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CORONARY SINUS REDUCER FOR REFRACTORY ANGINA: A NARRATIVE REVIEW OF EFFICACY, SAFETY AND VALUE

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ABSTRACT

BACKGROUND

Refractory angina remains a challenging clinical condition in patients with advanced coronary disease who are not eligible for further revascularisation and continue to experience disabling symptoms despite optimal medical therapy. The Coronary Sinus Reducer has emerged as a non-pharmacological treatment option aimed at symptom relief through modulation of coronary venous outflow.

AIMS

To provide a structured narrative synthesis of the available evidence on the clinical efficacy, safety, proposed mechanisms of action, and economic value of the Coronary Sinus Reducer in patients with refractory angina without further revascularisation options.

METHODS

A narrative review was conducted in accordance with methodological guidance for narrative synthesis. A structured literature search was performed in PubMed, Scopus, and Web of Science for human clinical studies published between 2015 and 2025 using predefined and comparable search terms. Inclusion and exclusion criteria were predefined. After removal of duplicates and non-eligible publications, randomised trials, observational registries, mechanistic cardiac magnetic resonance studies, and health-economic analyses were included for qualitative synthesis.

RESULTS

The review identified three randomised sham-controlled trials, one single-arm phase II trial in patients with microvascular dysfunction, eighteen observational real-world registries, six mechanistic studies, and two health-

economic evaluations, comprising approximately 3500 patients with CCS class II–IV refractory angina. Randomised and observational studies consistently demonstrated clinically meaningful reductions in angina severity and improvements in health-related quality of life, with effects sustained for up to one to three years. Improvements in exercise capacity were heterogeneous. Procedural success rates were high, and serious device- or procedure-related adverse events were uncommon. Mechanistic studies indicated preferential redistribution of myocardial blood flow toward ischaemic subendocardial regions without an increase in global myocardial perfusion. Health-economic analyses suggested potential cost effectiveness within commonly accepted European willingness-to-pay thresholds, contingent on persistence of clinical benefit beyond one year.

CONCLUSIONS

Current evidence supports the Coronary Sinus Reducer as a potentially useful adjunctive treatment for carefully selected patients with refractory angina who are not candidates for further revascularisation. However, conclusions are limited by the small number of randomised trials, the predominance of observational data, reliance on surrogate mechanistic endpoints, and the absence of direct comparative studies with alternative non-pharmacological therapies. Further adequately powered trials are required to more precisely define its long-term clinical and economic role.

Keywords: Angina Pectoris, Refractory Angina, Coronary Sinus Reducer, Coronary Sinus Stent, CSR.

INTRODUCTION

According to Global Burden of Disease estimates, angina from coronary artery disease affects about 112 million people worldwide (1.6% of the global population) [1], with most cases being chronic stable angina [2,3]. Of these, 5–10% have refractory angina [4,5], which means their symptoms are not controlled by medication with no options for revascularisation [6]. These symptoms are linked to much lower health-related quality of life, as measured by tools like the Seattle Angina Questionnaire (SAQ) and SF-36 [7,8,9]. Patients with refractory angina also use more healthcare resources because they are admitted to the hospital more often, need repeated tests, and have higher medical costs [10,11,12]. The Coronary Sinus Reducer was developed to help these patients. It is an hourglass-shaped stent placed into the coronary sinus to create a controlled narrowing of venous outflow, increase coronary sinus pressure, and redistribute blood flow [13,14,15]. Over the past decade, studies and clinical trials have shown that CSR implantation can improve angina class, quality of life, and exercise tolerance.

Despite the availability of non-pharmacological options for refractory angina, such as enhanced external counterpulsation and spinal cord stimulation, their clinical adoption remains limited, evidence is heterogeneous, and direct comparative data are scarce, leaving a substantial unmet need for alternative therapies with reproducible symptomatic benefit and a clearly defined mechanism of action [5,32–35].

Over the past decade, studies and clinical trials have shown that CSR implantation can improve angina class, quality of life, and exercise tolerance. However, the available evidence remains heterogeneous, spanning randomised sham-controlled trials, observational real-world registries, mechanistic cardiac magnetic resonance studies, and limited health-economic analyses, which have not previously been integrated into a single critically oriented narrative synthesis. The present review addresses this gap by systematically analysing and contextualising clinical efficacy, safety, mechanistic data, and economic value of the Coronary Sinus Reducer within a unified analytical framework, explicitly delineating the strengths and limitations of the current evidence base and its implications for clinical practice.

AIM OF THE PUBLICATION

The aim of this narrative review is to provide a systematic analysis of the clinical efficacy, safety, proposed mechanisms of action, and economic value of the Coronary Sinus Reducer device in patients with refractory angina who have no further options for revascularisation.

RESEARCH OBJECTIVES

1. To analyse data from randomised clinical trials evaluating the impact of the Coronary Sinus Reducer on angina severity, quality of life, and functional exercise tolerance in patients with refractory angina.
2. To summarise the results of observational registries and real world clinical practice in order to assess the durability of the clinical effect and the reproducibility of outcomes across different patient cohorts.
3. To review data on safety and the incidence of complications associated with Coronary Sinus Reducer implantation, including periprocedural and long term adverse events.
4. To analyse mechanistic studies using cardiac magnetic resonance imaging aimed at clarifying the effects of the device on myocardial perfusion and redistribution of coronary blood flow.
5. To evaluate available health economic studies with respect to treatment costs and cost effectiveness indicators

associated with the use of the Coronary Sinus Reducer in European healthcare systems.

METHODS

The narrative review was conducted in accordance with established methodological guidance for narrative synthesis, with transparent study identification, selection, and qualitative interpretation of the available evidence, following the approach described by Popay et al. [58].

This review is based on a search of the PubMed, Scopus and Web of Science databases. We searched for articles published between 2015 and 2025 using the following search terms: ("Angina Pectoris"[MeSH] OR "angina pectoris" OR "refractory angina" OR "refractory angina pectoris" OR "refractory chest pain") AND ("coronary sinus"[MeSH] OR "coronary sinus") AND ("reducer" OR "reducers" OR "coronary sinus device" OR "coronary sinus stent" OR "coronary sinus implant" OR "CSR" OR "CSRS").

STUDY SELECTION

A total of 532 records were retrieved. Following deduplication (n = 276), 256 records underwent title and abstract screening. After removing reviews, case reports, and pre-clinical studies, 30 clinical studies were included in this review (see Tables 1–3).

Four studies were prospective clinical trials: three were sham-controlled trials in patients with obstructive coronary artery disease (CAD), and one was a phase II trial in patients with coronary microvascular dysfunction (see Table 1). Eighteen more studies were observational registries, either prospective or retrospective, that looked at clinical outcomes (see Table 2). Six mechanistic studies and two health-economic studies were also reviewed separately (see Table 3).

Table 1: Clinical Trials

No.	Name or Main Title of the Study	Authors	Date of Publication	n Included	Type of publication	References
1	COSIRA	Verheye et al.	2015 Feb	104	Phase II RCT	16,17
2	ORBITA-COSMIC	Foley et al.	2024 Apr	50	RCT	18,19
3	Coronary Sinus Reducer Improves Angina, Quality of Life, and Coronary Flow Reserve in Microvascular Dysfunction	Tryon et al.	2024 Dec	30	Phase II Clinical Trial	20
4	CROSSROAD	Mrak et al.	2023 May	25	RCT	38

Table 2: Observational Studies

No.	Name or Main Title of the Study	Authors	Date of publication	n Treated with CSR	Type of publication	References
1	RESOURCE	Ponticelli et al.	2021 Aug	658	Observational study	54
2	REDUCER-I	Verheye et al.	2024 Dec	400	Observational study	21,22

3	Impact of Coronary Sinus Reducer on Angina Symptoms in Patients With Myocardial Ischemia Without Obstructive Coronary Artery Disease	Giannini et al.	2025 Aug	285	Observational study	47
4	Efficacy of coronary sinus reducer in patients with refractory angina and chronic total occlusion	Konigstein et al.	2025 Aug	262	Observational study	42
5	Efficacy of coronary sinus Reducer in patients with refractory angina and diabetes mellitus	Vescovo et al.	2022 Feb	219	Observational study	40
6	Efficacy of Coronary Sinus Reducer in Patients With Non-revascularized Chronic Total Occlusions	Zivelonghi	2020 Apr	205	Observational study	48
7	Usefulness of Coronary Sinus Reducer Implantation for the Treatment of Chronic Refractory Angina Pectoris	D'Amico et al.	2021 Jan	187	Observational study	23
8	REDUCE	Giannini et al.	2018 Jan	141	Observational study	53
9	The Coronary Sinus Reducer; 5-year Dutch experience	Silvis et al.	2020 Dec	132	Observational study	41
10	Long-term outcomes of patients undergoing coronary sinus reducer implantation - A multicenter study	Konigstein et al.	2021 Feb	99	Observational study	57

11	Effectiveness of coronary sinus reducer implantation in routine clinical practice: 12-month outcomes	Włodarczak et al.	2025 May	67	Observational study	24,36,37
12	Coronary Sinus Reducer Implantation for the Treatment of Chronic Refractory Angina: A Single-Center Experience	Giannini et al.	2018 Apr	50	Observational study	25,26
13	Initial experience with the coronary sinus reducer for the treatment of refractory angina in Spain	Rodriguez-Leor et al.	2022 Dec	48	Observational study	39
14	Coronary Sinus Reducer implantation improves symptoms, ischaemia and physical capacity in patients with refractory angina unsuitable for myocardial revascularisation: a single-centre experience	Konigstein et al.	2018 Jul	48	Observational study	44
15	Effects of coronary sinus Reducer implantation on oxygen kinetics in patients with refractory angina	Zivelonghi et al.	2021 Apr	37	Observational study	55
16	Coronary sinus Reducer device for the treatment of refractory angina: A multicenter initial experience	Reis et al.	2023 Feb	26	Observational study	49

17	Safety and efficacy of a device to narrow the coronary sinus for the treatment of refractory angina: A single-centre real-world experience	Abawi et al.	2016 Sep	23	Observational study	43
18	Efficacy of coronary sinus reducer implantation in patients with chronic total occlusion of the right coronary artery	Mrak et al.	2022	23	Observational study	45

Table 3: Additional mechanistic and health-economic studies on the CSR

No.	Name or Main Title of the Study	Authors	Date of publication	n Treated with CSR	Type of publication	References
1	Cost-effectiveness of the coronary sinus Reducer and its impact on the healthcare burden of refractory angina patients	Gallone et al.	2020 Jan	215	Observational study	29
2	Baseline Left Ventricle Longitudinal Strain as a Predictor for Clinical Improvement Following Coronary Sinus Reducer Implantation	Chen et al.	2023 Oct	41	Observational study	46
3	Feature tracking and mapping analysis of myocardial response to improved perfusion reserve in patients with refractory angina treated by coronary sinus Reducer implantation: a CMR study	Palmisano et al.	2021 Jan	28	Observational study	27

4	INROAD	Tebaldi et al.	2024 Jan	24	Research support	52
5	The impact of coronary sinus narrowing on diastolic function in patients with refractory angina	Szekely et al.	2019 Sept	24	Observational study	50
6	The impact of the coronary sinus reducer upon left ventricular function in patients with refractory angina pectoris	Tzanis et al.	2020 May	19	Observational study	51
7	Segmental redistribution of myocardial blood flow after coronary sinus reducer implantation demonstrated by quantitative perfusion cardiovascular magnetic resonance	Cheng et al.	2025 Summer	16	Observational study	28
8	A budget impact model and a cost–utility analysis of reducer device (Neovasc) in patients with refractory angina	Fortunato et al.	2024 Mar	None	Health economic modelling study	56

RESULTS

EFFECTIVENESS OF THE CORONARY SINUS REDUCER IN RANDOMISED TRIALS IN PATIENTS WITH OBSTRUCTIVE CAD

The phase II COSIRA trial randomised 104 patients with refractory angina (CCS class III–IV) despite optimal pharmacological treatment, objective evidence of reversible ischaemia, and no further revascularisation options to Reducer implantation or a sham procedure. After 6 months, 35% of patients who received CSR improved by at least 2 CCS classes versus 15% in the control group (p=0.02). Additionally, at least 1 CCS class improvement was achieved in 71% of the reducer group versus 42% in the control group (p=0.003). Quality of Life (QoL), assessed using the Seattle Angina Questionnaire, improved in patients with the device (mean change in the QoL domain: +17.6 vs. +7.6; p=0.03). Changes in exercise duration and dobutamine stress echocardiography wall-motion index did not differ significantly between groups [16]. A post hoc reanalysis by Jolicoeur et al. of the COSIRA trial confirmed that Reducer implantation improved symptoms and health-related quality of life compared with the sham procedure group. While the original COSIRA trial showed a non-significant improvement in exercise duration in the CSR group, the reanalysis demonstrated a mean improvement of 27.2% with 96.2% probability of superiority compared to sham intervention [17].

The ORBITA-COSMIC proof-of-concept trial enrolled 51 patients with CCS class II–IV refractory angina, without further treatment options (medication, PCI, or CABG), and with confirmed epicardial CAD on adenosine-stress perfusion CMR. Researchers randomised them 1:1 to Coronary Sinus Reducer implantation or sham intervention. 182 days after implantation, the primary symptom endpoint showed a significant reduction in daily angina burden

compared with placebo, with an OR of 1.40 (95% CI 1.08–1.83). Other clinically meaningful improvements were associated with the SAQ angina frequency (Benefit probability with coronary sinus reducer versus placebo 99.7%) as well as the MacNew Heart Disease Health-Related Quality of Life questionnaire (Benefit probability with coronary sinus reducer versus placebo 99.4%). The remaining questionnaires show no difference between the two groups. Treadmill duration exercise duration did not differ between groups [18,19].

In a sham-controlled, randomized clinical trial conducted at a single centre in Slovenia, Mrak et al. randomized 25 patients and evaluated them 6 months after CSR implantation. However, in contrast to previous studies, there were no significant differences in either CCS class improvement or any SAQ domain, although exercise parameters differed. Exercise capacity, measured by peak oxygen consumption, increased by 2.46 mL/kg/min in the reducer group compared with a decrease of 0.52 mL/kg/min in the control group ($p = 0.03$) [38].

EFFECTIVENESS OF THE CORONARY SINUS REDUCER IN PATIENTS WITH ANOCA

A single-arm, phase II trial by Tryon D et al. enrolled 30 patients with angina and no obstructive coronary artery disease (ANOCA) with invasively confirmed coronary microvascular dysfunction (CMD), and CCS class III–IV symptoms despite medical therapy. At the 120-day mark, Coronary Sinus Reducer implantation led to significant improvement in invasive indices of microvascular function. In patients with reduced baseline coronary flow reserve (CFR), median CFR increased from about 2.1 to 2.7 ($p=0.0011$). Those with abnormal coronary blood flow (CBF) responses to acetylcholine shifted from a negative to a positive hyperaemic response ($p=0.042$). Clinically, median CCS angina class improved from 4.0 to 2.0 ($p<0.001$), and all domains of the Seattle Angina Questionnaire increased significantly ($p<0.006$ for all), indicating better symptom control and quality of life [20].

The subsequent observational study conducted by Giannini et al. on 287 patients suffering from refractory angina without or with CAD confirmed that the CCS class improvement 12 months after CSR implantation does not differ significantly among these groups of patients (-1.4 vs -1.3; $p=0.67$) [47].

EFFECTIVENESS OF THE CORONARY SINUS REDUCER IN OBSERVATIONAL REAL-WORLD STUDIES

In RESOURCE multicentre, retrospective observational study, 658 patients with refractory angina after CSR implantation were observed in median 502 days follow-up. Improvement by at least 2 classes of CCS score (primary endpoint) was obtained by 39.7% followed by improvement by at least 1 class by 76% of patients (baseline vs follow-up CCS score $p<0.0001$) [54].

In the REDUCER-I multicentre, non-randomised, open-label study, 400 patients with CCS class II–IV angina despite optimal medical therapy, confirmed reversible ischemia, and no further revascularisation options underwent Reducer implantation. At 6-month follow-up, the mean CCS class decreased from 2.8 to 1.8 (mean CCS change = -0.9; $n = 344$; $p < 0.0001$), 69.8% of patients experienced an improvement of ≥1 CCS class, while 24.1% improved by ≥2 classes. The number of patients with severe angina (CCS III/IV) fell from about 72% to 18%. Improvements in angina burden translated into better functional capacity and quality of life exhibited by an increase in six-minute walk distance (325.2 vs 359.0 meters; $p<0.0001$), longer exercise duration (355.7 vs 387.0 seconds; $p<0.0001$), significant gains in SAQ ($p<0.0001$ for all domains) and EQ-5D-5L (overall $p<0.0001$) (6). Also, the EuroIntervention 2021 interim REDUCER-I showed a reduction in emergency department (ED) visits for angina compared with the year before Reducer implantation (0.69 vs 0.19 visits per patient-year; $p<0.0001$) [21]. The researchers confirmed that the benefits were sustained at 1, 2, and 3-year intervals, with reductions in the number of CCS III/IV class patients and improvements in QOL [21,22].

In a large Italian multicentre, single-arm registry, D'Amico et al. evaluated 187 patients with chronic refractory angina (CCS class II–IV) despite maximal tolerated pharmacological therapy, who were considered unsuitable for further PCI or CABG. Enrolled patients underwent CSR implantation. Over a median follow-up of 18.4 months, 82.8% of individuals experienced improvement in CCS by at least 1 class, with 49% improving by at least 2 classes. The mean CCS class decreased from 3.2 at baseline to 1.8 at follow-up ($p<0.001$). These symptomatic benefits were accompanied by significant gains in quality of life, as assessed by the SAQ ($p<0.001$ for all domains), and a reduction in the average number of anti-anginal drugs from 2.77 to 2.00 per patient ($p<0.001$) [23].

A prospective registry conducted at a single centre in Poland, Włodarczak et al. evaluated 67 individuals with refractory angina (CCS class II–IV) who were not eligible for further revascularisation and had either obstructive (n=61) or nonobstructive (n=6) coronary artery disease. All participants received a coronary sinus Reducer and were evaluated at multiple time points up to 1 year. After 12 months, 86.6% of patients showed an improvement of at least one CCS class relative to baseline ($P<0.001$). Additionally, substantial improvements were seen in patient-reported outcomes - SAQ-7 scores (rising from 39.9 to 54.6) and SF-36 scores (increasing from 98.4 to 112.7) (both $p<0.001$). Six-minute walking distance improved from 234.9 m at baseline to a peak of 310.6 m at 3 months ($p<0.001$) and remained significantly higher than baseline at 12 months (265.9 m; $p=0.03$). Anti-anginal medication burden did not change substantially (4 versus 3.9; $p=0.88$) [24,36,37].

In a prospective, single-centre observational study, Giannini et al. treated 50 patients with chronic refractory angina and objective evidence of myocardial ischaemia who were deemed unsuitable for further revascularisation with coronary sinus Reducer implantation. At 4-month follow-up, the mean CCS angina class decreased from 2.98 to 1.67; 80% of patients experienced improvement of ≥1 CCS class, and 40% of patients experienced improvement of ≥2 CCS classes ($p<0.001$). Symptomatic improvement was accompanied by New York Heart Association (NYHA) class reduction from 1.68 to 1.35 ($p<0.001$), significant gains in SAQ ($p<0.001$ for all domains) and a marked increase in six-minute walk distance (287.0 vs 388.6 meters; $p=0.004$), as well as a reduction in anti-anginal medication use in approximately one-third of patients (3 (IQR: 2-3) vs 3 (IQR: 2-4);$p=0.001$). The clinical efficacy and improvements in quality of life documented at the 4-month interval were sustained at the subsequent 1-year follow-up [25]. In a later two-year assessment of the identical cohort, Ponticelli et al. confirmed the persistence of these effects: CCS class improved by ≥1 class in 75.6% and by ≥2 classes in 35.6% of patients, with mean CCS decreasing from 2.98 at baseline to 1.74 ($p<0.001$), and four of five Seattle Angina Questionnaire domains remained significantly improved ($p<0.001$ in all domains but angina stability which showed $p=0.08$). Only the enhancement in NYHA classification was ultimately forfeited by the two-year follow-up assessment (1.68 vs 1.67; $p=1$) [26].

In the observational study conducted by Konigstein et al. 262 patients suffering from refractory angina and (131 patients) with or without (also 131) chronic total occlusion (CTO) underwent CSR implantation. 77% of patients showed at least 1 CCS class improvement and 42% at least 2 classes with similar results for patients with and without CTO. Only change in 6MWT was significantly lower in the CTO group (median 16 vs 50 meters; $p=0.009$) [42]. In another study patients with CTO LAD groups and CTO RCA were compared and exhibited no difference between groups in CCS class improvement ($P=0.35$) [45].

In an observational, multicentre study by Vescovo et al., 219 patients were included, of whom 116 (53%) had diabetes mellitus, and all underwent CSR implantation. Over a median follow-up of 393 days, the overall cohort showed a significant improvement in CCS class ($p<0.0001$), with no significant difference between patients with and without diabetes (72% vs 80%, respectively, achieved a ≥1-class reduction in CCS; $p = 0.28$) [40].

In a multicentre prospective single-arm pre–post study conducted by Zivelonghi et al. 37 patients underwent cardiopulmonary exercise testing (CPET) followed by CSR implantation. Then at 6 months follow-up CPET was repeated showing significant improvement in VO2 max (12.2 vs 13.2 ml/kg/min; $p=0.026$) and workload (68 vs 81 W; $p=0.05$) after treatment which exhibited an objective increase in exercise capacity [55].

SAFETY OF THE CORONARY SINUS REDUCER

In the COSIRA trial, the control group experienced 1 death and 3 myocardial infarctions (MIs), while the Reducer group had 1 periprocedural MI and no deaths. Overall, 34 serious adverse events were documented, with 10 cases occurring in the Reducer group and 24 in the control group. The analysis revealed 76 adverse events in the Reducer group, compared with 93 in the control group [16,17]

In the ORBITA-COSMIC trial, no deaths, myocardial infarctions, strokes or major haemorrhages occurred during the 6-month follow-up. Device embolisation occurred in 2 out of 25 patients in the CSR arm (8%) [18,19].

In the study by Tryon et al., device implantation was successful in 94% of attempts. Two patients experienced coronary sinus perforation (~7%), both occurring early in the centre’s experience. There were no periprocedural deaths or myocardial infarctions [20].

In the RESOURCE study, 658 patients underwent 663 CSR implantations of which 641 were successful. A total number of 42 complications were recorded. These complications did not lead to periprocedural death, myocardial infarction or require bailout surgery. Kaplan–Meier analysis showed no significant differences in long-term outcomes between patients with procedural complications and those without, for MACE ($p = 0.24$) or all-cause mortality ($p = 0.60$) [54].

In the REDUCER-I study, despite patients' complex medical history (the majority with extensive CAD, prior PCI or CABG, and other comorbidities), procedural success was high (97.1% of 382 procedures). Within the first 30 days following implantation, 7 patients (1.6%) experienced Major Adverse Cardiac Events (MACE). Device- or procedure-related serious adverse events (SAEs) occurred in 4 patients (1.1%) and included one case of pericardial tamponade, as well as three myocardial infarctions. Also, three device migrations were reported (0.8% of patients), but without the need for intervention. There were no periprocedural deaths or strokes [21,22].

In the study conducted by D’Amico et al., technical and procedural success rates were 98% and 95%, respectively, with an in-hospital device- or procedure-related complication rate of 4.3%. Complications included one coronary sinus dissection, two perforations, one embolisation, and four device migrations, all managed percutaneously without cardiac surgery, and no periprocedural deaths or myocardial infarctions were observed. All-cause mortality and myocardial infarction rates during follow-up were 7.9% each, but there is a lack of a control group to compare the data with [23].

In the study conducted by Włodarczak et al., CSR deployment was successful in all patients; periprocedural complications were infrequent, limited mainly to six access-site haematomas and a single case of device migration into the pulmonary artery, which was managed percutaneously with immediate successful re-implantation. Whereas rehospitalisation for CAD progression occurred in 8 patients (11.9%), 4 of whom (5.9%) needed further PCI [24,36,37].

In the study by Gallone et al., procedural success was achieved in 98.1% of patients, with one device migration without clinical complications. No additional intra-procedural or subsequent adverse events linked to the implantation of the Reducer were reported. During the median of 15-month follow-up interval, there were reported 15 non-fatal MIs, and 21 deaths, 10 of them were due to cardiovascular origin [27].

In the study by Palmisano et al., the procedure was successful in all cases, without device-related complications [28].

In the study by Giannini et al., procedural success was achieved in all implantations, and no device-related adverse events occurred during the procedure or follow-up [25]. In the Ponticelli et al. study, 2-year follow-up of Giannini et al. study, 10 patients (22%) underwent PCI, 3 after MI. 5 patients died, 1 of whom died due to cardiac arrest [26].

In the study by Konigstein et al. at median follow-up of 3.9 years all-cause mortality was 15.1% which is comparable to earlier observations in patients with stable ischemic heart disease [57].

In addition to the studies presented above, several other studies have reported consistent signals of effectiveness of the coronary sinus reducer, including a meaningful decrease in CCS class and improvements across SAQ domains, with infrequent device-related serious adverse events without new outcomes [39,41,43,44,48,49,53]. However, the certainty of these findings is limited by small sample sizes and potential selection bias; nevertheless, they support the role of CSR as a therapeutic option for refractory angina.

MECHANISTIC IMAGING STUDIES

In an observational single-centre study by Chen et al., the authors investigated changes in left ventricular global longitudinal strain (LV-GLS) as a predictor of functional improvement after CSR implantation. A lack of increase in LV-GLS (i.e., no improvement in LV-GLS after the procedure) was associated with a substantially lower likelihood of improvement in 6MWT ($p = 0.029$) [46].

In a single-centre, prospective, single-arm CMR study, Palmisano et al. evaluated the mechanistic impact of CSR implantation on myocardial function and microstructure in 20 patients with refractory angina (CCS ≥ II) and inducible ischaemia on baseline stress CMR who were not qualified for further revascularisation. All patients underwent multiparametric stress CMR and clinical evaluation at baseline and 4 months after CSR implantation. CSR therapy caused a significant improvement in global left ventricle systolic function, with median LVEF change from 61% to 67% ($p=0.0079$) and the restoration of normal global longitudinal and circumferential strain (GLS from −16% to −19%; $p=0.0192$, GCS from −18% to −21%; $p=0.0017$). Myocardial perfusion also improved, as reflected by a reduction in ischaemic burden (13% to 11% of LV mass; $p=0.0135$) and an increase in myocardial perfusion reserve index (MPRi) (1.10 vs 1.30; $p=0.0085$). Furthermore, the endocardial-to-epicardial ratio of the myocardial perfusion reserve index increased significantly in segments with subendocardial (0.80 vs 0.87; $p=0.0173$) and transmural defects (0.67 vs 0.96; $p=0.0107$), but did not change in segments without ischemia (0.90 vs 0.91; $p=0.0773$). Importantly, native T1, extracellular volume, matrix and cellular volumes, and scarring fibrosis remained unchanged, suggesting no adverse microstructural remodelling or diastolic impairment [27]. Previous studies conducted by Konigstein et al. in Israel confirm the beneficial effect of CSR on LVEF during the dobutamine test (51 vs 56.5%; $p=0.004$) and WSMI (1.58 vs 1.37; $p=0.004$) [43]. Other studies included in this review also suggest potential beneficial effects of CSR on left ventricular function without new outcomes [50,51].

Following multicentre research support study conducted by Tebaldi et al. evaluated coronary flow reserve (CFR) of 21 patients who underwent CSR implantation. IMR values decreased from index to 4-month assessments (33.35 to 15.42; $P<0.001$), while coronary flow reserve increased from 2.46 to 4.20 ($P=0.007$) [52].

In the ORBITA-COSMIC trial, the primary endpoint related to mechanism of action - change in stress myocardial blood flow (MBF) in ischaemic segments (not transmurally infarcted) after 6 months - showed no significant difference between groups (0.06 mL/min/g; 95% CI -0.09 to 0.20). One of the secondary endpoints - the ratio of endocardial-to-epicardial MBF during stress increased in ischaemic segments compared to non-ischaemic ones in the CSR group (0.10; 95% CI 0.02 to 0.19), indicating preferential improvement in subendocardial perfusion [18,19].

In a single-centre, retrospective observational cohort study, Cheng et al. investigated the effects of CSR implantation on quantitative myocardial perfusion using fully automated perfusion mapping CMR in 16 patients with refractory angina undergoing Reducer implantation. Rest and adenosine stress perfusion CMR were performed before and at a median of 5 months after the procedure. A high proportion of myocardial segments was visually assessed as ischaemic at baseline (208/254, 81.9%), which significantly decreased after CSR implantation (175/254, 68.9%; $P = 0.001$). Despite this, there were no significant changes in global myocardial blood flow (MBF), global strain values, or

myocardial perfusion reserve (MPR). However, after segments were divided into two groups according to baseline MPR above or below 1.88 (the threshold used in previous studies to identify CAD evaluated with pressure-wire), the MPR increased significantly in ischemic segments compared to non-ischemic ones (+0.44 vs -0.19; p<0.001). Analogous patterns were discerned within both the left and right coronary artery regions [28].

HEALTH-ECONOMIC EVIDENCE

In addition to the clinical evidence, the economic impact of CSR therapy has been evaluated in a large, multicentre observational study by Gallone et al., which included 215 consecutive patients with refractory angina who underwent Reducer implantation in Belgium, the Netherlands, and Italy. Using a pre–post design, angina-related healthcare resource use and quality-of-life data were compared between a standard-of-care period (from diagnosis of refractory angina to CSR implantation) and the post-implantation "Reducer period". CSR therapy was associated with a significant reduction in overall ambulatory visits for angina (2.1 vs 0.7; p<0.001), angina-driven hospitalisations (1.3 vs 0.2; p<0.001), coronary angiograms (1.0 vs 0.2; p<0.001) and PCI procedures (0.3 vs 0.1; p=0.029) per patient-year, which translated into lower healthcare costs. Only the reduction in emergency department admissions for angina per patient-year didn't show a relevant change (0.2 vs 0.1; p=0.751). When costs and utilities over one year of standard care were compared with those over one year after CSR implantation, the Reducer yielded higher QALYs (0.665 vs 0.580; P<0.001) at incremental costs, resulting in ICERs of 53,197, 34,948 and 63,146 €/QALY gained in Belgium, the Netherlands and Italy, respectively. Under modelled assumptions of a 2–3-year duration of CSR efficacy with 30% annual waning, ICERs ranged from 1,977 to 20,796 €/QALY, well below the Dutch willingness-to-pay threshold (50,000 €/QALY) [29].

Fortunato et al. conducted a budget impact model suggesting that CSR implantation may become cost-saving compared with standard of care by year 3 (−€59,772.44). The estimated savings increased further in years 4 and 5 (−€360,120.16 and −€669,464.86, respectively) [56].

DISCUSSION

This narrative review addressed predefined research objectives related to the clinical efficacy, safety, mechanisms of action, and economic value of the Coronary Sinus Reducer in patients with refractory angina without further revascularisation options.

Regarding the first objective, evidence from randomised sham controlled trials demonstrates a consistent reduction in angina severity and a clinically meaningful improvement in health related quality of life following Coronary Sinus Reducer implantation [16–19,38]. These effects are supported by improvements in patient reported outcome measures, whereas results for exercise capacity are heterogeneous and less consistent across studies [16–19,38]. This suggests that symptomatic relief represents the most robust efficacy endpoint, while functional performance outcomes require confirmation in larger trials.

The second objective was addressed through the analysis of observational registries and real world clinical studies. Large multicentre and single centre cohorts consistently report sustained reductions in CCS angina class and improvements in quality of life over follow-up periods of up to three years [21–26,36-37,39-45,47-49,51,53-55]. These findings indicate durability of clinical benefit and reproducibility across different healthcare settings, although the non randomised design of these studies introduces potential selection and reporting biases.

In relation to safety, the reviewed studies demonstrate high technical and procedural success rates with a low incidence of device or procedure related serious adverse events [16–26,36-45,47-49,51,53-55]. Most complications were infrequent and manageable, even in populations characterised by advanced coronary artery disease and multiple comorbidities. However, the lack of long term controlled safety data limits definitive conclusions regarding rare or delayed adverse outcomes.

Mechanistic studies using cardiac magnetic resonance imaging partially clarify the mode of action of the device. The available evidence indicates that symptom relief is primarily associated with redistribution of myocardial blood flow toward ischaemic subendocardial regions rather than an increase in global myocardial perfusion [18,19,28,29,46,50,52]. This mechanistic consistency supports the biological plausibility of the observed clinical effects.

Finally, health economic analyses suggest that Coronary Sinus Reducer therapy may represent a cost effective intervention within commonly accepted European willingness to pay thresholds, particularly if clinical benefits persist beyond one year [27,56]. Nevertheless, economic evidence is limited to observational analyses and remains sensitive to assumptions regarding durability of effect.

LIMITATIONS OF THE STUDY

The evidence base reviewed in this article has several fundamental limitations that directly arise from the analysed sources. Randomised evidence is limited to three sham controlled trials and one single arm phase protocol, which

restricts statistical power and does not allow a reliable assessment of the impact of the intervention on hard clinical endpoints [16–20,38]. The majority of clinical data are derived from non randomised real world registries that differ in study design, inclusion criteria, endpoint structure, and duration of follow-up, increasing the risk of selection bias and complicating direct comparison of results [21–26,36-37,39-45,47-49,51,53-55].

Mechanistic conclusions are based on a limited number of cardiac magnetic resonance studies with small sample sizes and a predominant use of surrogate imaging markers, without direct validation of their association with long term clinical outcomes [18,19,28,29,46,50,52]. Health economic evaluation relies on a single observational analysis with model based assumptions regarding the durability of clinical benefit, which reduces the reliability of result extrapolation [27,56].

The absence of direct comparative studies with other non pharmacological treatments for refractory angina, such as enhanced external counterpulsation and spinal cord stimulation, substantially limits precise positioning of the Coronary Sinus Reducer within therapeutic algorithms and precludes well founded conclusions regarding its comparative clinical and economic effectiveness [12,33,35].

CONCLUSIONS

The available evidence indicates that Coronary Sinus Reducer implantation is associated with clinically meaningful reductions in angina severity and improvements in health related quality of life in patients with refractory angina who have no further revascularisation options. These effects are consistently observed across randomised trials and real world registries and appear to be sustained for follow-up periods of up to one to three years, although durability beyond this timeframe remains insufficiently documented.

Symptomatic benefits have been reported both in patients with obstructive coronary artery disease and in selected patients with microvascular dysfunction. Procedural success rates are high, and serious device or procedure related complications are uncommon in observational cohorts, even in elderly patients with advanced disease and multiple comorbidities. However, the current safety profile is derived predominantly from non randomised data and limited duration of follow-up.

Mechanistic studies support the concept that the clinical effect of the Coronary Sinus Reducer is mediated by redistribution of myocardial blood flow toward ischaemic regions rather than by an increase in global myocardial perfusion, providing biological plausibility for the observed symptom relief. Nevertheless, these conclusions are based on small imaging studies using surrogate endpoints.

Economic evaluations suggest that Coronary Sinus Reducer therapy may be cost effective within commonly accepted European willingness to pay thresholds if clinical benefits persist beyond one year. This conclusion remains conditional, as it relies on observational data and modelling assumptions.

Taken together, the current evidence supports the Coronary Sinus Reducer as a potentially useful adjunctive treatment for carefully selected patients with refractory angina who are not candidates for further revascularisation. At the same time, the limited number of randomised trials, the predominance of observational data, and the absence of direct comparisons with alternative non pharmacological therapies underscore the need for further adequately powered studies to more precisely define its clinical role.

DISCLOSURE

AUTHORS' CONTRIBUTIONS

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CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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USE OF AI

Artificial Intelligence had been used for the purpose of style and language correction.

REFERENCES

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2163–2196. DOI: 10.1016/S0140-6736(12)61729-2.
2. De Luca L, Rosano GMC, Spoletini I. Post-percutaneous coronary intervention angina: from physiopathological mechanisms to individualized treatment. Cardiol J. 2022;29(5):850–857. DOI: 10.5603/CJ.a2021.0042. Epub 2021 Apr 12. PMID: 33843042; PMCID: PMC9550331.
3. Tarkin, Jason M, and Juan Carlos Kaski. "Pharmacological treatment of chronic stable angina pectoris." Clinical medicine (London, England) vol. 13,1 (2013): 63-70. DOI: 10.7861/clinmedicine.13-1-63
4. Mannheimer C, Camici P, Chester MR, Collins A, DeJongste M, Eliasson T, et al. The problem of chronic refractory angina: report from the ESC Joint Study Group on the Treatment of Refractory Angina. Eur Heart J. 2002;23(5):355–370. DOI: 10.1053/euhj.2001.2706.
5. Vervaat FE, van der Gaag A, Teeuwen K, van Suijlekom H, Wijnbergen I. Neuromodulation in patients with refractory angina pectoris: a review. Eur Heart J Open. 2023;3(1):oeac083. DOI: 10.1093/ehjopen/oeac083.
6. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary arterydisease of the European Society of Cardiology. Eur Heart J. 2013;34(38):2949–3003. DOI: 10.1093/eurheartj/eht296.
7. Andréll P, Ekre O, Grip L, Währborg P, Albertsson P, Eliasson T, et al. Fatality, morbidity and quality of life in patients with refractory angina pectoris. Int J Cardiol. 2011;147(3):377–382. DOI: 10.1016/j.ijcard.2009.09.538.
8. Moore RK, Groves D, Bateson S, Dunn G, Moore R. Health related quality of life of patients with refractory angina before and one year after enrolment onto a refractory angina program. EurJ Pain. 2005;9(3):305–310. DOI: 10.1016/j.ejpain.2004.07.013.
9. McGillion M, Arthur HM, Cook A, Carroll SL, Victor JC, L'Allier PL, et al. Management of patients with refractory angina: Canadian Cardiovascular Society/Canadian Pain Society joint guidelines. Can J Cardiol. 2012;28(2 Suppl):S20–S41. DOI: 10.1016/j.cjca.2011.07.007.
10. Moore RKG, Groves DG, Griffith J, Grey C, Newbery K, Bennett MI, et al. A brief cognitive-behavioral intervention reduces hospital admissions in refractory angina patients. J Pain Symptom Manage. 2007;33(3):310–316. DOI: 10.1016/j.jpainsymman.2006.10.009.
11. Reynolds MW, Frame D, Scheye R, Burns LR, Cheng JW, Baty PJ, et al. A systematic review of the economic burden of chronic angina. Am J Manag Care. 2004;10(11 Suppl):S347–S357.
12. Lawson WE, Hui JC, Cohn PF. Enhanced external counterpulsation is cost-effective in reducing hospital costs in refractory angina patients. Clin Cardiol. 2015;38(6):344–349. DOI: 10.1002/clc.22395.
13. Banai S, Ben Muvhar S, Parikh KH, Medina A, Sievert H, Seth A, et al. Coronary sinus Reducer stent for the treatment of chronic refractory angina pectoris: a prospective, open-label, multicenter, safety feasibility first-in-man study. J Am Coll Cardiol. 2007;49(17):1783–1789. DOI: 10.1016/j.jacc.2007.01.061.
14. Ugo F, Ponticelli F, Trabattoni D, Buffon A, Chieffo A, Briguori C, et al. Coronary sinus Reducer: history, current applications, and future perspectives. Rev Cardiovasc Med. 2025;26(11):[online ahead of print]. DOI: 10.31083/RCM39309.
15. Konigstein M, Giannini F, Banai S. The Reducer device in patients with angina pectoris: mechanisms, indications, and perspectives. Eur Heart J. 2018;39(11):925–933. DOI: 10.1093/eurheartj/ehx486.
16. Verheye S, Jolicoeur EM, Behan MW, Pettersson T, Sainsbury P, Hill J, et al. Efficacy of a device to narrow the coronary sinus in refractory angina. N Engl J Med. 2015;372(6):519–527. DOI: 10.1056/NEJMoa1402556.
17. Jolicœur EM, Verheye S, Schwartz M, Choudhury T, Behan MW, Pettersson T, et al. A novel method to interpret early phase trials shows how the narrowing of the coronary sinus concordantly improves symptoms, functional status and quality of life in refractory angina. Heart. 2021;107(1):41–46. DOI: 10.1136/heartjnl-2020-316644.
18. Foley MJ, Petraco R, Forfar JC, Al-Lamee R, Khan FZ, Elmariah S, et al. Coronary sinus Reducer for the treatment of refractory angina (ORBITA-COSMIC): a randomised, placebo-controlled trial. Lancet. 2024;403(10436):1543–1553. DOI: 10.1016/S0140-6736(24)00256-3.
19. Foley MJ, Petraco R, Forfar JC, Al-Lamee R, Khan FZ, Rubimbura V, et al. A double-blind, randomised, placebo-controlled trial of the coronary sinus Reducer in refractory angina: design and rationale of the ORBITA-COSMIC trial. EuroIntervention. 2024;20(3):e216–e223. DOI: 10.4244/EIJ-D-23-00567.

20. Tryon D, Petraco R, Chowdhary S, Shah R, King L, Khan FZ, et al. Coronary sinus Reducer improves angina, quality of life, and coronary flow reserve in microvascular dysfunction. JACC Cardiovasc Interv. 2024;17(24):2893–2904. DOI: 10.1016/j.jcin.2024.09.018.
21. Verheye S, Bergmark BA, Banai S, Avraham H, Al-Lamee R, Bajraktari G, et al. Coronary sinus narrowing for treating refractory angina: REDUCER-I multicenter "real-world" observationalstudy primary endpoint analysis. JACC Cardiovasc Interv. 2024;17(24):2908–2918. DOI: 10.1016/j.jcin.2024.08.047.
22. Verheye S, Jolicœur EM, Behan MW, Williams T, Parsons R, Pettersson T, et al. Coronary sinus narrowing for the treatment of refractory angina: a multicentre prospective open-label clinicalstudy (the REDUCER-I study). EuroIntervention. 2021;17(7):561–568. DOI: 10.4244/EIJ-D-20-00873.
23. D'Amico G, Tarantini G, Briguori C, Di Mario C, Berti S, Colombo A, et al. Usefulness of coronary sinus Reducer implantation for the treatment of chronic refractory angina pectoris. Am J Cardiol. 2021;139:22–27. DOI: 10.1016/j.amjcard.2020.09.045.
24. Włodarczak S, Barylski M, Hawranek M, Ochała A, Januszek R, Małyszko J, et al. Effectiveness of coronary sinus Reducer implantation in routine clinical practice: 12-month outcomes. Pol Arch Intern Med. 2025;135(5):16986. DOI: 10.20452/pamw.16986.
25. Giannini F, Baldetti L, Konigstein M, Ballerini G, Tzanis G, Calvo F, et al. Coronary sinus Reducer implantation for the treatment of chronic refractory angina: a single-center experience. JACC Cardiovasc Interv. 2018;11(8):784–792. DOI: 10.1016/j.jcin.2018.01.251.
26. Ponticelli F, Ugo F, Andreini D, Chiesa R, Trabattoni D. Safety and efficacy of coronary sinus Reducer implantation at 2-year follow-up. Int J Cardiol. 2019;292:87–90. DOI: 10.1016/j.ijcard.2019.05.026.
27. Gallone G, Baldetti L, Tzanis G, D'Ascenzo F, Angelini F, Latib A, et al. Cost-effectiveness of the coronary sinus Reducer and its impact on the healthcare burden of refractory angina patients. Eur Heart J Qual Care Clin Outcomes. 2020;6(1):32–40. DOI: 10.1093/ehjqcco/qcz027.
28. Palmisano A, Vignale D, Benedetti G, Mandurino-Mirizzi A, Magagnoli S, Banai S, et al. Feature tracking and mapping analysis of myocardial response to improved perfusion reserve in patients with refractory angina treated by coronary sinus Reducer implantation: a CMR study. Int J Cardiovasc Imaging. 2021;37(1):291–303. DOI: 10.1007/s10554-020-01964-9.
29. Cheng K, Ludwig DR, Dastidar AG, Levelt E, Krishna SB, Oxley P, et al. Segmental redistribution of myocardial blood flow after coronary sinus Reducer implantation demonstrated by quantitative perfusion cardiovascular magnetic resonance. J Cardiovasc Magn Reson. 2025;27(1):101868. DOI: 10.1016/j.jocmr.2025.101868.
30. Shockwave Medical, Inc. Efficacy of the COronary SInus Reducer in Patients With Refractory Angina II (COSIRA-II). ClinicalTrials.gov Identifier: NCT05102019.
31. Imperial College London. Reducing Microvascular Dysfunction in Patients With Angina, Ischaemia and Unobstructed Coronary Arteries – a pilot study (REMEDY-PILOT). ClinicalTrials.govIdentifier: NCT05492110.
32. Madeira S, Brito D, Aguiar C. Non-pharmacological treatment of refractory angina: the coronary sinus Reducer, the new kid on the block. Rev Port Cardiol. 2021;40(5):371–382. DOI: 10.1016/j.repce.2020.09.003.
33. Zhang C, Zhang Y, Yang J, Zhang J, Fu F, Qin X, et al. Efficacy of enhanced external counterpulsation in patients with chronic refractory angina on Canadian Cardiovascular Society (CCS) angina class: an updated meta-analysis. Medicine (Baltimore). 2015;94(47):e2002. DOI: 10.1097/MD.0000000000002002.
34. Vrints C, Knuuti J, Valgimigli M, Bueno H, Collet J-P, Crea F, et al. 2024 ESC guidelines for the management of chronic coronary syndromes. Eur Heart J. 2024;45(36):3415–3537. DOI: 10.1093/eurheartj/ehae177.
35. Bondesson S, Pettersson T, Währborg P, Rydén L, Edvardsson N. Comparison of patients undergoing enhanced external counterpulsation and spinal cord stimulation for refractory angina pectoris. Coron Artery Dis. 2008;19(8):627–634. DOI: 10.1097/MCA.0b013e3283162489.
36. Włodarczak, Szymon et al. "Coronary Sinus Reducer implantation in refractory angina: Short-term outcomes based on the Lower Silesia Sinus Reducer Registry (LSSRR)." Kardiologia polska vol. 81,5 (2023): 508-511. DOI: 10.33963/KP.a2023.0057
37. Włodarczak, Szymon et al. "Safety and Effectiveness of Coronary Sinus Reducer in the Therapy of Refractory Angina Pectoris-Mid-Term Results of the Real-Life Cohort." Journal of clinicalmedicine vol. 13,15 4413. 28 Jul. 2024, DOI: 10.3390/jcm13154413
38. Mrak M, Pavšič N, Žižek D, Ležaić L, Bunc M. Effect of Coronary Sinus Reducer Implantation on Aerobic Exercise Capacity in Refractory Angina Patients-A CROSSROAD Study. J Cardiovasc Dev Dis. 2023 May 26;10(6):235. DOI: 10.3390/jcdd10060235. PMID: 37367400; PMCID: PMC10299361.
39. Rodríguez-Leor, Oriol et al. "Initial experience with the coronary sinus reducer for the treatment of refractory angina in Spain." Revista espanola de cardiologia (English ed.) vol. 76,5 (2023): 381-383. DOI: 10.1016/j.rec.2022.10.012

40. Vescovo, Giovanni M et al. "Efficacy of coronary sinus Reducer in patients with refractory angina and diabetes mellitus." Heart and vessels vol. 37,2 (2022): 194-199. DOI: 10.1007/s00380-021-01909-9
41. Silvis, M J M et al. "The Coronary Sinus Reducer; 5-year Dutch experience." Netherlands heart journal : monthly journal of the Netherlands Society of Cardiology and the Netherlands HeartFoundation vol. 29,4 (2021): 215-223. DOI: 10.1007/s12471-020-01525-8
42. Konigstein, Maayan et al. "Efficacy of coronary sinus reducer in patients with refractory angina and chronic total occlusion." Clinical research in cardiology : official journal of the German Cardiac Society, 10.1007/s00392-025-02723-3. 19 Aug. 2025, DOI: 10.1007/s00392-025-02723-3.
43. Abawi, M et al. "Safety and efficacy of a device to narrow the coronary sinus for the treatment of refractory angina: A single-centre real-world experience." Netherlands heart journal : monthlyjournal of the Netherlands Society of Cardiology and the Netherlands Heart Foundation vol. 24,9 (2016): 544-51. DOI: 10.1007/s12471-016-0862-2
44. Konigstein, Maayan et al. "Coronary Sinus Reducer implantation improves symptoms, ischaemia and physical capacity in patients with refractory angina unsuitable for myocardialrevascularisation: a single-centre experience." EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology vol. 14,4 e452-e458. 20 Jul. 2018, DOI: 10.4244/EIJ-D-18-00102
45. Mrak, Miha et al. "Efficacy of coronary sinus reducer implantation in patients with chronic total occlusion of the right coronary artery." Kardiologia polska vol. 80,1 (2022): 25-32. DOI: 10.33963/KP.a2021.0132
46. Elimelech, Chen et al. "Baseline Left Ventricle Longitudinal Strain as a Predictor for Clinical Improvement Following Coronary Sinus Reducer Implantation." The American journal of cardiology vol. 204 (2023): 77-83. DOI: 10.1016/j.amjcard.2023.07.026
47. Giannini, Francesco et al. "Impact of Coronary Sinus Reducer on Angina Symptoms in Patients With Myocardial Ischemia Without Obstructive Coronary Artery Disease." Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions vol. 106,4 (2025): 2313-2320. DOI: 10.1002/ccd.70072
48. Zivelonghi, Carlo et al. "Efficacy of Coronary Sinus Reducer in Patients With Non-revascularized Chronic Total Occlusions." The American journal of cardiology vol. 126 (2020): 1-7. DOI: 10.1016/j.amjcard.2020.03.042
49. Ferreira Reis, João et al. "Coronary sinus Reducer device for the treatment of refractory angina: A multicenter initial experience." Revista portuguesa de cardiologia : orgao oficial da Sociedade Portuguesa de Cardiologia = Portuguese journal of cardiology : an official journal of the Portuguese Society of Cardiology vol. 42,5 (2023): 413-420. DOI: 10.1016/j.repc.2022.05.010
50. Szekely, Yishay et al. "The impact of coronary sinus narrowing on diastolic function in patients with refractory angina." International journal of cardiology vol. 291 (2019): 8-12. DOI: 10.1016/j.ijcard.2019.03.041
51. Tzanis, Georgios et al. "The impact of the coronary sinus reducer upon left ventricular function in patients with refractory angina pectoris." Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions vol. 95,6 (2020): 1104-1108. DOI: 10.1002/ccd.28408
52. Tebaldi, Matteo et al. "Coronary Sinus Narrowing Improves Coronary Microcirculation Function in Patients With Refractory Angina: A Multicenter Prospective INROAD Study." Circulation. Cardiovascular interventions vol. 17,1 (2024): e013481. DOI: 10.1161/CIRCINTERVENTIONS.123.013481
53. Giannini, Francesco et al. "Safety and efficacy of the reducer: A multi-center clinical registry - REDUCE study." International journal of cardiology vol. 269 (2018): 40-44. DOI: 10.1016/j.ijcard.2018.06.116
54. Ponticelli, Francesco et al. "Safety and efficacy of coronary sinus narrowing in chronic refractory angina: Insights from the RESOURCE study." International journal of cardiology vol. 337 (2021): 29-37. DOI: 10.1016/j.ijcard.2021.05.034
55. Zivelonghi C, Konigstein M, Azzano A, Agostoni P, Topilski Y, Banai S, Verheye S. Effects of coronary sinus Reducer implantation on oxygen kinetics in patients with refractory angina. EuroIntervention. 2021 Apr 2;16(18):e1511-e1517. DOI: 10.4244/EIJ-D-19-00766. PMID: 32091397; PMCID: PMC9724877.
56. Fortunato A, Valentini I, Rumi F, Antonini D, Siviero L, Di Brino E, Basile M, Cicchetti A. A budget impact model and a cost-utility analysis of reducer device (Neovasc) in patients with refractory angina. Front Cardiovasc Med. 2024 Mar 18;11:1307534. DOI: 10.3389/fcvm.2024.1307534. PMID: 38562187; PMCID: PMC10982321.
57. Konigstein M, Ponticelli F, Zivelonghi C, Merdler I, Revivo M, Verheye S, Giannini F, Banai S. Long-term outcomes of patients undergoing coronary sinus reducer implantation - A multicenterstudy. Clin Cardiol. 2021 Mar;44(3):424-428. DOI: 10.1002/clc.23566. Epub 2021 Feb 19. PMID: 33605473; PMCID: PMC7943892.
58. Popay J, Roberts H, Sowden A, Petticrew M, Arai L, Rodgers M, et al. Guidance on the conduct of narrative synthesis in systematic reviews. J Public Health. 2006;28(2):427–431.

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