

# Technical aspects in coronary sinus Reducer implantation



**Francesco Giannini**<sup>1\*</sup>, MD; Georgios Tzanis<sup>2</sup>, MD; Francesco Ponticelli<sup>2</sup>, MD; Luca Baldetti<sup>2</sup>, MD; Ozan M. Demir<sup>2</sup>, MD; Satoru Mitomo<sup>2</sup>, MD; Guglielmo Gallone<sup>2</sup>, MD; Shmuel Banai<sup>3</sup>, MD; Antonio Colombo<sup>1</sup>, MD

1. Interventional Cardiology Unit, GVM Care & Research Maria Cecilia Hospital, Cotignola, Italy; 2. Unit of Cardiovascular Interventions, IRCCS San Raffaele Scientific Institute, Milan, Italy; 3. Department of Cardiology, Tel-Aviv Medical Center, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel

This paper also includes supplementary data published online at: <https://eurointervention.pronline.com/doi/10.4244/EIJ-D-18-01180>

## KEYWORDS

- diffused disease
- prior CABG
- stable angina

## Abstract

Refractory angina is a growing problem, predominantly due to advanced coronary artery disease, associated with a reduced quality of life and an increased hospitalisation rate with a corresponding impact on healthcare resources. There is an unmet clinical need to be addressed by novel therapeutic approaches. Over the last few years, a treatment approach causing a controlled coronary sinus narrowing by implantation of a balloon-expandable, hourglass-shaped, stainless steel mesh (i.e., the coronary sinus Reducer) has arisen with promising initial short-term and midterm results, in terms of reducing angina and ischaemia burden and improving quality of life. Guidance with proper implantation algorithms and knowledge on how to address potential complications will improve interventional outcomes and foster a wider application of this novel therapeutic approach. In this review, we summarise the implantation technique, the causes of potential complications, and algorithms focusing upon their practical management, based on the experience of the authors.

\*Corresponding author: Interventional Cardiology Unit, GVM Care & Research Maria Cecilia Hospital, Via Madonna di Genova 1, 48033 Cotignola, Italy. E-mail: [giannini\\_fra@yahoo.it](mailto:giannini_fra@yahoo.it)

## Abbreviations

<b>CS</b>	coronary sinus
<b>LAO</b>	left anterior oblique

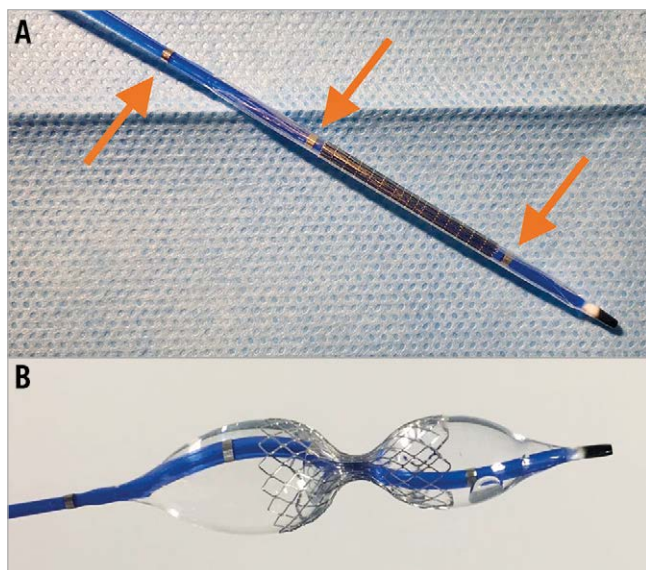
## Introduction

The coronary sinus (CS) Reducer™ (Neovasc Inc., Richmond BC, Canada) is designed to reduce disabling symptoms and improve quality of life of patients suffering from refractory angina (Table 1). A single randomised, sham-controlled clinical trial<sup>1</sup> and a few observational studies<sup>2-5</sup> have demonstrated the safety and efficacy of this novel device. The Reducer consists of a balloon-expandable, hourglass-shaped, stainless steel mesh, which is implanted in the CS to create a controlled narrowing of the lumen and a pressure gradient across it.

While the CS Reducer's clinical efficacy on reducing angina burden is apparent, technical aspects of this procedure, including prevention and management of potential complications, have never been described systematically. In this review, we provide recommendations relating to the practical aspects of this procedure and we report potential procedural complications focusing upon their practical management. The technical aspects described below are based on our initial experience of approximately 500 cases performed by operators among the authors.

## Coronary sinus Reducer device and the implantation procedure

The Reducer is a balloon-expandable hourglass-shaped stainless steel device, with flexible longitudinal struts without welding points (Figure 1). The device is delivered via an over-the-wire hourglass-shaped balloon catheter. The proximal and distal portions of the balloon have differing diameters so that once expanded



**Figure 1.** Coronary sinus Reducer. A) The Neovasc coronary sinus Reducer system mounted on a balloon with radiopaque markers (arrows). B) Device during deployment.

they conform to the tapered anatomy of the CS. Two radiopaque markers (on the catheter shaft) outline the proximal and distal ends of the Reducer mounted on the deployment balloon. A third marker, located just proximally to the balloon, is used to assist the operator in visualising when the balloon section of the catheter is distal to the guide catheter (Figure 1).

## THE PROCEDURE

Aims and considerations that should be taken into account during the procedure are presented in Figure 2. Based on the authors' experience, patients undergoing Reducer implantation should be pretreated with 75-100 mg aspirin daily for a minimum of 72 hours prior to device implantation in addition to either clopidogrel, prasugrel or ticagrelor. Dual antiplatelet therapy should be continued for at least one month after implantation. During the procedure, a bolus of unfractionated heparin (100 U/kg) should be administered after the introducer sheath is inserted into the jugular vein.

The Reducer system kit (Figure 3) contains:

- 1) The Neovasc Reducer pre-mounted on a balloon catheter
- 2) A 9 Fr straight guide catheter (VISTA BRITE TIP™ 55 cm, no.598-943P; Cordis [now Cardinal Health], Milpitas, CA, USA)
- 3) A rotating haemostatic valve (MEDEX Inc., MX336LBP1)

The delivery system is designed to be used via the internal jugular vein; the right internal jugular access is preferable to avoid the tortuosity of the left. Sedation of the patient is not required for the procedure, only local anaesthesia at the jugular vein puncture site.

## VENOUS ACCESS AND PRELIMINARY MEASURES

Supplementary Appendix 1 and Supplementary Figure 1 provide information on the CS anatomy. After central venous access via the right jugular vein has been obtained, a 9 Fr sheath is introduced. A multipurpose diagnostic catheter is then advanced into the right atrium over a standard 0.035" wire and the right atrial pressure is measured. If the mean pressure is above 15 mmHg, the procedure is abandoned as the effect of the Reducer (aiming to increase the cardiac venous system pressure) is unlikely to be beneficial<sup>1</sup>. Another contraindication for Reducer implantation is biventricular pacing (Table 1). In this condition, the presence of the pacing lead in the CS makes the procedure technically challenging with the additional risk of lead fracture.

## ANGIOGRAPHIC PROJECTIONS AND CORONARY SINUS ENGAGEMENT

The majority of CS ostia can be engaged in the left anterior oblique (LAO) 30° view, advancing and gently rotating a 5 or 6 Fr multipurpose catheter. Manual injection of radiopaque contrast medium via a 10 ml Luer-lock syringe can be used to confirm CS engagement. If engaging the CS is difficult with a multipurpose catheter, the use of an Amplatz Left 1, Amplatz Left 2, XB 3.5 or Josephson electrophysiology catheter may be considered. Importantly, if an Amplatz catheter is used to engage the CS ostium and to advance a wire distal into the vessel, it should not be advanced deep into the CS. Therefore, once the wire is advanced distal into the CS, the Amplatz

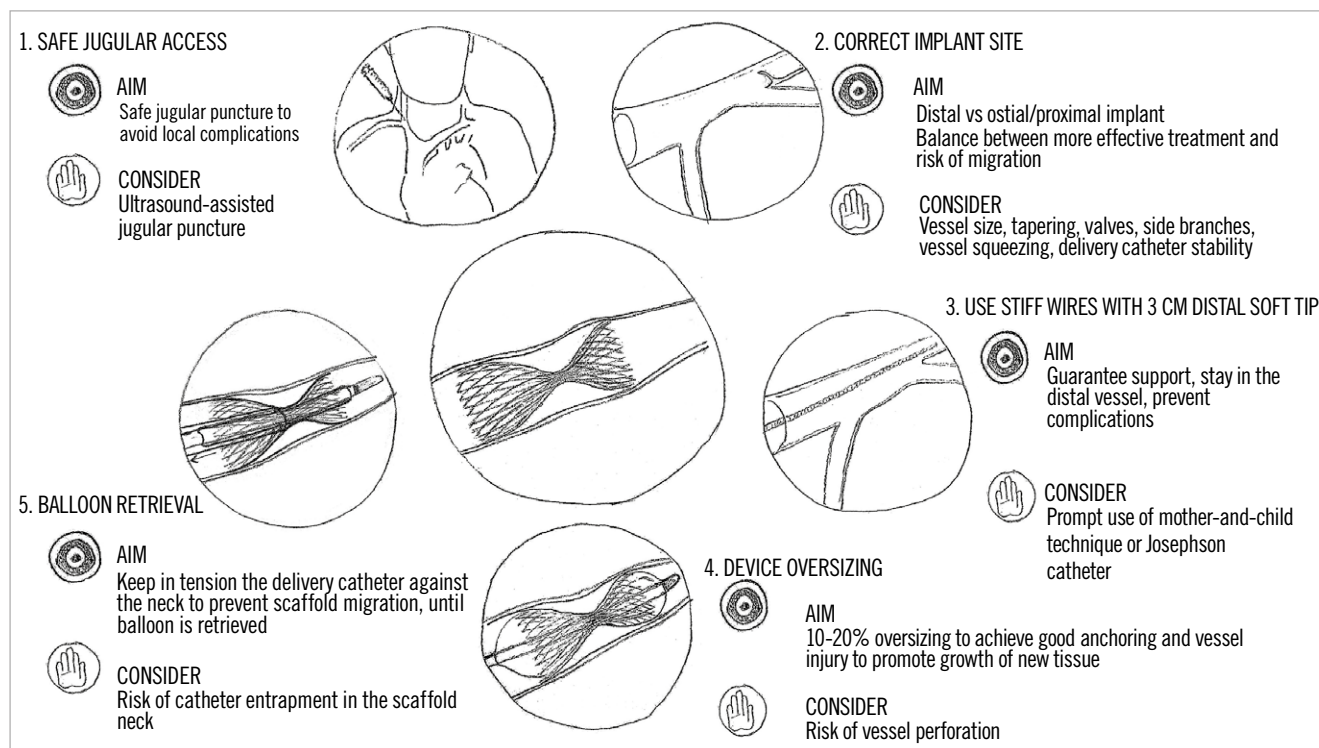


Figure 2. Coronary sinus Reducer implantation; aims and considerations.

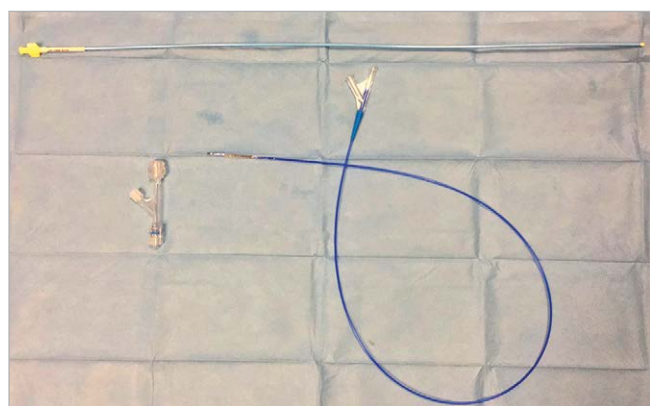


Figure 3. Coronary sinus Reducer kit. Device kit consists of a scaffold pre-mounted on a balloon catheter, a 9 Fr straight guide catheter and a rotating haemostatic valve.

catheter should be exchanged for the multipurpose catheter, which can easily be advanced deeper into the CS. If engagement of the CS is still difficult, visualising the CS anatomy by contrast injection into the left coronary artery in the venous phase in the 30° LAO view can be helpful. Rarely, in the most difficult cases, a coronary wire can be advanced into the left circumflex artery to act as a landmark.

**CORONARY SINUS VENOGRAPHY AND SCAFFOLD RELEASE**

After engagement of the ostium, a standard 0.035” wire is advanced distal into the CS and the catheter is then gently advanced over the wire as distally as possible. During this manoeuvre, the catheter

Table 1. Details concerning the CS Reducer procedure.

Device	Clinical experience
Centres performing the procedure	– Around 100 centres – Mostly in Europe, Italy, Germany, Spain, the Netherlands, Belgium, England, Sweden, Canada, Israel, Saudi Arabia
Countries with most experience	Italy and Germany
Device reimbursement	Reimbursement varies from country to country
Stable coronary artery disease indications	Refractory angina in patients: – Optimal medical therapy – Unsuitable for further revascularisation – Myocardial ischaemia in the territory of left coronary artery
Risks with Reducer implantation	– Reducer implantation is a very safe procedure. The complications rate is very low (<2%) – Potential procedural complications are access-site haematoma, device migration/ embolisation, CS perforation
Contraindications	– Presence of biventricular pacing – Patients with right atrial pressure >15 mmHg are excluded
Sedation	– Local anaesthesia at the jugular vein puncture site – General anaesthesia is not required
CS: coronary sinus	

can sometimes be dislodged into the right ventricle. With the catheter distally positioned in the CS, a venography is performed for CS sizing and to identify the location of collateral branches. Prior to

contrast injection for venography, a small amount of contrast should be carefully injected to make sure that the tip of the diagnostic catheter is not located in a small branch. Device implantation is usually 1.5-3 cm distal to the CS ostium, where the vessel diameter is of adequate dimension for device deployment. The landing site should be chosen carefully to avoid side branches and, once chosen, can be re-identified by using bony landmarks. Then, a bolus of unfractionated heparin should be administered, and the Reducer system should be prepared (**Supplementary Figure 2**). It is important not to exceed a 20%:80% contrast/saline ratio inside the inflater in order to facilitate balloon deflation and retrieval after scaffold deployment. A standard CS Reducer procedure is presented in **Figure 4**.

A 0.035" wire is then advanced within the catheter and placed distally in the great cardiac vein and the catheter is removed. Since adequate support is needed for the advancement of the Reducer system, we now routinely use the 0.035" Hi-Torque Supra Core® peripheral wire (Abbott Laboratories, Abbott Park, IL, USA). The Hi-Torque Supra Core peripheral wire provides greater support and features a soft, shapeable radiopaque tip that helps to prevent venous injury.

The supplied 9 Fr guiding catheter tip should be manually curved to facilitate progression into the CS. It is important to advance the 9 Fr catheter and the device together, with the device protruding a few millimetres from the catheter in order to prevent vessel injury. Another strategy is to insert a 5 Fr multipurpose catheter into the 9 Fr catheter ("mother and child" technique) without the balloon in order to reach the distal part of the CS (**Supplementary Figure 3**). At this point, the 5 Fr catheter is removed and the balloon with the pre-mounted Reducer advanced. In cases of challenging anatomy, the use of a Josephson electrophysiology catheter with the mother and child technique may be needed (**Supplementary Figure 4**).

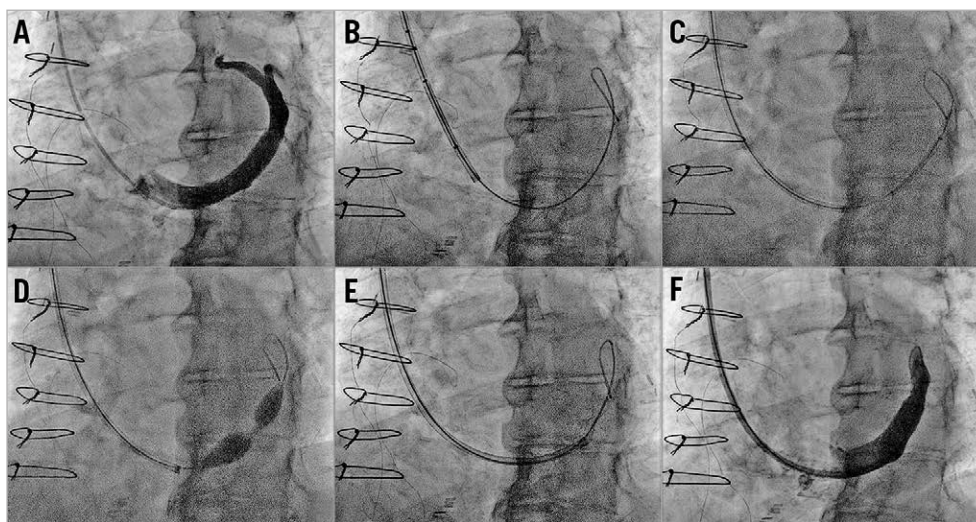
After reaching the landing zone, the guiding catheter is carefully retracted, exposing the Reducer system. The two distal markers, which identify the edges of the Reducer, enable correct positioning, using the bony landmarks previously identified. Importantly, before deploying the Reducer device, the 9 Fr guiding catheter must be withdrawn to the third proximal marker, so that the balloon can be fully expanded. Supraventricular and ventricular extrasystoles during CS engagement (related to catheter and device manipulation) are potential arrhythmias during the procedure.

The Reducer is deployed by inflating the delivery balloon at 4-6 atmospheres for at least 60 seconds. It is imperative to oversize the device by 10-20% relative to the CS. The CS sizing could be performed by visual estimation, but quantitative coronary angiography (QCA) is recommended especially for the first procedures. Oversizing helps to anchor the scaffold to the CS vessel wall, thus preventing device migration, and favours the activation of injury-induced tissue growth mediators that promote device endothelialisation. As valves of the CS might prevent proper scaffold oversizing, the proximal and distal portions of the Reducer should be implanted in valve-free segments. It is recommended to locate the narrowed centre segment of the Reducer on a valve, if possible.

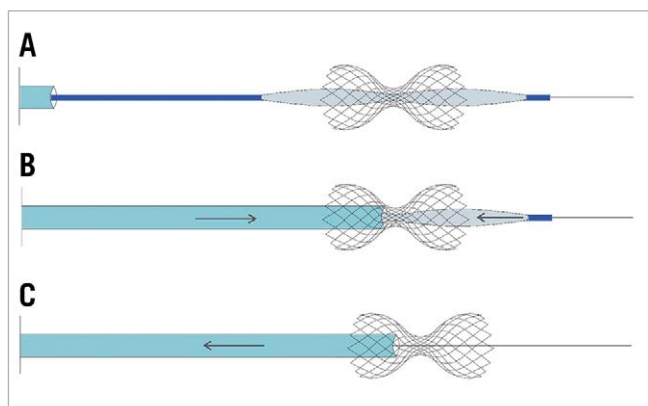
#### BALLOON RETRIEVAL

Balloon retrieval must be performed with caution, preferably by two operators, to avoid displacement of the Reducer. A proposed technique is presented in **Figure 5**. This is achieved by advancing the guiding catheter to the narrow neck of the scaffold to provide support so that the balloon can be retrieved safely. This needs to be performed carefully due to the large profile of the balloon.

A final venography check is performed to confirm the correct position of the scaffold and to exclude potential complications.



**Figure 4.** Standard coronary sinus Reducer procedure. A) Venography in left anterior oblique view (30°) with the catheter distal in the coronary sinus. B) A 0.035" wire is advanced distally in the great cardiac vein. C) Advancement of the Reducer system with the device protruding a few millimetres from the guide catheter. D) Reducer is deployed by inflating the delivery balloon at 4-6 atmospheres. E) Balloon catheter is retrieved by a simultaneous support of the 9 Fr guiding catheter. F) Final venography to confirm the correct position of the scaffold and exclude complications.



**Figure 5.** Proposed balloon catheter retrieval. A) The balloon is fully deflated, and a negative intraluminal pressure is established. B) The 9 Fr guiding catheter tip should be advanced against the neck of the scaffold. Retraction of the balloon catheter is accompanied by a parallel tension/support of the 9 Fr guiding catheter, supporting the Reducer during the manoeuvre. C) After passage of the balloon catheter from the narrow neck, the balloon is fully retrieved by the first operator. The 9 Fr catheter should be retrieved by the second operator to avoid entrapment inside the scaffold neck causing device displacement.

### Potential complications

Although evidence on CS Reducer safety is limited to the COSIRA trial and a few observational studies<sup>1,2,4,6</sup>, initial experience shows rare periprocedural or midterm device-related complications.

According to the technical steps of the Reducer procedure, our experience and a few case reports recently published, we here describe potential procedural complications (**Table 1**) including their prevention and management.

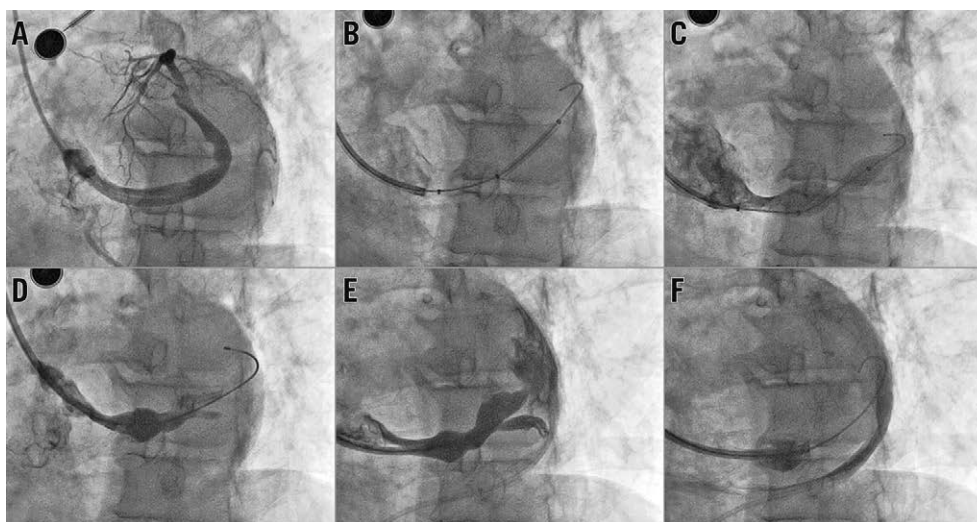
### CS DISSECTION AND PERFORATION

Coronary sinus dissection and perforation are serious, potentially fatal, complications observed in patients undergoing electrophysiological procedures during the placement of the CS lead<sup>7-10</sup> or during CS lead extraction<sup>11</sup>. Since the first CS Reducer implantation in 2004, only two cases of perforation have been reported so far with this procedure<sup>12</sup>. In the first case, the complication was addressed successfully with protamine sulphate administration to reverse the heparin effect and long semi-compliant balloon (5×12 mm) prolonged (five minutes) inflation at 10 atm in order to seal the perforation, while in the second case there was need for urgent surgery.

Coronary sinus dissection during Reducer implantation may happen because of manipulation of this “delicate” vessel. However, both catheter and wire are directed against the downstream flow during scaffold implantation, thus dissections rarely evolve into complete perforation and can usually be managed conservatively<sup>9,13</sup>.

Perforation might be caused by excessive oversizing during scaffold deployment and distal migration of the wire tip. Perforation might also be secondary to wire migration into a small side branch during device advancement; in such cases, when the scaffold is deployed across the main branch and a small side branch, it will result in CS perforation due to oversizing, at the site of the side branch origin (**Figure 6**).

Attention to the following steps may prevent perforation and dissection of the CS: advancement of the catheters over the wire; the use of a stiffer wire or mother and child technique; maintaining the wire in the distal CS segment and adequate scaffold oversizing in the correct position. Moreover, we recommend routinely ensuring adequate backflow from the catheter before performing any strong manual injection and confirming the correct wire position before device deployment. The first tip will avoid injection against the vessel wall or in a small branch, while the second one



**Figure 6.** Coronary sinus perforation during Reducer deployment. Clinical case. A) Large CS directed upwards at the standard 30° LAO projection. B) Guidewire and catheter positioning. The guidewire tip is in a branch vessel. C) The Reducer was deployed by inflating the delivery balloon. The patient became hypotensive. D) & E) Coronary sinus venography revealing coronary sinus perforation. F) Contrast in the pericardial space. The patient was managed surgically and discharged a few days after the rescue operation.

will guarantee device deployment in the correct position (avoiding small vessel damage in case of wire migration).

Management of CS perforation depends on its severity and associated haemodynamic compromise. It is based on the emergent requirement to stop coronary extravasation and ensure haemodynamic stability in the shortest possible time<sup>11,14</sup>.

**Figure 7** illustrates a proposed algorithm, mainly based on the authors' consensus, for the potential approaches to CS perforation during Reducer implantation and highlights the different management strategies.

Once this complication is confirmed, unfractionated heparin may be neutralised with intravenous administration of protamine. Moreover, a balloon of similar size or slightly larger than that of the vessel should be immediately positioned at the perforation site, to achieve immediate haemostasis<sup>15</sup>. The balloon should be placed at the perforation site or distally and should be inflated at the lowest possible pressure to promote haemostasis (as verified by contrast injection at regular intervals). When a large pericardial effusion is associated with tamponade, emergent pericardiocentesis is indicated<sup>8</sup>. Aspirated blood should immediately be re-infused into a vein to promote haemodynamic stability, especially in case of severe perforation.

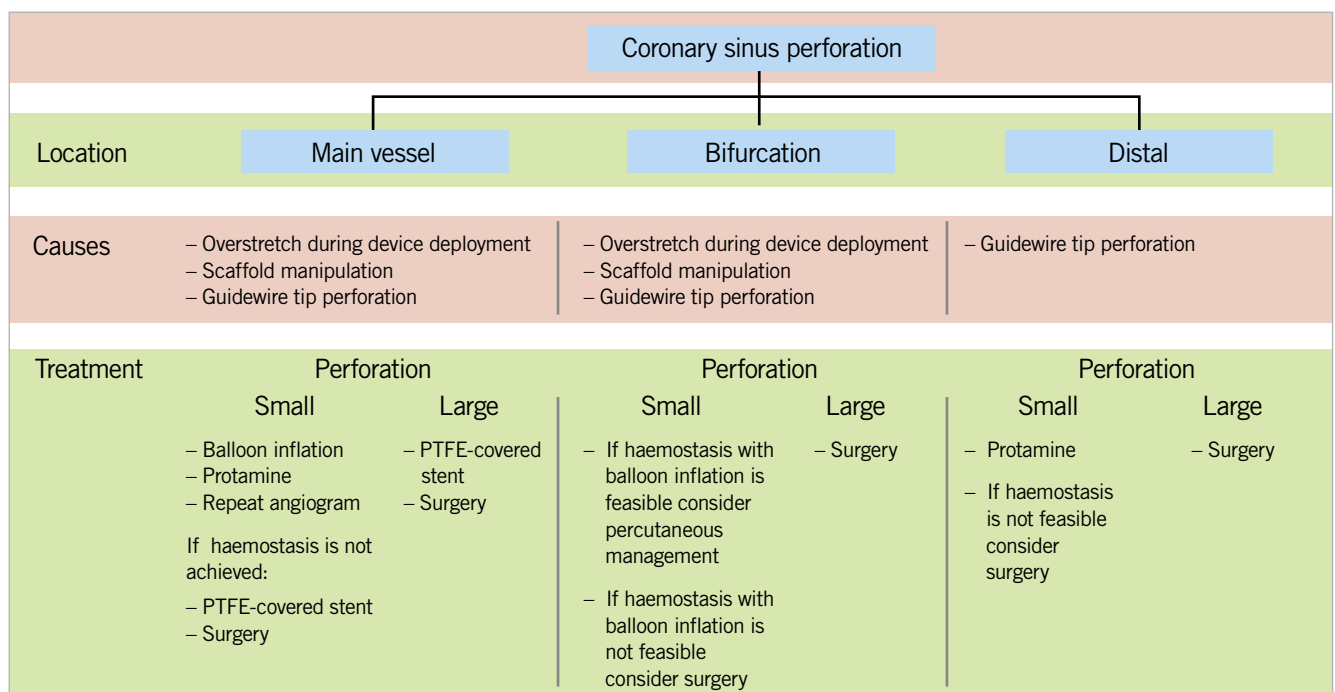
While most perforations should resolve without intervention or should generally be treated with the proposed measures, cases of more severe perforation may be associated with persistent extravasation despite prolonged balloon inflations<sup>16</sup>. In these instances, the implantation of polytetrafluoroethylene (PTFE) stents should be considered<sup>17</sup>; however, emergency cardiac surgery may be required immediately<sup>16,18</sup>.

Another increasingly common cause of perforation is the inadvertent distal migration of guidewires (most commonly hydrophilic wires), resulting in tip-related perforation<sup>19</sup>. Although many of these perforations are small and self-limiting after protamine administration, the reverse venous flow and the distal location of the injury make subcutaneous fat or coils ineffective; thus, cardiac surgery should be considered if leakage persists and the patient remains haemodynamically compromised.

**GUIDING CATHETER ENTRAPMENT INTO THE SCAFFOLD NECK**

Balloon retrieval, following Reducer deployment, is performed with caution to avoid proximal displacement of the Reducer by the large profile of the deflated balloon. This is achieved by advancing the guiding catheter against the narrow neck of the scaffold before pulling the balloon into the guiding catheter's tip, so that the catheter provides support and stabilises the Reducer and the balloon can be retrieved safely. Once the balloon is back into the catheter, the tip of the catheter is pulled back and away from the narrowed centre of the Reducer by pushing on the wire. This manoeuvre should prevent catheter tip entrapment within the narrowed centre of the Reducer. If the Reducer had been implanted with an inflation pressure >6 atmospheres (not recommended), the guiding catheter might cross the neck of the Reducer.

In rare cases of catheter tip entrapment, the first manoeuvre is an attempt to pull the guiding catheter back gently while pushing on the wire deep into the CS and trying to detach it from the scaffold. When an adequate scaffold oversizing has been performed, the guiding catheter should be easily detached by performing this



**Figure 7.** Proposed algorithm for coronary sinus perforation management.

manoeuvre. If it is unsuccessful and the catheter is still inside the scaffold, a second balloon may be advanced over the wire and inflated at the distal part of the device with the intention of trapping it. While the scaffold is trapped by the balloon, the guiding catheter should be gently pulled back (**Figure 8**).

If the guiding catheter went through the neck distal to the scaffold, two different strategies may be considered. A larger catheter may be advanced over the first against the scaffold neck; while the larger catheter is pushed against the neck, the second catheter should be pulled back. An alternative approach would be to get additional venous access and advance a second guide catheter into the right atrium and to engage the CS. Subsequently, a 0.035" wire is advanced from the second guide catheter into the scaffold struts at the level of the neck, then the second catheter is advanced over the wire against the scaffold neck. While the scaffold is maintained *in situ* pushing the second catheter, the first catheter should be pulled back gently and detached from the scaffold.

In most cases, percutaneous measures alone are successful; however, emergency cardiac surgery may be required<sup>20</sup>.

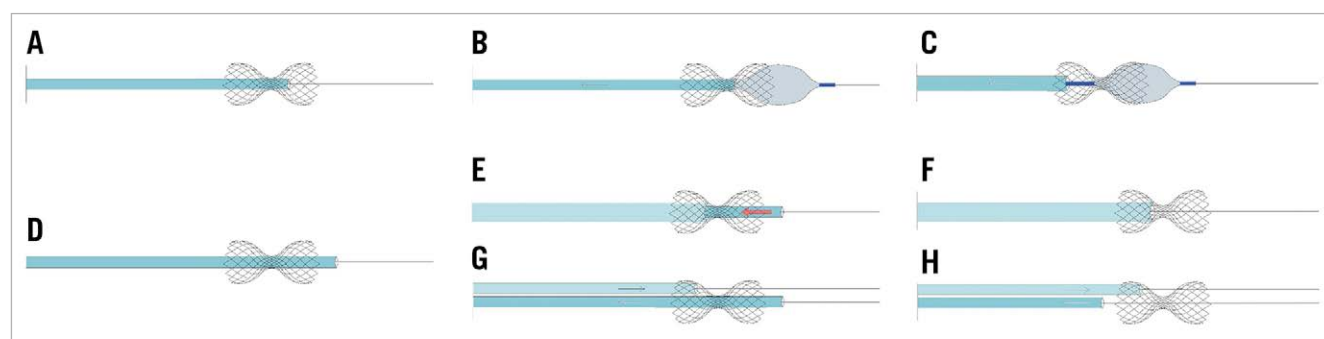
### SCAFFOLD MIGRATION

Scaffold migration may occur in different phases of the procedure<sup>21</sup>. The proposed management algorithm for Reducer "loss" (on wire) is presented in **Figure 9**. When this complication occurs but the device is at least in part overlapping with the balloon, we recommend inflating the balloon and partially deploying the scaffold; then, a second balloon (sized according to the vessel diameter) should be advanced in order to expand the scaffold fully. When the dislodged device is not overlapping with the balloon, the interventional techniques utilised following stent loss retrieval in coronary arteries should be considered. Firstly, device retrieval with a gooseneck snare should be considered.

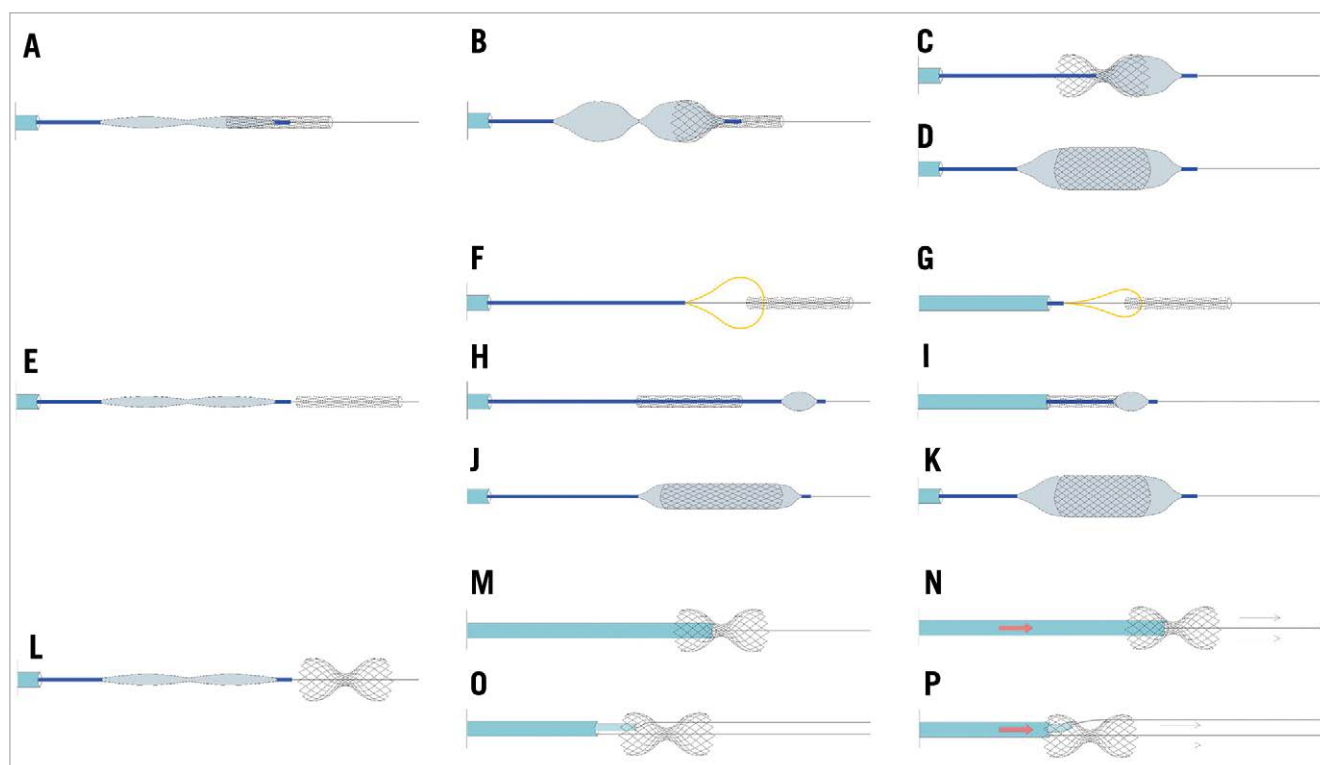
If this proves unsuccessful, and the Reducer remains on the wire, a valid option is to try to advance a small balloon beyond the device, inflate it, and retrieve the scaffold by "dragging" it back with the balloon. Alternatively, a small balloon can be used to dilate the scaffold partially, making room for progressively larger balloons to expand the scaffold fully against the vessel walls. If the previous strategies fail, surgical removal should be considered, although in our and published experiences this has never been necessary.

Device migration may occur after its deployment (**Figure 9, Supplementary Figure 5-Supplementary Figure 8**). This occurs mainly during balloon retrieval when scaffold oversizing is insufficient, balloon refolding is not properly performed, and/or the guiding catheter is not advanced to the neck for support. In such cases, the migration of the scaffold out of the CS is prevented by the correct position of the wire in the distal vessel. A gentle attempt at re-advancing the scaffold in the correct position by pushing the guiding catheter against its neck may be performed (**Figure 9M, Figure 9N, Supplementary Figure 5**). If this attempt is unsuccessful, a second 0.035" wire is advanced through the device mesh at the neck level, and a 5 Fr diagnostic multipurpose catheter is advanced over the second wire inside the 9 Fr catheter and pushed against the neck to advance the scaffold in the correct position (**Figure 9O, Figure 9P, Supplementary Figure 6**). As described in the clinical case presented in **Supplementary Figure 6**, this manoeuvre may result in a distal crushing of the device. If this happens, after removal of the 0.035" wire, two 0.014" wires may be advanced into the distal CS and the crushed device may be post-dilated, inflating two coronary balloons simultaneously (**Supplementary Figure 6**).

In case of scaffold migration outside the CS with the device no longer over the wire, it should be snared (capturing it from the



**Figure 8.** Guide catheter entrapment into the device neck. Proposed management techniques. A) Catheter entrapment into the device neck. B) A second balloon is advanced over the wire and inflated at the distal part of the device with the intention of trapping it. C) While the scaffold is trapped, the 9 Fr guiding catheter is gently pulled back without scaffold displacement. D) Catheter entrapment into the device neck, with catheter tip beyond the Reducer. Two different strategies may be helpful. E) A larger catheter is advanced against the scaffold neck over the 9 Fr guiding catheter utilising the "mother and child" technique. While the larger catheter is pushed against the neck, the 9 Fr trapped catheter is pulled back until it is fully retracted (F). G) As an alternative option, a second guide catheter is advanced to engage the CS. From the second guiding catheter a 0.035" wire is advanced through the scaffold struts at the level of the neck, then the second catheter is advanced over the wire against the scaffold neck. H) While the scaffold is maintained *in situ* pushing the second catheter, the first catheter is gently pulled back and detached from the scaffold.



**Figure 9.** Coronary sinus Reducer loss on wire. Proposed management techniques. *A)* The migrated device is still at least partially overlapping the balloon. *B)* Reducer balloon inflation in order to deploy the scaffold partially. *C)* Attempt to advance and deploy a second balloon to expand the distal part of the device and reshape the scaffold or fully expand it and lose the narrow neck (*D*). *E)* When the uncrimped device is not overlapping the balloon, the use of gooseneck snares should be considered first (*F* & *G*). *H)* If this proves unsuccessful, and the Reducer remains on the wire, a small balloon can be advanced beyond the device and inflated, trying to retrieve the scaffold by “dragging” it back with the balloon (*I*). *J)* Alternatively, a small balloon can be used to dilate the scaffold partially, making room for progressively larger balloons to expand the scaffold fully against the vessel walls (*K*). If the previous strategies fail, surgical removal should be considered. *L)* Scaffold migration after deployment. In most cases, the migration of the scaffold out of the CS is prevented by the guidewire. *M)* A gentle attempt at re-advancing the scaffold in the correct position by pushing the guiding catheter against its neck (*M* & *N*). *O)* If this attempt is unsuccessful, a second 0.035” wire is advanced through the device mesh at the neck level, and a 5 Fr diagnostic multipurpose catheter is advanced over the second wire inside the 9 Fr catheter and pushed against the neck to advance the scaffold in the correct position (*P*).

neck) and retrieved from an 18 Fr introducer placed through the femoral vein (**Supplementary Figure 7, Supplementary Figure 8**).

### CORONARY SINUS THROMBOSIS

Coronary sinus thrombosis is an extremely rare and often fatal condition<sup>22,23</sup>. Acute CS occlusion is not well tolerated and immediate action to resolve the complication should be taken<sup>24</sup>. Such a complication has never been described with the Reducer. An old, experimental study showed that sudden occlusion of the CS was associated with a high operative mortality, while partial obstruction of the CS was associated with a lower mortality rate after a subsequent sudden occlusion of the left anterior descending artery and also diminished the extent of the infarction<sup>25</sup>, highlighting a “double-edged sword” phenomenon when referring to CS manipulation.

Acute coronary sinus occlusion increases pressure within the coronary venous system, inducing ischaemia, arrhythmia, progression to infarction, and sudden cardiac death. Chronic progressive

occlusion has been described after electrophysiology procedures<sup>26</sup>. It has been well tolerated, probably due to the development of the Thebesian venous system.

Management of coronary sinus thrombosis, after ablation procedures, is poorly described, although thrombectomy and subsequent anticoagulation therapy have been employed<sup>22</sup>. Coronary sinus thrombosis during or following Reducer implantation is a potential complication, although no cases of CS thrombosis have yet been reported since 2007<sup>1</sup>.

### Conclusion

After the initial promising results of CS Reducer implantation, with efficacy in terms of reducing angina burden and reduction of myocardial ischaemia burden<sup>1-5</sup>, a forthcoming wider application of this approach should be expected. Although the Reducer procedure is safe<sup>1-5</sup>, a proper implantation algorithm and knowledge of how to address potential complications will



improve patient outcomes and enable the wider application of this novel technique.

## Conflict of interest statement

F. Giannini is a consultant for Neovasc Inc. S. Banai is the medical director of Neovasc Inc. The other authors have no conflicts of interest to declare.

## References

- Verheye S, Jolicœur EM, Behan MW, Pettersson T, Sainsbury P, Hill J, Vrolix M, Agostoni P, Engstrom T, Labinaz M, de Silva R, Schwartz M, Meyten N, Uren NG, Doucet S, Tanguay JF, Lindsay S, Henry TD, White CJ, Edelman ER, Banai S. Efficacy of a device to narrow the coronary sinus in refractory angina. *N Engl J Med*. 2015;372:519-27.
- Konigstein M, Meyten N, Verheye S, Schwartz M, Banai S. Transcatheter treatment for refractory angina with the Coronary Sinus Reducer. *EuroIntervention*. 2014;9:1158-64.
- Abawi M, Nijhoff F, Stella PR, Voskuil M, Benedetto D, Doevendans PA, Agostoni P. Safety and efficacy of a device to narrow the coronary sinus for the treatment of refractory angina: A single-centre real-world experience. *Neth Heart J*. 2016;24:544-51.
- Giannini F, Baldetti L, Ponticelli F, Ruparella N, Mitomo S, Latib A, Montorfano M, Jabbour RJ, Aurelio A, Ferri L, Mangieri A, Regazzoli D, Ancona M, Pagnesi M, Faccini A, Chieffo A, Azzalini L, Carlino M, Colombo A. Coronary Sinus Reducer Implantation for the Treatment of Chronic Refractory Angina: A Single-Center Experience. *JACC Cardiovasc Interv*. 2018;11:784-92.
- Giannini F, Baldetti L, Konigstein M, Rosseel L, Ruparella N, Gallone G, Colombo A, Banai S, Verheye S. Safety and efficacy of the reducer: A multi-center clinical registry - REDUCE study. *Int J Cardiol*. 2018;269:40-4.
- Konigstein M, Bazan S, Revivo M, Banai S. Coronary Sinus Reducer implantation improves symptoms, ischaemia and physical capacity in patients with refractory angina unsuitable for myocardial revascularisation: a single-centre experience. *EuroIntervention*. 2018;14:e452-8.
- Van Rees JB, de Bie MK, Thijssen J, Borleffs CJ, Schalijs MJ, Van Erven L. Implantation-related complications of implantable cardioverter-defibrillators and cardiac resynchronization therapy devices: a systematic review of randomized clinical trials. *J Am Coll Cardiol*. 2011;58:995-1000.
- León AR, Abraham WT, Curtis AB, Daubert JP, Fisher WG, Gurley J, Hayes DL, Lieberman R, Petersen-Stejskal S, Wheelan K; MIRACLE Study Program. Safety of transvenous cardiac resynchronization system implantation in patients with chronic heart failure: combined results of over 2,000 patients from a multicenter study program. *J Am Coll Cardiol*. 2005;46:2348-56.
- de Cock CC, van Campen CM, Visser CA. Major dissection of the coronary sinus and its tributaries during lead implantation for biventricular stimulation: angiographic follow-up. *Europace*. 2004;6:43-7.
- Nägele H, Behrens S, Azizi M. What can happen during coronary sinus lead implantation: dislocation, perforation and other catastrophes. *Herzschrittmacherther Elektrophysiol*. 2007;18:243-9.
- Banaszewski M, Stepińska J. Right heart perforation by pacemaker leads. *Arch Med Sci*. 2012;8:11-3.
- Cortese B, di Palma G, Latini R. Coronary sinus perforation during reducer implantation. *Catheter Cardiovasc Interv*. 2018;91:1291-3.
- Yoda M, Hansky B, Koerfer R, Minami K. Coronary sinus dissection during left ventricular pacing electrode implantation. *Ann Thorac Cardiovasc Surg*. 2007;13:275-7.
- Bhatta L, Luck JC, Wolbrette DL, Naccarelli GV. Complications of biventricular pacing. *Curr Opin Cardiol*. 2004;19:31-5.
- Bosa F, Bethencourt M, Vargas M, Ferrer J, Rodriguez A, Marrero F. Prolonged inflation of coronary angioplasty balloon as treatment for subocclusive dissection of the coronary sinus during implantation of a coronary sinus pacing lead. *J Interv Card Electrophysiol*. 2008;23:139-41.
- Palmisano P, Accogli M, Zaccaria M, Luzzi G, Nacci F, Anaclerio M, Favale S. Rate, causes, and impact on patient outcome of implantable device complications requiring surgical revision: large population survey from two centres in Italy. *Europace*. 2013;15:531-40.
- Briguori C, Nishida T, Anzuini A, Di Mario C, Grube E, Colombo A. Emergency polytetrafluoroethylene-covered stent implantation to treat coronary ruptures. *Circulation*. 2000;102:3028-31.
- Bartel T, Kocher A, Feuchtner G, Müller S, Bonatti JO, Metzler B. Spontaneous rupture of the dissected coronary sinus mimicking acute coronary syndrome. *J Thorac Cardiovasc Surg*. 2009;137:e1-3.
- Abushabha G, Abujalala S, Butt M. Treatment of Distal Left Anterior Descending Artery Perforation with Fat Embolization. *Heart Views*. 2016;17:159-63.
- Al-Moghairi AM, Al-Amri HS. Management of retained intervention guide-wire: a literature review. *Curr Cardiol Rev*. 2013;9:260-6.
- Tzani G, Durante A, Mitomo S, Giannini F. Percutaneous management of periprocedural coronary sinus Reducer migration. *Catheter Cardiovasc Interv*. 2019;93:E235-7.
- Yeo KK, Davenport J, Raff G, Laird JR. Life-threatening coronary sinus thrombosis following catheter ablation: case report and review of literature. *Cardiovasc Revasc Med*. 2010;11:262.
- Hazan MB, Byrnes DA, Elmquist TH, Mazzara JT. Angiographic demonstration of coronary sinus thrombosis: a potential consequence of trauma to the coronary sinus. *Cathet Cardiovasc Diagn*. 1982;8:405-8.
- Kazui T, Lin TM, Lick SD. Coronary Sinus Rupture Repair: Patency Is Important. *Ann Thorac Surg*. 2018;106:e25-6.
- Gross L, Blum L, Silverman G. Experimental attempts to increase the blood supply to the dog's heart by means of coronary sinus occlusion. *J Exp Med*. 1937;65:91-108.
- de Voogt WG, Ruiters JH. Occlusion of the coronary sinus: a complication of resynchronization therapy for severe heart failure. *Europace*. 2006;8:456-8.

## Supplementary data

**Supplementary Appendix 1.** Coronary sinus anatomy.

**Supplementary Figure 1.** Coronary sinus anatomy.

**Supplementary Figure 2.** Coronary sinus Reducer; device preparation.

**Supplementary Figure 3.** Mother and child technique.

**Supplementary Figure 4.** Mother and child technique using the Josephson catheter.

**Supplementary Figure 5.** Coronary sinus Reducer dislocation following balloon withdrawal. Clinical case.

**Supplementary Figure 6.** Coronary sinus Reducer migration. Clinical case.

**Supplementary Figure 7.** Catheter entrapment into the device neck accompanied by device migration. Clinical case.

**Supplementary Figure 8.** Scaffold snaring. Clinical case.

The supplementary data are published online at:

<https://eurointervention.pconline.com/doi/10.4244/EIJ-D-18-01180>



## **Supplementary data**

### **Supplementary Appendix 1. Coronary sinus anatomy**

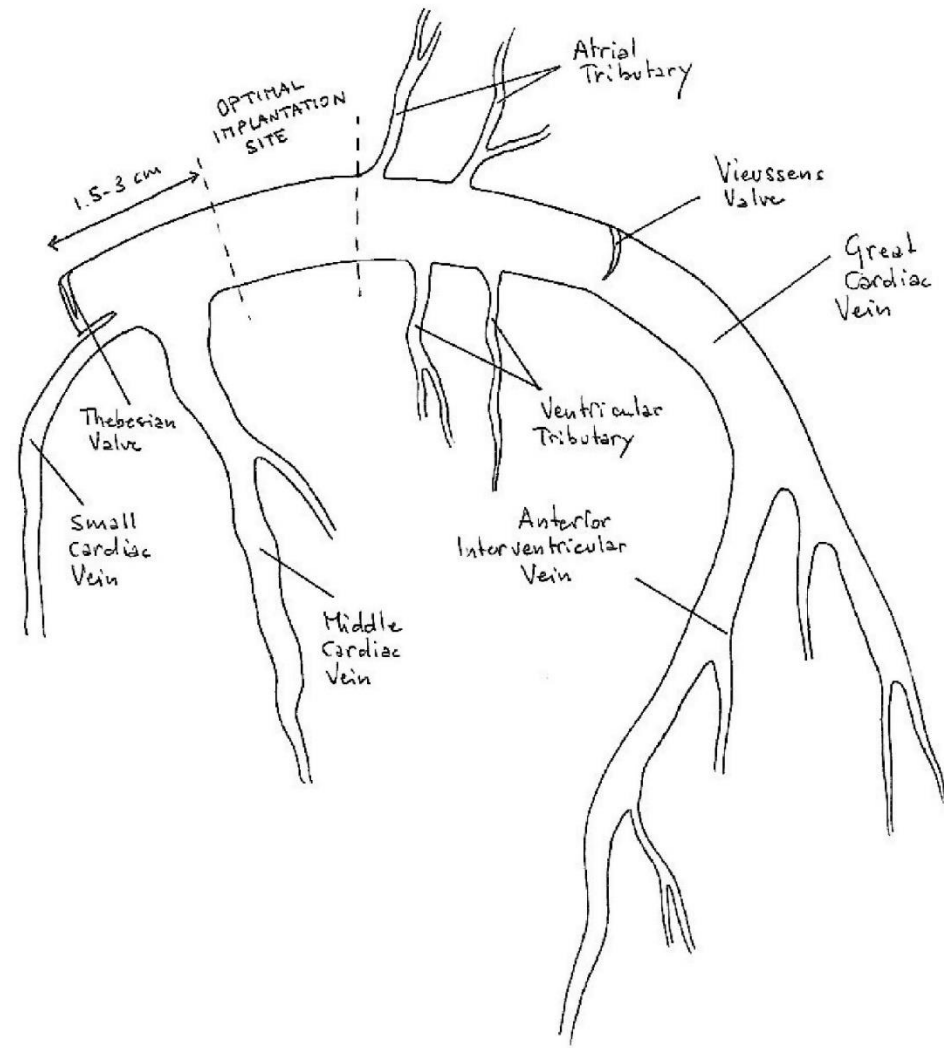
The CS is the main vessel of the greater venous system of the heart. It runs along the left side of the posterior atrioventricular sulcus, opening into the right atrium close to the interatrial septum.

The length of this vein is approximately 4 cm, usually between 3 and 5.5 cm. The CS extends between the CS ostium in the right atrium and its continuation into the great cardiac vein in the atrioventricular groove. The mean CS diameter is  $9.8 \pm 9.3$  mm; however, the CS is larger at the ostium due to its tapered conformation: mean diameter of the ostium of the CS is  $12.6 \pm 3.6$  mm (anteroposterior) x  $15.5 \pm 4.5$  mm (superoinferior). The CS ostium is often covered by the Thebesian valve. This valve usually covers the postero-superior contour of the CS ostium; however, in a minority of subjects (around 16%), the valve can be completely occlusive with only multiple fenestration to allow for blood drainage. In such circumstances, cannulation of the CS can be difficult, if not impossible. The transition of the CS into the great cardiac vein is usually identified by the presence of a valve (Vieussens valve; present in 65-87% of individuals) and by the confluence of the vein of Marshall coming from the left atrium; the Vieussens valve can occasionally interfere with distal advancement of wires.

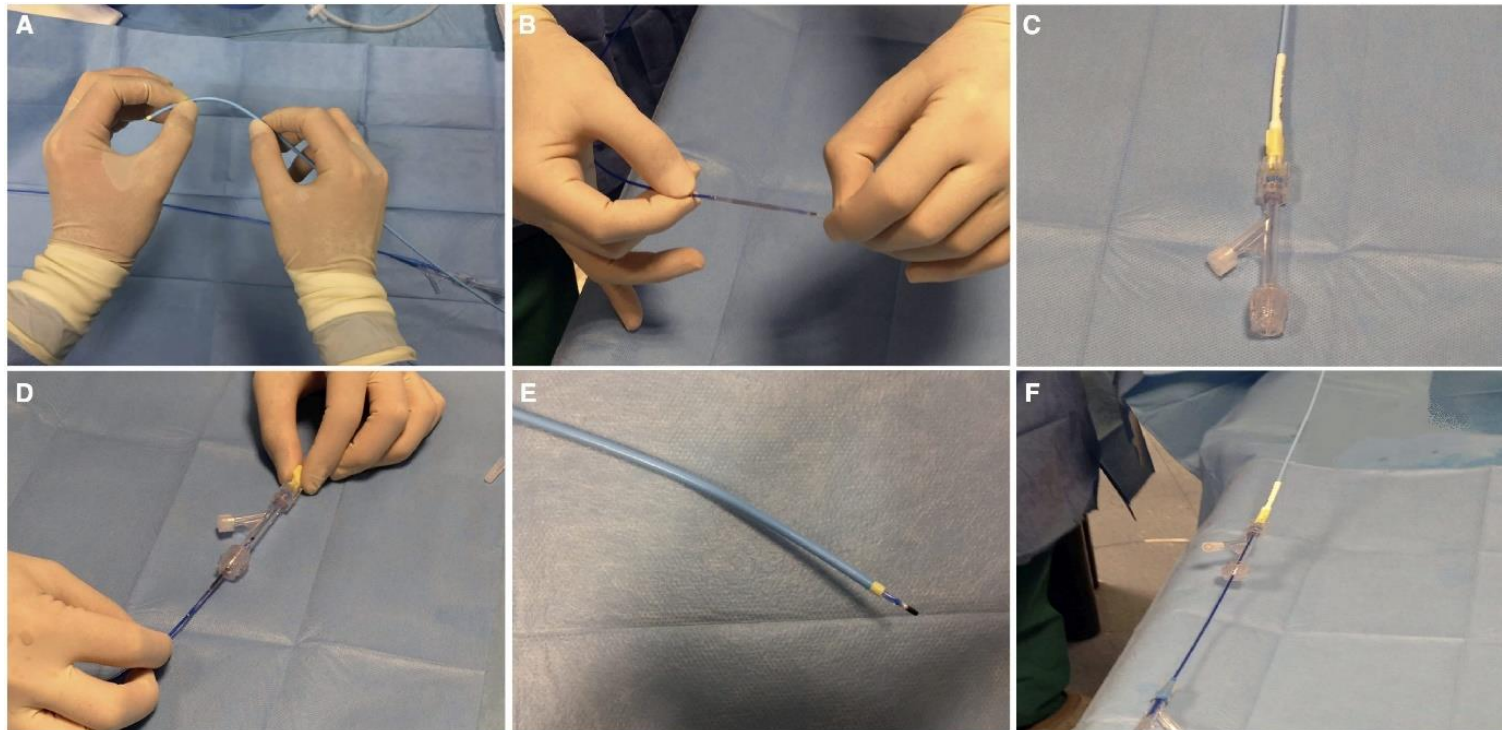
The CS has a number of tributaries - a median of three atrial and six ventricular veins. The most consistent tributary of the CS, in terms of frequency and location, is the middle cardiac vein. This vein follows the course of the posterior descending artery and joins the CS very close to the CS ostium. Lateral veins, the posterolateral vein and the posterior vein also drain into the CS along its course. These vessels can purposely or inadvertently be engaged during interventional CS procedures. As the origin of the middle cardiac vein is close to the CS ostium, the Reducer cannot be implanted proximally to it. Consequently, the myocardial territory drained from this vein is never involved in the treatment.

### ***Coronary sinus fluoroscopic anatomy***

Fluoroscopic views normally used to image the CS are the right and left anterior oblique (RAO and LAO) views. A characteristic landmark that may help to engage the CS ostium is the “fat stripe”. This is a linear radiopacity corresponding to the adipose tissue present in the atrioventricular groove. This marker is found in RAO 35-45° views and is best visualised during cine loops thanks to its systolic excursion. The CS ostium corresponds to the fat stripe base and, once cannulated, correct catheter advancement deep into the CS can be achieved following the fat stripe trajectory. In this projection, posterior or anterior shifts of the catheter tip may mean cannulation of atrial or ventricular veins, respectively. This view also allows evaluation of the anteroposterior position of the catheter with respect to the CS ostium. On the other hand, LAO views are commonly used to check the progressive catheter advancement in the CS, with each advance visible as a leftward movement. In this view, catheter movements are directly visualised, allowing the operator to modulate the force applied to the catheter to avoid excessive or abrupt advances.

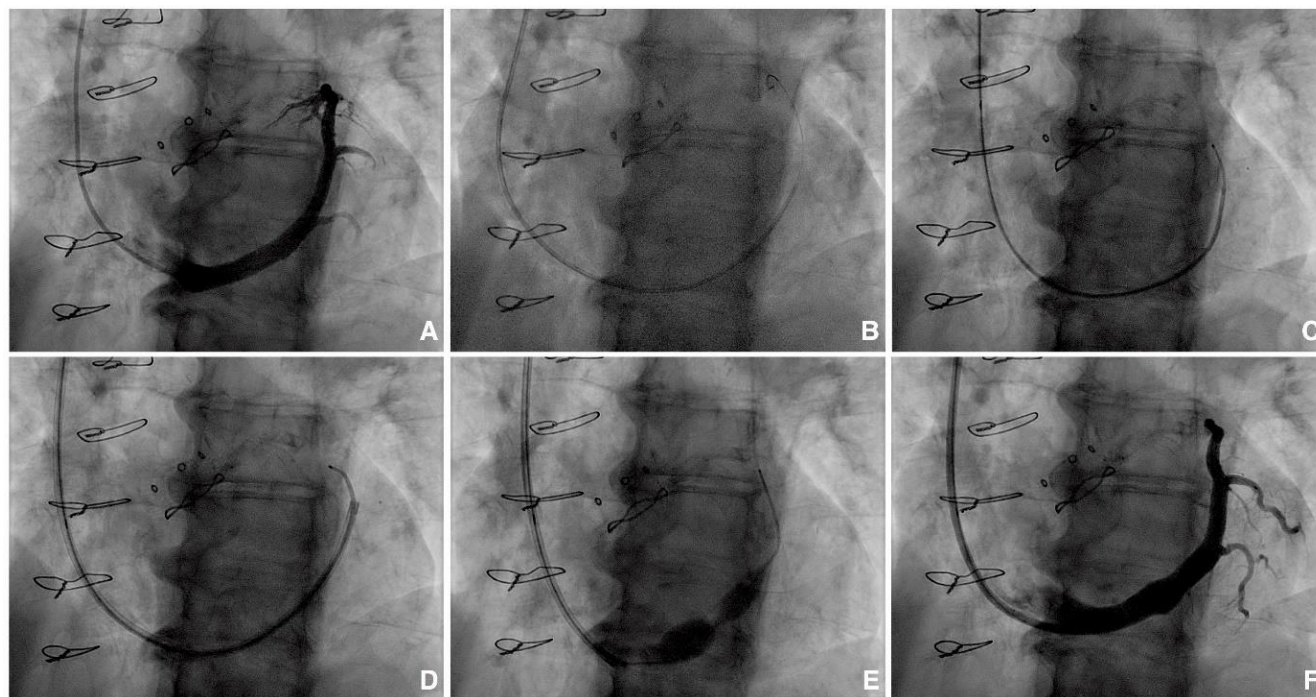


**Supplementary Figure 1.** Coronary sinus anatomy.



**Supplementary Figure 2.** Coronary sinus Reducer; device preparation.

- A) The 9 Fr guiding catheter tip is manually curved to facilitate progression into the coronary sinus.
- B) Removal of the protective covering.
- C) Connection of the haemostatic valve.
- D) Advancing the device-balloon catheter through the haemostatic valve.
- E) Protrusion of the device-balloon catheter a few millimetres from the guiding catheter.
- F) The whole system assembled. Advancing the system over a 0.035" wire.



**Supplementary Figure 3.** Mother and child technique.

A) Venography with the 5 Fr multipurpose catheter distal in the coronary sinus.

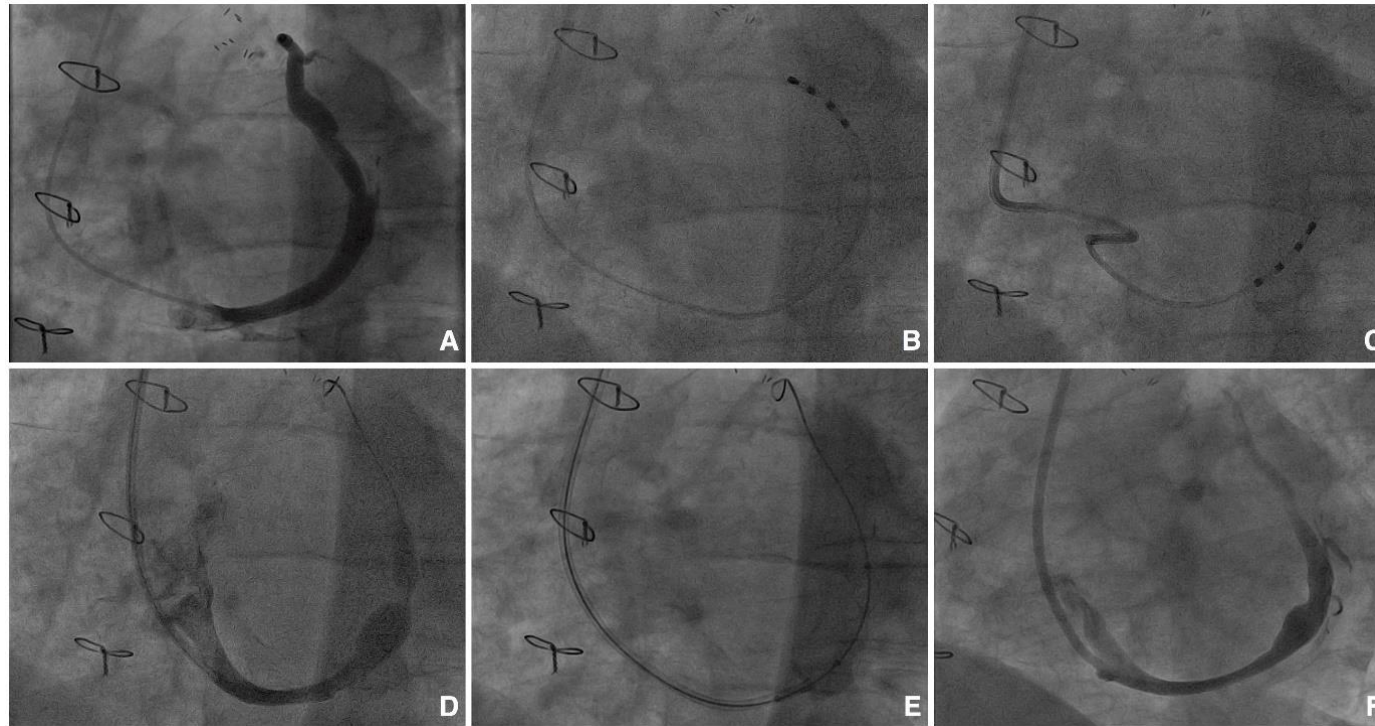
B) A 0.035" wire is placed distally in the coronary sinus.

C) The proximal part of the multipurpose catheter is cut and the 9 Fr guide catheter is advanced over the multipurpose catheter.

D) The 9 Fr catheter is advanced over the multipurpose catheter in order to reach the distal part of the coronary sinus.

E) The multipurpose catheter is removed and then the balloon catheter with the pre-mounted scaffold is advanced within the 9 Fr guide catheter to reach the landing zone. Guiding catheter is retracted, exposing the Reducer system, and the Reducer is deployed.

F) Final venography.



**Supplementary Figure 4.** Mother and child technique using the Josephson catheter.

A) Venography with the 5 Fr multipurpose catheter distal in the coronary sinus.

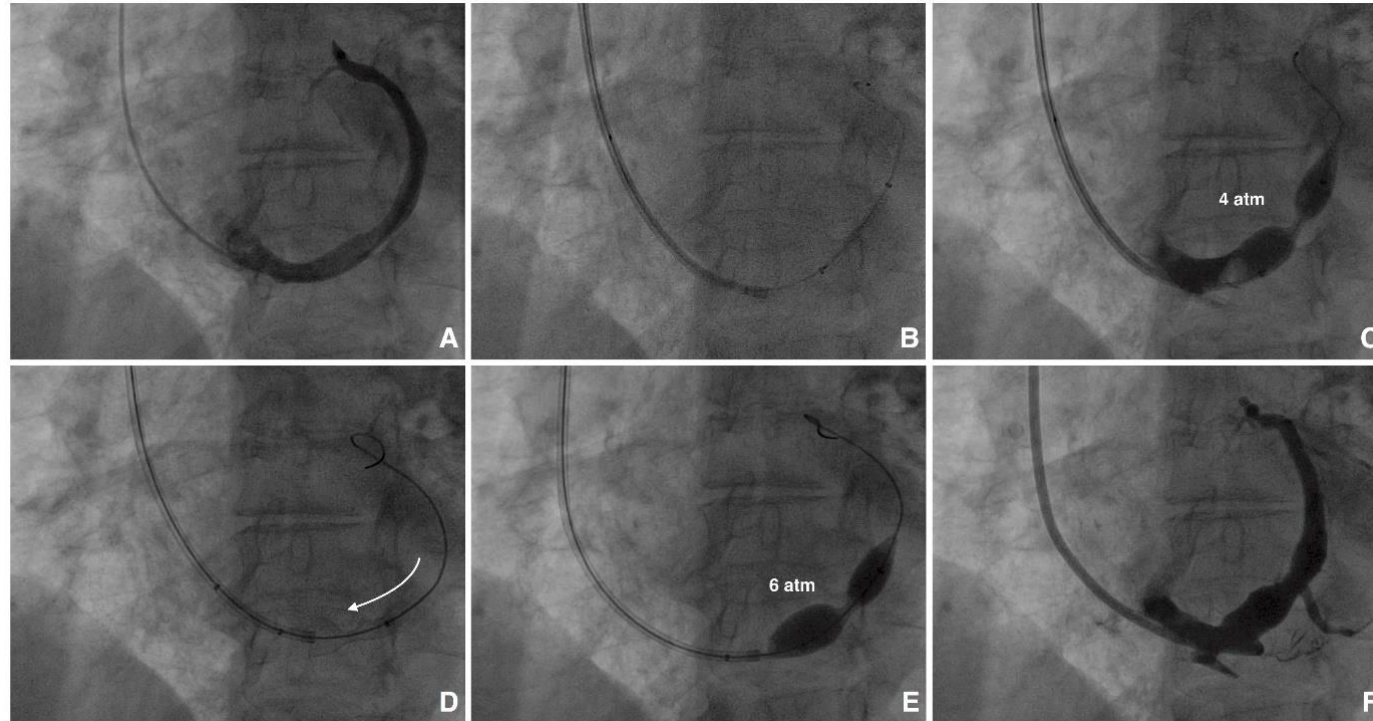
B) Re-engaging the coronary sinus with the Josephson catheter and advancing the catheter distally.

C) Difficulties in advancing the guide catheter over the Josephson catheter due to the tortuosity of the ostial vessel segment and the sharp take-off. The 9 Fr guiding catheter is advanced over the Josephson catheter utilising the mother and child technique.

D) The Josephson catheter is removed and the balloon with the pre-mounted scaffold is advanced. The Reducer is deployed.

E) Balloon catheter retrieval and deployed scaffold in place.

F) Final venography.



**Supplementary Figure 5.** Coronary sinus Reducer dislocation following balloon withdrawal. Clinical case.

A) Coronary sinus venography.

B) Reducer balloon catheter advanced in the preferred landing zone.

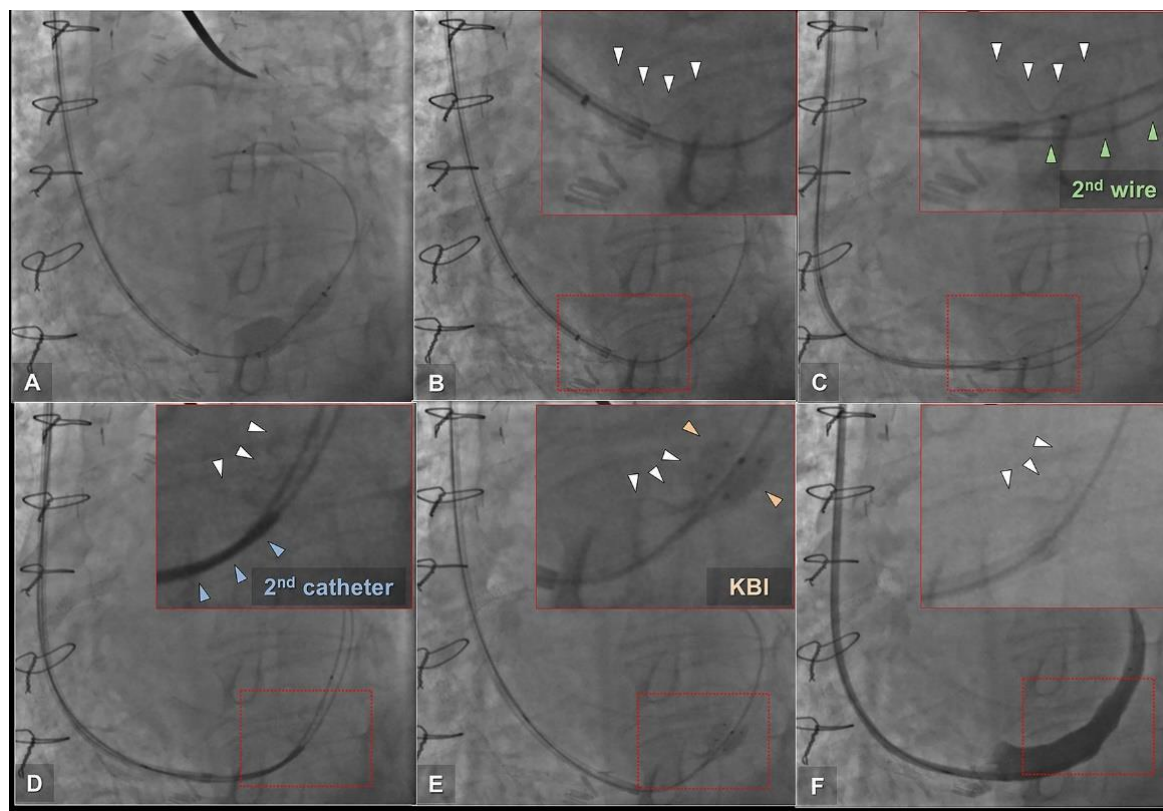
C) The Reducer was deployed by inflating the delivery balloon at 4 atmospheres with evidence of only mild oversizing.

D) Backward displacement of the Reducer (device migration) during balloon retrieval.

E) The balloon was re-advanced in the correct position, and re-inflated at 6 atmospheres to ensure proper oversizing and good anchoring to the vessel walls.

F) Final venography confirmed the correct device position with good oversizing.



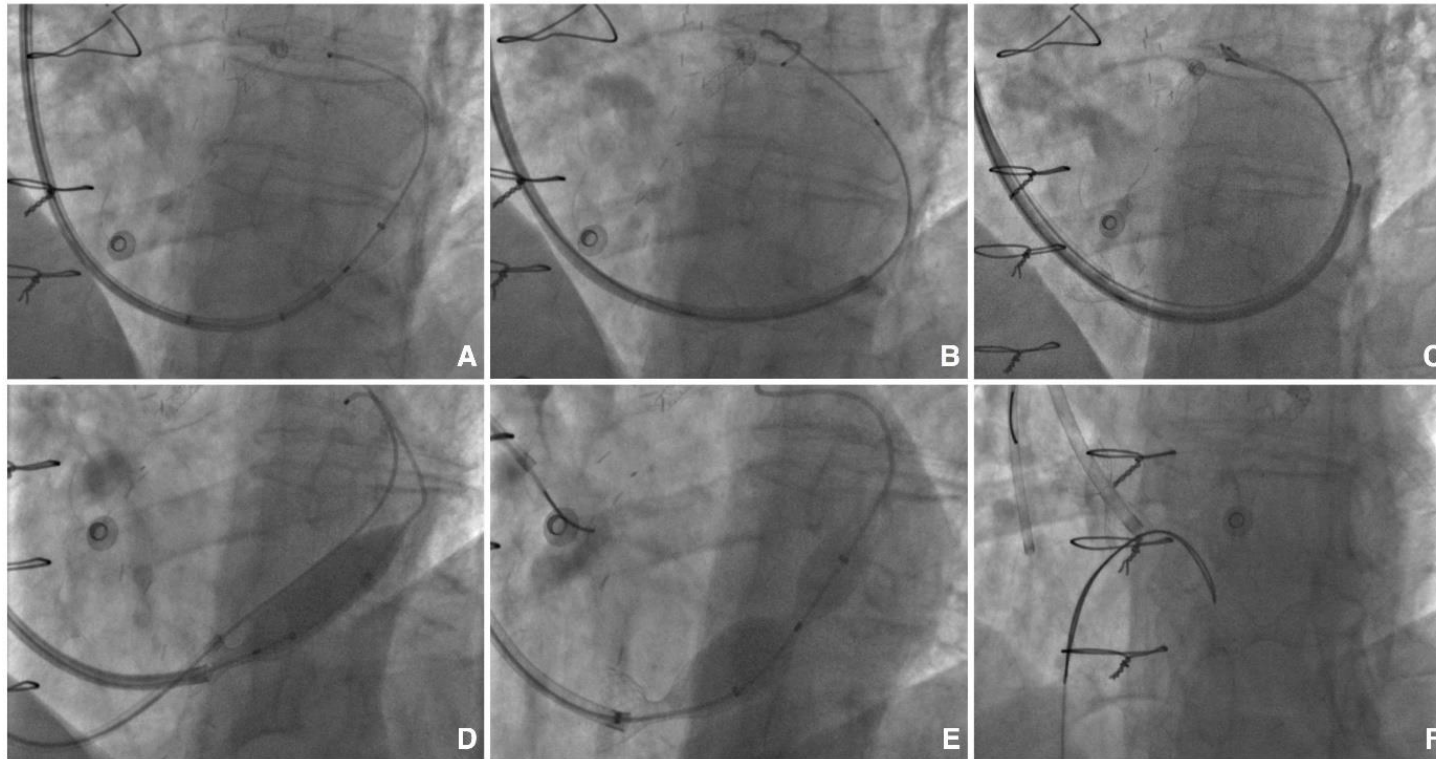


**Supplementary Figure 6.** Coronary sinus Reducer migration. Clinical case.

- A) The device was advanced to the landing zone and the Reducer was deployed.
- B) Following the retrieval of the balloon, catheter entrapment into the device neck was observed, with device dislodgement in the right atrium.
- C) Wiring of the Reducer, outside its neck, with a GLIDEWIRE<sup>®</sup> (second wire) (Terumo Corp., Tokyo, Japan).
- D) A multipurpose catheter was advanced over the GLIDEWIRE and was then pushed gently forward to advance the Reducer distally. After it was advanced, some distal deformation of the device was noticed. Therefore, the guidewire and the multipurpose catheter were removed.

E) New wiring of the Reducer, inside its neck, with two coronary guidewires and dilation of the distal portion of the device with kissing balloon inflation (5x8 mm each).

F) Final venography confirmed the correct position of the device.



**Supplementary Figure 7.** Catheter entrapment into the device neck accompanied by device migration. Clinical case.

A) Initial successful delivery of the scaffold.

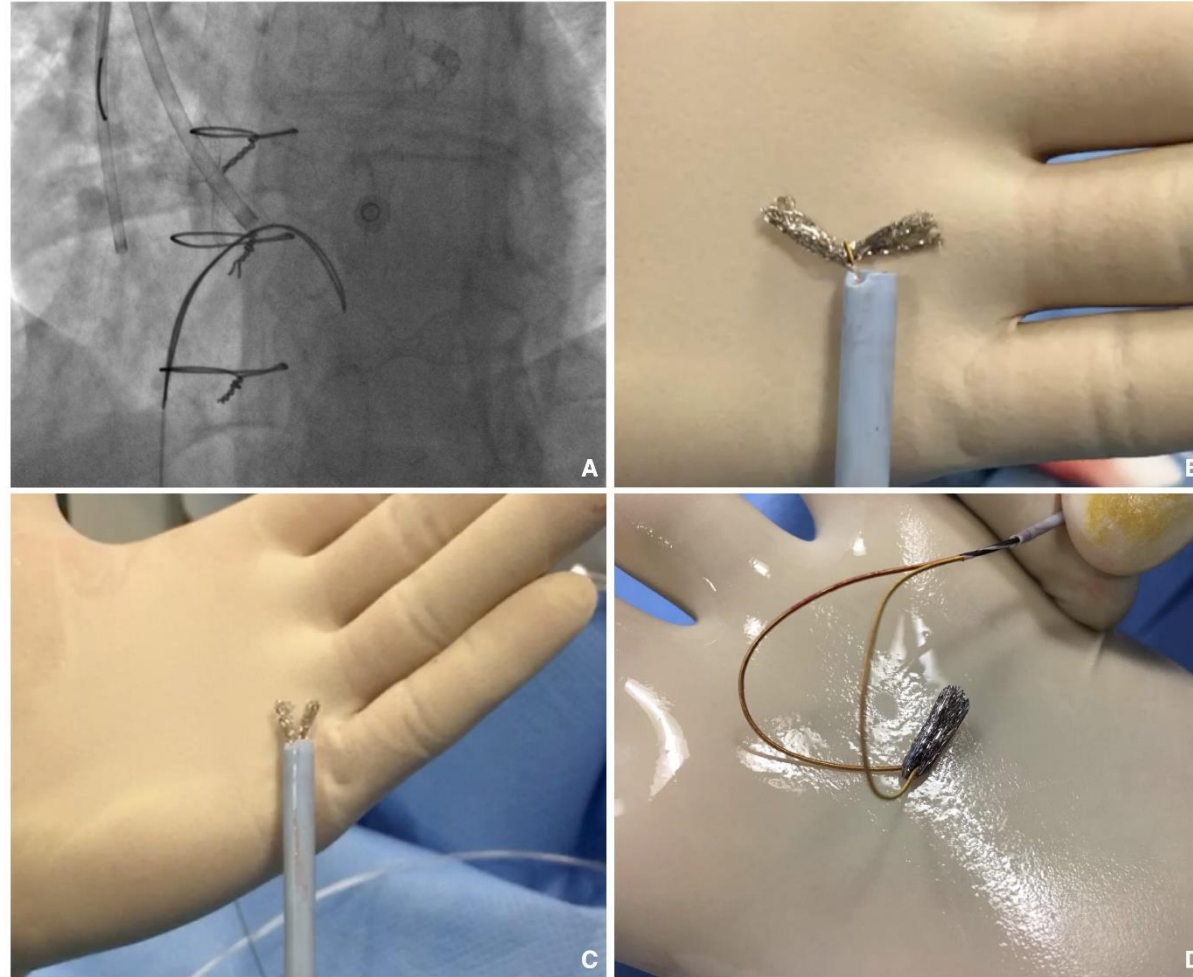
B) Despite the favourable anatomy of the CS, and initial successful delivery of the scaffold, the guide catheter was trapped inside the neck during balloon retrieval and progressively moved into the right atrium.

C) With the aid of a second catheter from the contralateral jugular vein, we tried to push the device back into position.

D) Following re-engagement of the CS, two 5 mm coronary balloons were used, unsuccessfully, to secure the device to the coronary sinus walls; a larger peripheral balloon was used next, again with no success.

E) In an attempt to stabilise the first scaffold, a second, more distal CS Reducer scaffold was deployed, in an attempt to entrap the distal portion of the first device.

F) Once this last approach had also failed, we opted for scaffold snaring and retrieval through the femoral vein. The first, displaced scaffold was retrieved successfully with no complications at the access site, and the second Reducer was correctly left in place. The patient was eventually discharged on the second post-procedural day with no adverse events recorded.



**Supplementary Figure 8.** Scaffold snaring. Clinical case.

A) During balloon retrieval, the 9 Fr catheter was entrapped in the scaffold neck. After second device implantation, retrieval of the migrated scaffold required the use of a 25 mm gooseneck snare (St. Jude Medical, St. Paul, MN, USA) inserted through the right femoral vein. With the 9

Fr catheter trapped inside the scaffold neck, a small guide was advanced inside the 9 Fr catheter and beyond the device to avoid scaffold loss in the right atrium. Then, snaring was attempted and succeeded after only a few attempts. The gooseneck snare was then tightened around the scaffold neck, which was finally freed from the 9 Fr catheter and brought into the inferior vena cava. The snared scaffold was then forced into a large, 18 Fr introducer (B & C) that had been inserted through the femoral vein. The flexible nature of the struts made retrieval possible and the crushed scaffold was extracted without complications from the right femoral vein (D).