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Coronary Sinus Reducer implantation in refractory angina: Short-term outcome of Lower Silesia Sinus Reducer Registry (LSSRR)

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INTRODUCTION

Despite the undeniable improvement in the field of pharmacological and interventional treatment of coronary artery disease (CAD) still, even up to 10% of patients [1] can experience refractory angina pectoris (RAP)-reversible myocardial ischemia which cannot be adequately controlled, despite the implementation of all available revascularization and pharmacological therapeutic options [2]. RAP has got heterogeneous pathophysiology and involves patients with CAD unsuitable for revascularization (diffuse disease, high risk-benefit profile; diseases affecting distal segments of arteries) along with other than obstructive CAD coronary disorder.

RAP significantly affects important from patients' perspective values — the quality of life and mortality rate [3]. Recently, a novel device dedicated to patients with RAP has been introduced to clinical practice [4] and had found a reflection in the latest ESC/ESH guidelines [2]. Coronary Sinus (CS) Reducer (Neovasc Inc., Richmond, Canada) is a balloon-expandable, hourglass-shaped, scaffold implanted percutaneously into the coronary sinus creating a narrowing to delay blood outflow and establishing a backward pressure gradient in the coronary artery system. Which is promoting blood redistribution from less ischemic to more ischemic myocardial regions. In this brief report, we present the short-term outcomes of the Copper CS Registry.

METHODS

This observational, single-center, single-arm registry included 22 consecutive patients who were referred to the Cardiac Department of Copper Health Center due to chronic disabling refractory angina pectoris (Canadian Cardiovascular Society [CCS] classes 2–4) despite maximally tolerated anti-angina medical therapy. All patients were evaluated by the local Heart Team and considered not amenable to percutaneous or surgical revascularization procedures. After the Heart Team evaluation patients were qualified for the procedure or Coronary Sinus Reducer implantation unless they meet one of the exclusion criteria. Study exclusion criteria involved: (1) recent acute coronary syndrome (<3 months); (2) recent coronary revascularization (<3 months); (3) a mean right atrial pressure higher than 15 mm Hg; (4) CS proximal diameter <10 mm and >14 mm; (5) life expectancy under 12 months; (6) heart failure (New York Heart Association [NYHA] classification, classes 3-–4); (7) potential CRT-D implantation candidate.

Initial patient evaluation (prior to device implantation) consisted of past medical history, actual clinical assessment with an evaluation of CCS class, Seattle Angina Questionnaire — 7 items (SAQ-7) scores, 6-minute walk distance (6-MWT) test, and echocardiography. First, a follow-up visit was scheduled 1 month after the implantation procedure. All patients provided informed consent for the Reducer Implantation procedure and written consented to participate in this study. The study had the approval of the local etic community (Lower Silesian Medical Chamber, ref number 02/BOBD/2022 date of approval- 13.07.2022). The study had a license agreement with Outcomes Instruments, LLC, Missouri for the use of SAQ-7 (Project ID: 11117).

Statistical analysis

Depending on the normality of distribution (assessed by the Shapiro-Wilk test) the data is presented as the mean with the standard deviation (SD) or the median with the interquartile range (IQR). Categorical data were analyzed using McNemar-Bowker test, continuous data were analyzed using Student's paired t-test or Wilcoxon paired signed rank test depending on the results of the Shapiro-Wilks test for normality. Changes in levels of CCS were compared using McNemar-Bowker test. For t-test a sample mean and 95% confidence interval for mean was used and for Wilcoxon's test, a sample pseudomedian and 95% confidence interval for pseudomedian was shown. A significance level of alpha = 0.05 was assumed for all tests. All analyses were made using the R statistical package.

RESULTS AND DISCUSSION

We retrospectively analyzed short-term outcomes of 22 consecutive subjects with implanted Reducer Device w performed between April, and September 2022. There were no specific exclusion criteria from the study, in this paper we presented data of all patients qualified for CS Reducer implantation in which a full 1-month follow-up was available. The vast majority of patients were male (86.3%) with an average age of 71.1 years and rich in history of previous coronary revascularization. In the study cohort, we noticed a high prevalence of cardiovascular risk factors (hypertension (100%), hyperlipidemia (81.8%), and diabetes (63.6%). Despite previous revascularization procedures and intensive pharmacological treatment (average of four antianginal drugs per patient), in the vast majority of subjects, clinical symptoms of angina were poorly controlled (90.9% initially referred with III or IV class of CCS). In our cohort study, we observed the successful implantation of CS Reducer in all subjects. Apart from one case (hospitalization prolonged due to symptomatic gastric ulcer disease), all patients were discharged the next day after the procedure. In terms of clinical outcome after a one-month follow-up in 9 subjects, we observed improvement by one CSS class (CCS IV to III — 1 subject; CCS III to II — 6 subjects; CCS II to I — 2 subjects). In 10 patients we reported the reduction of symptoms by two CSS classes (CCS IV to II — 2 subjects; CCS III to I — 8 subjects). One subject achieved the highest possible improvement in symptom control (de-escalation from CCS IV to CCS I). All clinical data are presented in Table 1.

Refractory angina pectoris is resistant to classical therapeutic options for patients with CAD. The prevalence of this disorder is relatively high and can reach up to 5%–10% of the stable CAD population [5]. It is well documented [1, 3, 5] that RAP is associated with poor quality

of life, resulting in the recurrence of hospitalizations, leading to a high level of healthcare resource utilization(in our cohort nearly four angina-related hospitalizations in cardiology departments per year for each study subject). In the current paper, we present the first polish experience with CS Reducer. What needs to be emphasized so far available data from our country are mainly related to case-reports studies [6, 7].

The main findings of the study are: (1) CS Reducer implantation was a relatively safe procedure. In the presented study cohort despite high comorbidity, no serious adverse events related to the procedure were observed; (2) short-term clinical effectiveness was noticeable and showed significant improvement in angina control along with the increase in 6-MWT, and in terms of quality of life assessed by the SAQ-7 score.

Despite the CS Reducer having found its place in actual guidelines for the management of chronic coronary syndromes [2], still “real-world” data related to the safety and efficacy of this device is limited to small-number studies [4, 8, 9]. In our study cohort, all procedures finished with successful implantation of the CS Reducer device, without any periprocedural complications- all patients were discharged the next day after the implantation procedure. Similar to our funding, recently published data confirmed the safety and efficacy of the procedure [7–11]. Nevertheless, we observed a slightly higher success rate in comparison to other studies. Our encouraging results are undeniably related to an advanced proctoring program applied in our Cardiac Center along with the relatively high number of procedures performed in a short period of training. It allowed achieving a quick gain of the necessary experience and flattened the learning curve The clinical outcome obtained in our registry are encouraging, we noticed a statistically significant improvement in all evaluated angina gauges (6-MWT and CCS score). Additionally, significant improvement was observed in terms of quality of life rate (SAQ-7 score). All data regarding clinical outcomes were pooled in table 1.

The present study has limitations that should be acknowledged. It is a single-center observational registry with a relatively small number of patients enrolled and the absence of a control group. Additionally, the study refers to short-term outcomes mainly related to the quality of life parameters. Despite these limitations, the study includes the largest number of patients treated with CS Reducer in Poland and confirmed the short-term safety and clinical efficiency of the CS Reducer device in real-world settings.

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Table 1. LSSRR clinical data

Variables	**Study cohort (n = 22)**
Age, mean (SD)	71.1 (7.2)
Male sex, n (%)	19 (86.3)
Female, n (%)	3 (13.6)
BMI [kg/m2], mean (SD)	29.4 (4.4)
Hypertension, n (%)	22 (100)
Diabetes mellitus type 2, n (%)	14 (63.6)
Hyperlipidemia, n (%)	18 (81.8)
Cigarette smoker, n (%)	7 (31.8)
Atrial fibrillation, n (%)	7 (31.8)
Peripheral arterial disease, n (%)	11 (50)
LVEF, %, median (IQR)	55 (40–60)
Heart failure, n (%)	9 (40.9)
Coronary artery disease – illness duration, years, mean (SD)	18.4 (8.3)
Antianginal drugs, median (IQR)	4 (3–4.75)
Admissions to Department of Cardiology – during previous year, median (IQR)	3 (3–4.75)
History of revascularization	
PCI, n (%)	19 (86.4)
CABG, n (%)	18 (81.8)

PCI + CABG, n (%)					15 (68.2)	
History of ACS						
STEMI, n (%)					8 (36.4)	
NSTEMI, n (%)					8 (36.4)	
STEMI + NSTEMI, n (%)					2 (9.1)	
Change in CCS class*					***P* = 0.003**	
CCS Class		1-month FU				
		I	II	III	IV	total
Baseline	I	0	0	0	0	0 (0%)
	II	2	0	0	0	2 (9.1%)
	III	8	6	2	0	16 (72.7%)
	IV	1	2	1	0	4 (18.2%)
	total	11 (50%)	8 (36.4%)	3 (13.6%)	0 (0%)	22 (100%)
6MWT		**Baseline**	**1-month FU**	***P*-value**	**Group difference and Cl**	
Distance, m, mean (SD)		224.4 (99.9)	300.7 (124.1)	<0.001	76.33 (41.5 to 111.14)	
Duration, sec, median (IQR)		360 (247.5–360)	360 (338.5–360)	0.02	79.48 (20 to 162.5)	
Borg’s scale score, mean (SD)		3.05 (1.36)	1.68 (1.36)	0.001	-1.36 (-2.11 to -0.62)	
SAQ-7		**Baseline**	**1-month FU**	**P**	**Group difference and Cl**	

SAQ-7 total score, mean (SD)	33.3 (13.88)	54.53 (19.44)	<0.001	21.24 (12.16 to 30.32)
SAQ-7-PL, mean (SD)	35.23 (18.71)	54.17 (22.23)	<0.001	18.94 (9.39 to 28.49)
SAQ-7-AF median (IQR)	40 (22.5–57.5)	65 (52.5–80)	0.001	30 (15 to 45)
SAQ-7-QL median (IQR)	18.75 (12.5–37.5)	43.75 (25–59.4)	<0.001	25 (12.5 to 43.75)

Abbreviations: 6MWT, six-minute walk test; ACS, acute coronary syndrome; BMI, body mass index; CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; CI, mean or pseudomedian difference 95% confidence interval; FU, follow up; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-segment elevation myocardial infraction; PCI, percutaneous coronary intervention; SAQ-7, Seattle Angina Questionnaire-7 item; SAQ-7-AF, Angina Frequency Score; SAQ-7-PL, Physical Limitation Score; SAQ-7-QL, Quality of Life Score; SD, standard deviation; STEMI, ST-segment elevation myocardial infraction

*Table cells colored red corresponds to increase in CCS grade, yellow cells corresponds to no change in CCS grade, green cells corresponds to decrease in CCS grade