

Double Reducer implantation in the coronary venous system for treatment of refractory angina: a case report

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Background

The coronary sinus (CS) Reducer can be considered for the treatment of refractory angina in patients unsuitable for coronary revascularization, but its effect can be influenced by the significant heterogeneity in the anatomy of the cardiac venous system.

Case summary

We report the case of a 70-year-old woman with recurrent episodes of rest angina refractory to optimal medical therapy [Canadian Cardiovascular Society (CCS) Class IV] and inducible ischaemia in a large myocardial territory. Given the diffuse and peripheral nature of the coronary disease, the patient was considered ineligible for percutaneous or surgical revascularization and she was regarded as a good candidate for a CS occluder. Since coronary venous angiography showed the middle cardiac vein (MCV) to be at least as relevant as the CS, successful implantation of two devices, one in the CS and the second in the MCV, was performed. At 6-month follow-up, the patient reported a significant improvement in angina, resulting in a reduction of the CCS class from Grades IV to III.

Discussion

In patients affected by refractory angina and regarded as good candidates for Reducer implantation, a thorough comprehension of the cardiac venous pathway drainage is of pivotal importance to guarantee the therapeutic success of the procedure. In this patient, since the CS and the MCV seemed to contribute equally to coronary venous drainage, Reducer implantation in both vessels allowed to obtain a significant improvement of symptoms. The clinical effectiveness of this strategy needs to be validated in randomized clinical trials.

Keywords

Angina • Case report • Coronary sinus • Coronary sinus Reducer • Revascularization

ESC Curriculum

3.1 Coronary artery disease • 3.3 Chronic coronary syndrome

Learning points

- Coronary sinus (CS) Reducer can be considered for the treatment of refractory angina. In 15–30% of patients, the procedure does not provide a significant clinical benefit and this may be accounted for by the anatomical variability of coronary venous system.
- The comprehension of the cardiac venous pathway drainage is of pivotal importance to guarantee the therapeutic success of the procedure.
- In up to one-third of cases, the middle cardiac vein may be at least as relevant as the CS in the venous drainage system: in these patients, Reducer implantation in both vessels may be useful in order to achieve a significant improvement of symptoms.

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Introduction

The coronary sinus (CS) Reducer (Neovasc Inc., Richmond, BC, Canada) is a percutaneous balloon-expandable, hourglass-shaped device designed to create controlled narrowing of the CS. The device is intended to increase coronary venous pressure, thus improving perfusion to ischaemic territories of the myocardium by forcing redistribution of blood from the less ischaemic subepicardium to the more ischaemic subendocardium.^{1,2}

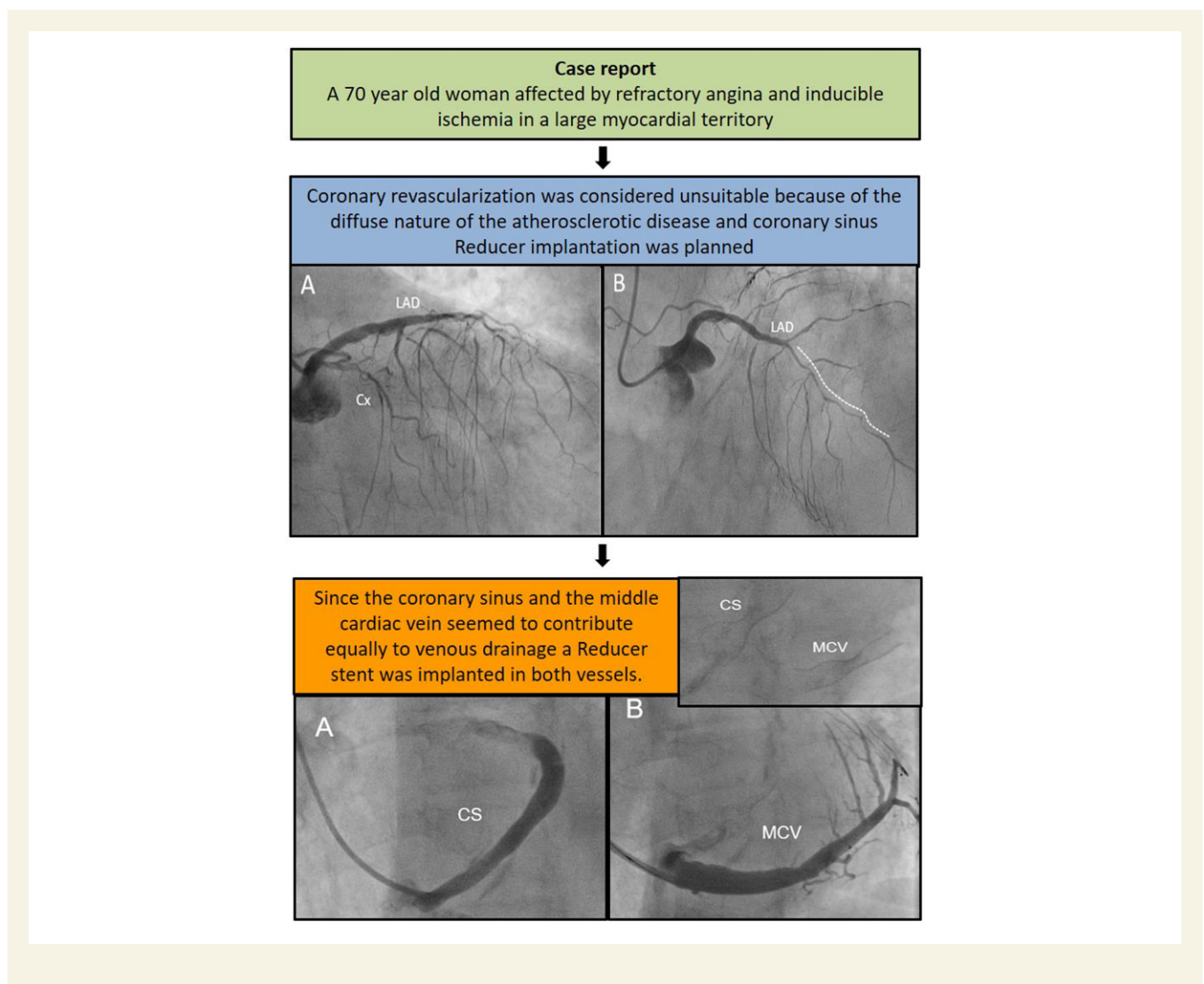
Coronary sinus Reducer implantation can be considered for the treatment of refractory angina in patients unsuitable for coronary revascularization, with symptom improvement in 70–85% of patients.³ Why the remaining 15–30% of patients do not gain clinical benefit is a matter of debate: anatomical variability in the coronary venous system may play a pivotal role, and the presence of alternative venous drainage systems to the CS may be crucial in determining whether patients benefit from this intervention.^{4,5}

Timeline

Case presentation

A 70-year-old Caucasian woman with a history of dyslipidaemia, hypertension, and Stage 3 chronic kidney disease was referred to our clinic due to daily recurrent episodes of rest angina (Canadian Cardiovascular Society Grade IV) refractory to optimal medical therapy.

At the age of 65, she was admitted to our department because of unstable angina: since coronary angiography showed a diffuse disease of the left anterior descending unsuitable for coronary revascularization, a conservative strategy was adopted. As the patient continued to complain of angina, with significant limitation of ordinal physical activity, antianginal therapy was progressively implemented: low-dose beta-blocker therapy was started and bisoprolol was slowly titrated to 5 mg once daily with a final basal heart rate of 55 b.p.m. To achieve better control of anginal symptoms, isosorbide mononitrate was added and titrated up to 80 mg twice daily; no further dose improvement was achievable because systolic blood pressure ranged from 90 to 100 mmHg. Ivabradine was contraindicated by the resting heart rate of <70 b.p.m., and both blood pressure and heart rate values did not allow the addition of calcium channel blockers. Ranolazine



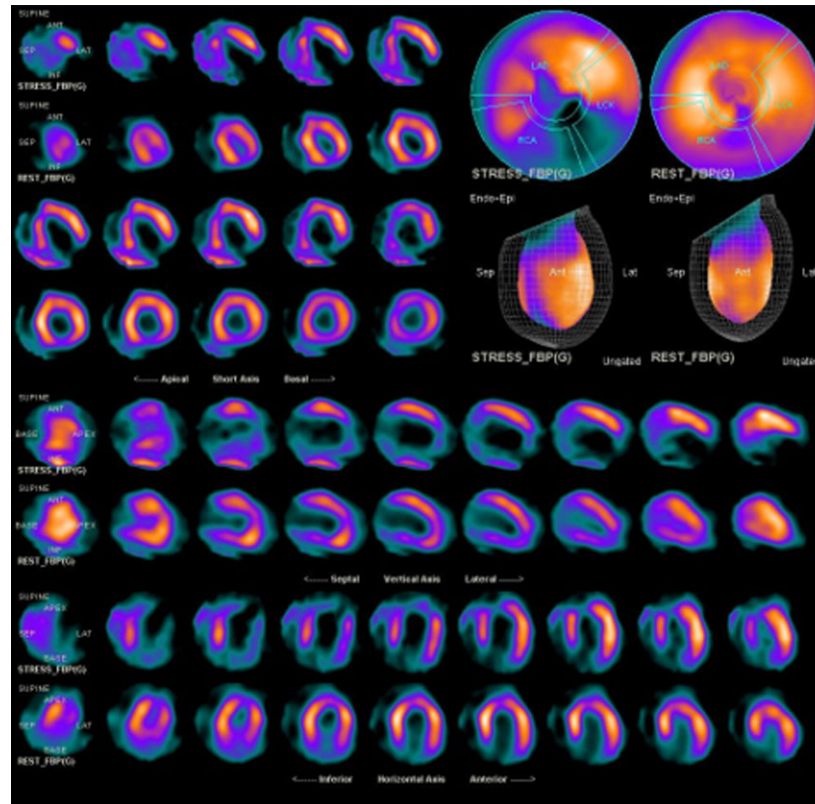


Figure 1 Dipyridamole nuclear stress test showing diffuse ischaemia in the apical, septal, and inferior walls.

was initially administered at the lowest dosage of 375 mg twice daily, but no relevant improvement in symptoms was obtained. Titration was not considered because of the Stage 3 chronic kidney disease, with an estimated glomerular filtration rate of 35 mL/min/1.73 m². After 1 month of treatment, the patient reported constipation and dizziness, and ranolazine was discontinued.

The physical examination at hospital admission was unremarkable: cardiovascular examination revealed a regular rhythm with a heart rate of 60 b.p.m., clear S1 and S2 and no murmurs or rubs. The lungs were clear to auscultation and the lower extremities were warm without oedema bilaterally.

Blood exams at hospital admission showed a mild anaemia with a haemoglobin value of 11.2 g/dL (normal range 12–16 g/dL) and a normal platelet count. The electrocardiogram revealed a sinus rhythm with a left bundle branch block pattern. Basal echocardiography documented a mildly dilated left ventricle with moderate systolic dysfunction (ejection fraction 40%) with a wall motion score index of 1.25.

A dipyridamole nuclear stress test was performed, revealing diffuse ischaemia in the apical, septal, and inferior walls (*Figure 1*). Coronary angiography revealed three-vessel coronary artery disease with diffuse narrowing of the mid and distal left anterior descending and circumflex. The right coronary artery (RCA) showed severe stenoses in the distal portion (*Figure 2*).

Given the diffuse and peripheral nature of the coronary disease, the patient was considered ineligible for percutaneous or surgical

revascularization, but given the high ischaemic burden, she was regarded as a good candidate for a CS occluder (Reducer).

Following pre-treatment with aspirin and clopidogrel, a nine Fr introducer sheath was inserted into the right jugular vein under local anaesthesia. A multipurpose catheter was advanced into the right atrium and a mean pressure of 7 mmHg was documented. After engagement of the CS ostium, the catheter was gently advanced distally and venography was performed, revealing a normal size CS (*Figure 3A*). The Reducer was implanted without complications after the exchange with the delivery system.

Coronary sinus venography showed the absence of side branches draining the lateral and posterior walls. Selective angiography of the middle cardiac vein (MCV) was performed, documenting a large vessel draining just proximal to the CS ostium in the right atrium and receiving several collateral branches (*Figure 3B*). Based on the results of the nuclear stress test, showing inducible ischaemia in a large myocardial territory involving the inferior wall, a Reducer was also implanted in the MCV (*Figure 3C*).

The patient was discharged after 24 h. At 6-month follow-up, she reported a significant improvement in angina, resulting in a reduction in angina from Grade IV to III. She reported an improvement in quality of life, assessed using the Seattle Angina Questionnaire⁶: baseline (physical limitation 13, angina stability 20, angina frequency 40, treatment satisfaction 25, quality of life 25), 6-month follow-up (physical limitation 40, angina stability 80, angina frequency 80, treatment satisfaction 75, quality of life 50).

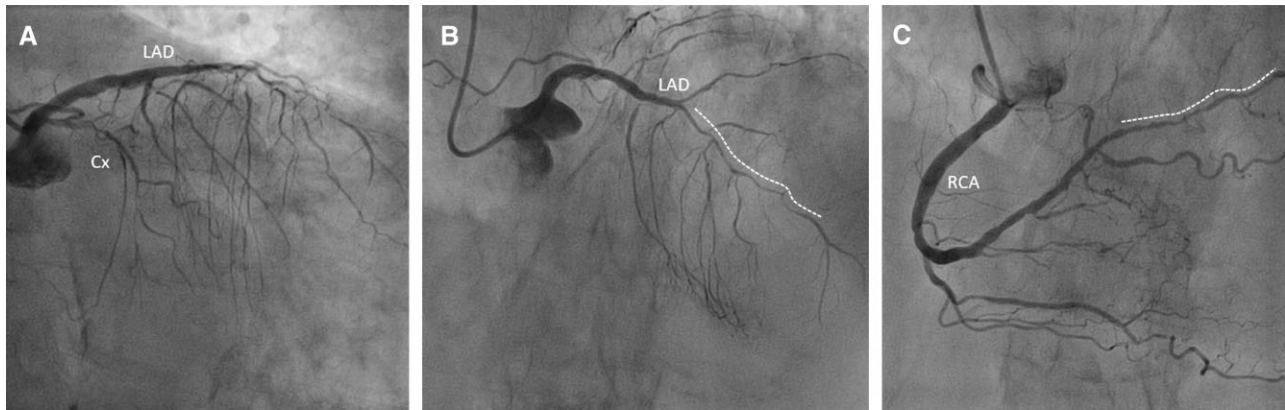


Figure 2 Coronary angiography: (A) caudal view of the left coronary artery demonstrating diffuse disease of the circumflex (Cx) and mid and distal left anterior ascending; (B) cranial view of left coronary artery showing severe narrowing of the left anterior ascending in the mid and distal segments (dotted line); (C) cranial view of the right coronary artery indicating diffuse disease of the distal segment (dotted line).

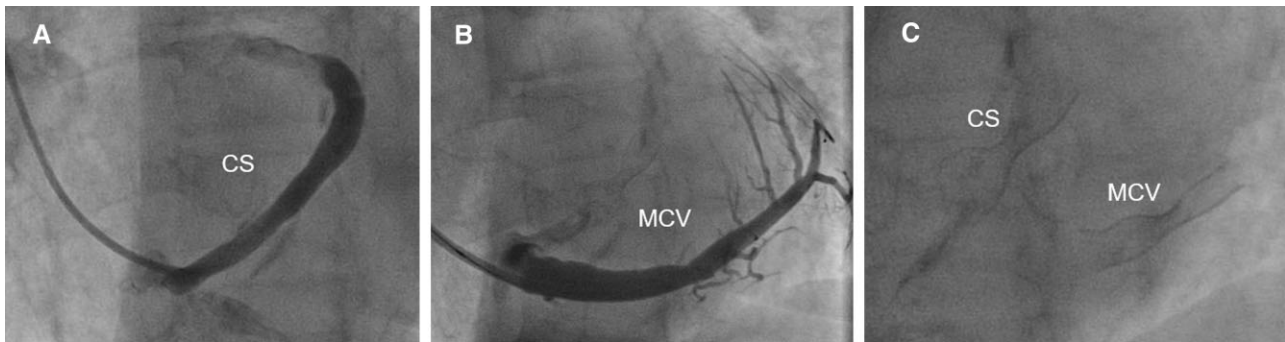


Figure 3 Reducer devices implanted in the coronary sinus: (A) selective angiography of the middle cardiac vein, documenting a large vessel draining just proximal to the CS ostium in the right atrium and (B) receiving several collateral branches; (C) based on the extension of the inducible myocardial ischaemia, a second Reducer device was implanted in the middle cardiac vein.

Discussion

The Reducer is intended to increase intracardiac venous pressure by partially obstructing drainage of venous blood through the CS: this effect can be influenced by the significant heterogeneity in the anatomy and physiology of the cardiac venous system. The MCV (or posterior or inferior interventricular vein) usually drains the diaphragmatic walls of the ventricular chambers and much of the muscular ventricular septum.⁷ However, Kawashima *et al.*⁸ demonstrated that the MCV may be as relevant as the great cardiac vein in ~52% of cases, and may be the dominant drainage vessel in around 36%.

In patients such as ours, with documented inducible ischaemia in a large myocardial territory involving the apical, septal, and inferior walls, understanding the cardiac venous pathway drainage is pivotal in guaranteeing therapeutic success. If coronary venous angiography shows the MCV to be at least as relevant as the CS, the option to implant a Reducer in both vessels could be considered.

We acknowledge that inducible ischaemia in our patient was also documented in the inferior wall and that Reducer implantation is usually recommended in patients with prevalent left coronary disease.

However, this indication is based on the inclusion criteria of the 'Efficacy of a Device to Narrow the Coronary Sinus in Refractory Angina' (COSIRA) trial, a randomized study testing the effectiveness of the device for refractory angina in subjects with evidence of reversible ischaemia attributable to the left coronary arterial system.³ Limited evidence is available about patients with inducible ischaemia due to RCA disease, but a recent study demonstrated the clinical efficacy of Reducer implantation in 22 subjects with ischaemia due to chronic total occlusion of the RCA.⁹ The 'Efficacy of the Coronary Sinus Reducer in Patients With Refractory Angina II' (COSIRA-II), a multicenter, randomized (1:1 ratio), double-blinded, sham-controlled clinical trial, is ongoing and is expected to provide more information about the clinical effectiveness of the Reducer system for the treatment of refractory angina (ClinicalTrials.gov Identifier: NCT05102019).

As our patient showed satisfactory improvement in symptoms, no further nuclear stress tests were performed after Reducer implantation. We acknowledge that the lack of an objective measurement of the reduction in myocardial ischaemia after CS occlusion is a limitation. Limited evidence is available supporting a reduction in myocardial ischaemia after device implantation, but adequately powered

studies have not been conducted. The most widely accepted mechanism of action of the Reducer is blood redistribution from the less ischaemic subepicardium to the more ischaemic subendocardium, and this mechanism has been demonstrated by stress cardiac magnetic resonance in small-size studies.¹⁰

The Reducer device has a good safety profile, with low rates of periprocedural and mid-term complications in randomized trials and observational studies.^{3,11} The additional risk associated with a double implantation is believed to be limited because the procedure is carried out using the same vascular access and the extra time required to cannulate and wire the second vessel is usually limited. As the clinical success of the procedure is closely related to a precise knowledge of the coronary venous anatomy, the limited additional risk associated with double device implantation in the case of a large MCV is likely to be counterbalanced by the achievement of a significant improvement in anginal symptoms.

Reducer implantation in the MCV has been reported previously^{12,13} and, to the best of our knowledge, this is the first case of double implantation in the same coronary venous system.

Lead author biography



Dr Andrea Picchi is an interventional cardiologist at Misericordia Hospital, Grosseto, Italy. His research interests include coronary physiology assessment and coronary microvascular disease.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Acknowledgements

None declared.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidelines.

Conflict of interest: None declared.

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