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Coronary Sinus Reducer Implantation for the Treatment of Chronic Refractory Angina

A Single-Center Experience

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ABSTRACT

OBJECTIVES The aim of this study was to assess the safety and efficacy of the Reducer in a real-world cohort of patients presenting with refractory angina.

BACKGROUND The coronary sinus Reducer is a novel device to aid in the management of patients with severe angina symptoms refractory to optimal medical therapy and not amenable to further revascularization.

METHODS Fifty patients with refractory angina and objective evidence of myocardial ischemia who were judged unsuitable for revascularization were treated with coronary sinus Reducer implantation at a single center between March 2015 and August 2016. Safety endpoints were procedural success and the absence of device-related adverse events. Efficacy endpoints, assessed at 4- and 12-month follow-up, were a reduction in Canadian Cardiovascular Society angina class, improvement in quality of life assessed using the Seattle Angina Questionnaire, improvement in exercise tolerance assessed using the 6-min walk test, and reduction in pharmacological antianginal therapy.

RESULTS Procedural success was achieved in all patients, with no device-related adverse effects during the procedure or at follow-up. Regarding the efficacy endpoint, 40 patients (80%) had at least 1 reduction in Canadian Cardiovascular Society class, and 20 patients (40%) had at least 2 class reductions, with a mean class reduction to 1.67 ± 0.83 vs. 2.98 ± 0.52 ($p < 0.001$) at 4-month follow-up. All Seattle Angina Questionnaire items improved significantly ($p < 0.001$ for all). A significant increment in 6-min walk distance to 388.6 ± 119.7 m vs. 287.0 ± 138.9 m ($p = 0.004$) was observed. Sixteen patients (32%) and 3 patients (6%) demonstrated reductions of at least 1 or 2 antianginal drugs, respectively. The benefit of Reducer implantation observed at 4-month follow-up was maintained at 1 year.

CONCLUSIONS In this real-world, single-center experience, implantation of the coronary sinus Reducer appeared safe and was associated with reduction in anginal symptoms and improvement in quality of life in patients with refractory angina who were not candidates for further revascularization. (J Am Coll Cardiol Intv 2018;11:784–92) © 2018 by the American College of Cardiology Foundation.

Chronic angina refractory to medical and interventional therapies is a disabling and prevalent condition, predominantly due to severe obstructive coronary artery disease (CAD) (1–3). Although refractory angina does not adversely affect mortality compared with stable, chronic CAD, it is associated with a significant reduction in quality of life and increased cardiovascular hospitalizations, leading to increased health care–associated costs (4–6). Treatment of this population is thus directed primarily at improving quality of life by relieving symptoms (7). However, although a considerable

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number of innovative pharmacological and nonpharmacological therapeutic options have been studied in this patient group in recent years, none has demonstrated clear efficacy, leading to a weak recommendation supporting their use in the most recent guidelines (3,8).

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Coronary sinus (CS) Reducer (Neovasc, Richmond, British Columbia, Canada) implantation has emerged as a novel therapeutic treatment for patients with refractory angina (9), with a single randomized clinical trial (10) and 2 observational studies demonstrating safety and efficacy (11,12). The Reducer is a stainless steel, balloon-expandable, hourglass-shaped device that is percutaneously implanted in the CS to create a controlled narrowing of the CS lumen (9,13). This ultimately leads to an increase in coronary venous pressure, capillary and arteriolar dilatation, lower resistance to flow, and restoration of the normal endocardial/epicardial blood flow ratio, which is impaired in the ischemic myocardium.

Currently, there are limited real-world data describing the Reducer's use outside of clinical trials. We therefore report procedural and clinical outcomes of the first 50 consecutive patients who underwent CS Reducer implantation at our center.

METHODS

STUDY DESIGN AND POPULATION SELECTION CRITERIA. This was a single-center, single-arm, prospective, observational study including consecutive patients treated with the CS Reducer at our center between March 2015 and August 2016. Patients were considered eligible for Reducer implantation if they met all of the following criteria: 1) refractory angina of at least Canadian Cardiovascular Society (CCS) class 2, despite optimal or maximally tolerated medical antianginal therapy; 2) objective evidence of inducible myocardial ischemia in the left coronary artery distribution territory (as determined by myocardial perfusion imaging, dobutamine stress echocardiography, or stress perfusion cardiac magnetic resonance imaging); and 3) CAD not amenable to percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) because of unsuitable coronary anatomy, diffuse disease, or absence of satisfactory distal graft anastomosis sites, following evaluation by the heart team.

Exclusion criteria included ischemia related exclusively to the right coronary artery, the presence of a foreign body in the CS (e.g., a left ventricular pacemaker wire for cardiac resynchronization therapy), recent acute coronary syndrome (<3 months), recent coronary revascularization (<6 months), or a mean right atrial pressure higher than 15 mm Hg.

All patients provided informed consent for Reducer implantation after thorough explanation of the procedure, possible complications, and expected clinical benefits. All patients consented to participate in this study.

DEVICE AND IMPLANTATION PROCEDURE. The Reducer is a percutaneous, endoluminal, hourglass-shaped, balloon-expandable, stainless-steel stent that is designed for implantation in the CS to create a focal narrowing. A few weeks following implantation, the Reducer is fully endothelialized, and it is only at this time point that the device establishes a controlled narrowing of the CS. Device characteristics and procedural aspects have been previously described (9,13) and are summarized in the Online Appendix. Online Figure 1A describes the main procedural steps with the use of the 0.035-inch Hi-Torque Supra Core Peripheral Guide Wire (Abbott Laboratories, Abbott Park, Illinois), which, according to our experience, provides adequate support for device delivery and additionally features a soft, shapeable, and radiopaque tip that helps prevent venous vascular injury. Online Figures 1B and 1C illustrate alternative strategies that are sometimes helpful with challenging CS anatomy.

All study patients were pre-treated with aspirin 75 to 100 mg/day for a minimum of 72 h prior to device implantation in addition to clopidogrel (75 mg/day for at least 7 days prior to the procedure or a loading dose of 300 to 600 mg within 24 h prior to the procedure), prasugrel, or ticagrelor. Dual antiplatelet therapy (DAPT) was continued for at least 1 month after implantation.

BASELINE AND FOLLOW-UP EVALUATION. Prior to device implantation, all patients underwent a thorough clinical assessment with evaluation of CCS class, Seattle Angina Questionnaire (SAQ) scores, 6-min walk distance, echocardiography, and stress testing for inducible myocardial ischemia. Follow-up visits were scheduled 4 months after Reducer implantation and were performed by physicians who were not directly involved in the implantation procedure (M.A., D.R., A.M., L.F., M.P.), who evaluated angina status, administered the SAQ, performed the 6-min walk test, performed echocardiographic evaluation, and registered medical therapy and occurrence of

ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting

CAD = coronary artery disease

CCS = Canadian Cardiovascular Society

CS = coronary sinus

DAPT = dual antiplatelet therapy

IQR = interquartile range

PCI = percutaneous coronary intervention

SAQ = Seattle Angina Questionnaire