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# A prospective multicenter registry of laser therapy for degenerated saphenous vein graft stenosis: the COronary graft Results following Atherectomy with Laser (CORAL) trial☆,☆☆

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ABSTRACT

*Purpose:* The primary aim of this study was to prospectively evaluate the safety and efficacy of Excimer laser atherectomy as a primary treatment strategy in consecutively eligible patients presenting for percutaneous coronary intervention (PCI) of degenerated saphenous vein graft (SVG) lesions using a multicenter registry. Prior single-center experience suggested that laser atherectomy may decrease acute procedural complications during treatment of degenerated SVGs, including lesions not amenable to distal protection devices (DPDs).

*Methods and materials:* The COronary graft Results following Atherectomy with Laser investigators enrolled 98 patients at 18 centers between June 23, 2003, and October 4, 2004, with greater than 50% stenosis of an SVG who presented for PCI due to angina pectoris or objective evidence of myocardial ischemia in a concordant myocardial distribution. Laser atherectomy was planned. Patients were excluded if the operator planned to utilize a DPD. Inclusion and exclusion criteria were aligned to those in the Saphenous vein graft Angioplasty Free of Emboli Randomized (SAFER) trial.

*Results:* The primary end point [30-day major adverse cardiac events (MACE)] occurred in 18/98 (18.4%) patients driven primarily by non-q-wave myocardial infarction. Major procedural complications included no reflow ($n$=5) and major dissection ($n$=1). No perforations occurred. Univariate predictors of 30-day MACE included lesion length, vessel angulation, plaque burden, SVG degeneracy score, number of laser pulses used, and larger-sized laser catheters.

*Conclusions:* This study demonstrated that Excimer laser atherectomy of diseased SVGs is feasible with results comparable to the 30-day MACE in the control population from the SAFER trial. Whether the addition of laser to embolic protection devices is of any clinical utility remains to be tested in future studies.



## 1. Introduction

Saphenous vein graft (SVG) interventions for older degenerated grafts remain technically challenging, with a high risk for periprocedural events despite advances in therapy including the introduction of mechanical embolic protection. Although stent implantation for SVG stenosis has become the standard of care for diseased SVGs since the publication of the Saphenous Vein De Novo Trial in 1997 [1], outcomes were not significantly improved until stenting was performed in the presence of embolic protection. The Saphenous vein graft Angioplasty

☆ Disclosures: Dr. Giugliano served as a consultant to Spectranetics from 2003 to 2006. Dr. Ebersole has served as a consultant to Spectranetics. Dr. Ruggio served on the board of directors for Spectranetics.

☆☆ Summary: The CORAL registry was a multicenter prospective registry of Excimer laser atherectomy of diseased SVGs. Overall 30-day MACE rate was comparable to SVG PCI without the use of distal embolic protection from the SAFER trial.

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Free of Emboli Randomized (SAFER) trial enrolled 801 patients between June 1999 and August 2000 in a multicenter study in which patients undergoing SVG intervention of the body of the SVG were randomized to undergo stenting either over a conventional guidewire or over the GuardWire distal protection device (DPD) [2]. Prior therapies (e.g., glycoprotein IIb/IIIa inhibitors and covered stents) have not been effective in improving outcomes of SVG percutaneous coronary intervention (PCI) [3–5]. It has been noted that not all SVG lesions are amenable to DPD, and in 33%–57% of SVG PCIs, lesion location or the lack of a landing zone may not permit use of DPD [6]. However, these are the lesions that demonstrate the higher rates of periprocedural complications. Further, plaque and thrombus embolization may occur during attempted placement of the embolic DPD (first pass effect) prior to performing any definitive therapy of the diseased SVG [7]. In order to overcome this "first pass effect," proximal embolic protection is an alternative that has promise but adds technical complexity [8]. It has been shown that the embolic particulates consist of both plaque and platelet-rich thrombus [9]. This suggests that debulking the atherosclerotic plaque and ablating platelet-rich thrombus may decrease the adverse event rate during SVG PCI. Previous attempts at mechanical debulking of SVG lesions have demonstrated an increased risk of embolization, likely due to incomplete capture of plaque or lack of specific treatment for thrombus [10,11]. Excimer laser debulking has been utilized in complex lesion subsets including acute myocardial infarction, severe calcification, and thrombus-containing lesions [12–16]. Given the unique properties of the laser to ablate thrombus, its potential for benefit in treating SVG lesions has been suggested previously to reduce embolic complications in this high-risk lesion subset [17,18].

## 2. Methods

The **CO**ronary graft **R**esults following **A**therectomy with **L**aser (CORAL) trial was a prospective, multicenter registry of 98 non-randomized, consecutive patients with stenotic SVGs undergoing laser atherectomy and planned stenting without a DPD. Key exclusions included patients with recent myocardial infarction and creatine kinase-MB fraction elevated above normal, left ventricular systolic function less than 30%, and planned use of a DPD. The CORAL trial was initially designed as a randomized study of SVG PCI comparing stenting with DPD versus pretreatment with laser atherectomy followed by stenting plus DPD. Unfortunately, the randomized trial failed to enroll and was halted. The CORAL registry then enrolled a consecutive patient cohort that underwent SVG PCI using laser atherectomy without DPD from June 2003 to October 2004. The primary end point was 30-day major adverse cardiac events (MACE) defined as the composite of all-cause mortality, myocardial infarction (CK-MB more than three times the upper limit of normal), emergent bypass surgery, or target vessel revascularization. A comparison of the primary end point in this study with the SAFER trial was planned. Secondary end points included technical success (defined as successful crossing of the lesion and retrieval of the device from the body) and procedural success (defined as less than 50% residual stenosis and no MACE). Procedure-related complications were also evaluated to assess the safety and feasibility of performing laser atherectomy using the CVX-300 Excimer Laser (Spectranetics Corporation, Colorado Springs, CO, USA) followed by planned stenting of degenerated SVGs. The enrolling site was required to prespecify whether the patient would meet the primary operators' criteria for distal embolic protection. Definitive treatment of the SVG lesion was planned to be accomplished by stent implantation.

### 2.1. Excimer laser treatment protocol

The Spectranetics CVX-300 is a pulsed-wave xenon chloride laser that operates within a wavelength of 308 nm, with a pulse duration of 135 ns, and produces an output of 165 mJ per pulse. The size of the laser catheter(s) used was left to the discretion of the interventionalist based on reference vessel diameter, target lesion morphology, and degree of lesion obstruction. Protocol guidance was provided to the operators to ablate as much tissue as possible with the goal to achieve a minimal lumen diameter (MLD) postlaser of at least 2.0 mm (deemed optimal ablation). Laser catheter sizes of 1.7 mm and 2.0 mm were recommended for use in target vessels with a reference diameter greater than 2.3 mm. Smaller laser catheters (0.9 mm and 1.4 mm) were available for initial pretreatment if a larger catheter could not be passed or for smaller-diameter vessels. Manual flush saline infusion before and during ablation was required. Initial fluence and repetition rates were 45 mJ and 25 Hz, respectively. The fluence and repetition rates were increased at the discretion of the operator if the catheter could not be advanced. The laser catheter was slowly advanced at 1–5 mm per 5-s train of pulse. The operators were advised to follow the instructions for use of the Excimer laser catheter.

The CORAL registry was crafted to allow the use of the control arm of the SAFER trial (no DPD) as a comparison group by utilizing the same inclusion/exclusion criteria as the SAFER trial excluding planned DPD use. All patients underwent pretreatment of the diseased SVG using the Excimer laser followed by planned stent implantation. An independent angiographic core laboratory, skilled in the analysis of SVG therapies, evaluated the outcomes and also determined whether the SVG lesion would qualify for DPD based upon the SAFER trial criteria.

To compare the CORAL population to that in the SAFER trial, we utilized standard clinical and angiographic variables as well as previously established predictors of SVG MACE from the SAFER trial and filter wire study [19,20]. The independent angiographic core lab (Brigham and Women's Hospital Angiographic Core Laboratory, Boston, MA, USA) calculated the SVG percent degeneration score, defined in quartiles as the percentage (0%–25%, 26–50%, 51%–75%, >75%) of the treated graft with evident (>20% luminal narrowing) disease. Estimated lesion plaque volume, defined as the volume of a cylinder whose diameter was equal to the reference vessel diameter, and whose length was the core-lab-measured shoulder-to-shoulder lesion length, minus the volume of a cylinder of the same length and a diameter equal to the measured minimal lumen diameter, was also calculated. The degeneracy score captures the state of graft disease outside the target lesion, thus incorporating the diffuse nature of the disease within the entire graft. The estimated plaque volume is a lesion-specific variable which captures the amount of plaque at risk for embolization when the lumen of the target lesion is expanded during stent placement.

### 2.2. Statistical analysis

Continuous variables were compared using Student's $t$ test since the samples were large enough to approximate normal distributions. Binary variables were compared using $\chi^2$ with normal approximation or Fisher's Exact Test when appropriate. All data were analyzed based on the intention-to-treat principle. Logistic regression was used to identify univariable predictors of 30-day MACE. Selected demographic and angiographic characteristics recorded in the SAFER trial, as well as graft degeneration score and lesion plaque volume, were considered in univariable analyses as potential predictors. Due to the small number of events overall, multivariable modeling was not appropriate. A two-tailed $P$ value<.05 was considered significant. All statistical analyses were performed using STATA, version 7 (College Station, TX, USA).

## 3. Results

### 3.1. Baseline demographics

The CORAL registry enrolled 98 patients across 13 medical centers in the USA between June 2003 and October 2004. The patient