 15% diabetics. The angiographic findings of the SVG included a mean vessel reference diameter of 3.2 ± 0.64 mm and a mean lesion length of 8.9 ± 4.2 mm. There were no acute complications with 100% device and procedural success. The lesions were treated with a single stent in all but one patient who required two overlapping stents. There were no angiographic complications such as no-reflow/slow-flow, angiographic thrombus or dissection.

The secondary end point reported by the authors of 30-day MACE was 0% and the 9-month MACE was 14% driven by two target vessel revascularizations and one target lesion revascularization (at the overlapping stent). Additionally, two incidental chronic total occlusions were documented during the follow-up.

Although not planned as part of the initial protocol, the authors described paired data on intravascular ultrasound images at the time of the intervention and of the angiographic scheduled follow-up, which showed full apposition of the stents without tissue prolapsed and absence of thrombus or edge dissection. Moreover, in this subset of patients the volume of intimal hyperplasia was 49.6 ± 26.8 mm^3.

Significance

The treatment of diseased SVG remains one of the most challenging subsets of patients who have undergone percutaneous coronary intervention. The interesting acute results from Abizaid *et al.* with the SESAME stent brings back an old strategy of covered stents to treat diseased SVG [1].

In the past, the RECOVERS trial has evaluated the polytetrafluoroethylene (PTFE)-covered stent (JoStent™, Abbott) compared with the bare-metal stent. The patients who were randomized to the PTFE stent showed a higher incidence of MACE at 30 days (10.9 vs 4.1%; p = 0.047) and at 9-month follow-up, mainly, attributed to nonfatal myocardial infarction (12.8 vs 4.1%; p = 0.013) [14]. These results were confirmed in a similar randomized trial, STING, which demonstrated a trend toward a higher late occlusion rate in the stent graft group (7 vs 16%; p = 0.069) [15]. As a result, both studies failed to support the hypothesis of the PTFE-covered stent to act as a 'local filter' decreasing the probability of distal embolization and also the rationale of 'endoluminal sealing' to reduce the neointimal proliferation.

The results from Abizaid *et al.* are largely in contrast with these trials, especially regarding the 0% incidence rate of 30-day acute myocardial infarction even without the use of EPD, indicating a potential advance in the field.

Findings that can explain these results include: the fact that the PTFE stent is somewhat bulky, which is reflected by the higher pressure and the postdilatation necessary in order to completely expand the stent, which can affect the rates of myocardial infarction, and that the double layer may be detrimental considering the hyperplasia. On the other hand, the SESAME stent is self expandable with a microporous 5-µm thick all-metal external membrane without polymers, which has the potential to favor endothelialization. In addition, the all-metal mesh of the SESAME stent has a 'pillowing effect' on the plaque avoiding the plaque protrusion and the potential limitation of stent migration into the plaque.

However, as acknowledged by the authors, this represents a first experience with a limited sampled population. Furthermore, a selection bias towards enrollment of less complex diseased SVG patients should not be excluded.

From a clinical point of view, there was no mention on the clinical presentation of SESAME patients. It is well established that non-ST-elevation acute coronary syndromes have worse prognosis and are more likely to have vessels with thrombus-containing lesions. Secondly, the prevalence of diabetic patients was lower in the SESAME trial (14%) compared with the classical SVG trials (25–45%) [16].

The angiographic characteristics of patients treated in the SESAME study also diverge from the historical SVG trials. For example; the mean lesion length in the SESAME study was 8.9 mm compared with 14 mm in a recent study [17]. This difference is relevant because the lesion length has been demonstrated to be the strongest determinant of MACE (odds ratio: 2.81; 95% CI: 1.82–4.34/log increase in lesion length) and the strongest predictor of periprocedural myocardial infarction (odds ratio: 2.54; 95% CI: 1.59–4.04/log increase in lesion length) [17]. Interestingly, the age of SVG was not associated with periprocedural outcomes. Other angiographic differences included thrombus-containing lesions and SVG with high degeneration scores.

The rate of MACE at 9 months was approximately 14% in the 18 patients (90%) with complete follow-up driven by two target vessel revascularizations and the incidence of one target lesion revascularization (at the site of two overlapping stents). Nevertheless, the finding of two 'chronic total occlusions' documented during the angiographic follow-up should be interpreted with caution. Apparently they were not classified as stent thrombosis or target vessel failure, which despite being included in the methods section, was not described by the authors. In addition, the period of anti-platelet therapy was not mentioned.

The 9-month MACE outcomes of the SESAME stent appear to be as safe as the bare-metal arm of the recent randomized controlled trials with the great advantage of not using the EPD devices during the stent implantation [8,10]. This information can benefit most patients without anatomical criteria for the EPD device and make the procedure more cost effective.

Future perspective

The first-in-man SESAME stent trial is noteworthy owing to the acute performance on diseased SVG without the use of embolic protection

devices. Hypothetically, the causal pathway of periprocedural myocardial infarction was disrupted by an action of a 'local filter'. Apparently, the covered all-metal mesh membrane avoids the embolization of atherothrombotic particles and the protrusion of plaque through the stent struts during and after the procedure, resulting in the outcomes reported.

The concept of tissue prolapse and exposure of underlying atheromatous tissue through the stent struts is confirmed, in part, by the improved outcomes with the simple technique of select undersized stents in patients who underwent percutaneous treatment of diseased SVG [18].

The optimal percutaneous treatment of SVG remains to be established. Recent randomized trials have pointed out an angiographic benefit of drug-eluting stents over the bare-metal controls without major safety concerns [10]. However, the small sample size of these studies makes the capture of small-to-moderate treatment effects difficult. Two recently published meta-analysis showed a benefit of drug-eluting stents over bare-metal stents in the treatment of diseased SVG [19,20]. Of note, 11 of 19 studies included in the analysis included less than 150 patients. In addition, the heterogeneity reached statistical significance for some end points analyzed, which makes the conclusions underpowered. ISAR-CABG, the first trial adequately powered to clinical end points, will be a landmark study in the treatment of diseased SVG.

An adequately powered randomized trial comparison between the SESAME stent and a strategy with embolic protection including more complex lesions would be appropriate as the next step. Just after this 'placement test', the SESAME stent can potentially be included in the armamentarium of treatment for diseased SVG.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Executive summary

Background

- The percutaneous treatment of saphenous vein graft (SVG) disease represents overall 5–15% of all percutaneous coronary interventions. The use of embolic protection devices (EPDs) has been associated with improved acute outcomes. However, in daily clinical practice the use of EPD represents less than 25% of cases.

Methods

- This is a first-in-man prospective study of 20 patients with 21 SVG lesions undergoing percutaneous intervention with a novel nanosynthesized, membrane-covered self-expanding all-metal stent (SESAME stent™) without EPD. The end points were to evaluate the technical feasibility and the incidence rates of major adverse cardiac events (MACE) at 30 days and 9 months.

Results

- There were no acute complications with 100% device and procedural success. The incidence rate of 30 day and 9 month MACE was 0 and 14%, driven by two target vessel revascularizations and one target lesion revascularization.

Significance

- The first-in-man SESAME stent trial is noteworthy owing to the acute performance on SVG lesions without the use of EPD.

Future perspective

- A randomized trial including more complex SVG lesions would be appropriate as the next step to include the SESAME stent in the armamentarium of SVG lesions.

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