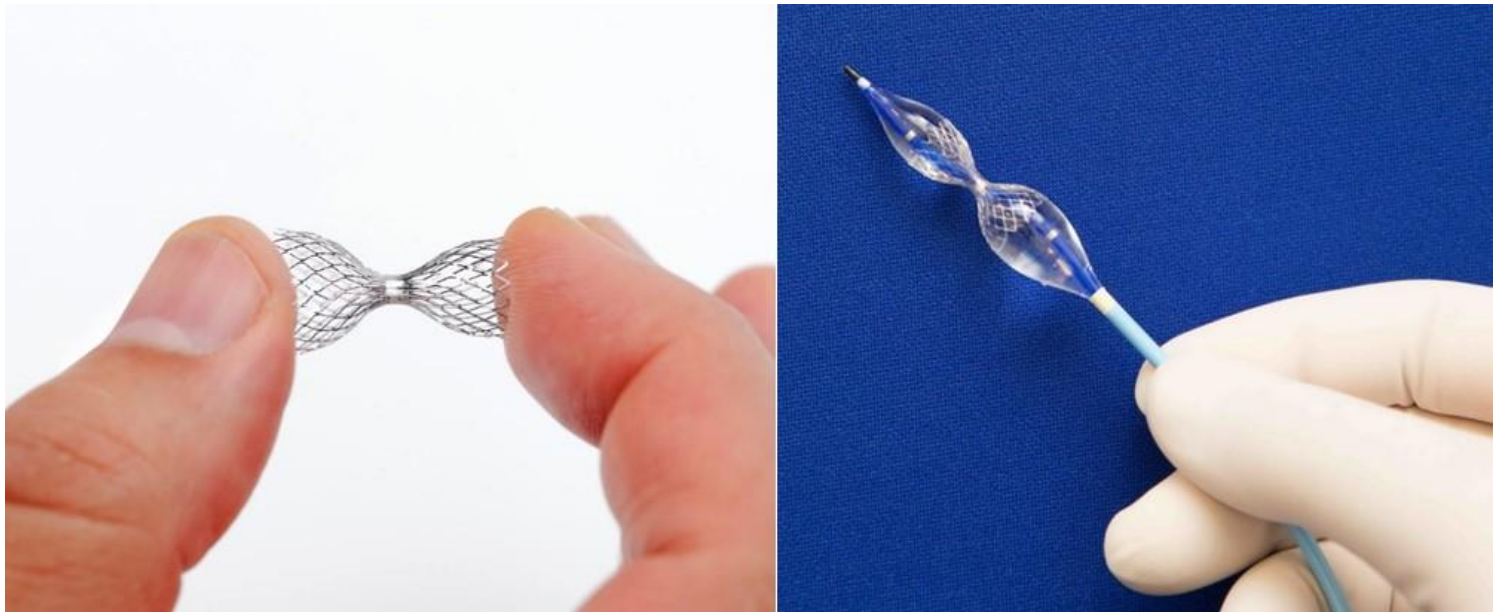
The coronary sinus Reducer for the treatment of Refractory Angina Pectoris



Shmuel Banai, MD
Director, Division of Cardiology
The Tel Aviv Medical Center

The Problem:
Chronic angina pectoris, refractory to medical and interventional therapies

- A common and disabling medical condition
- A major public health problem

1. AHA Heart disease and stroke statistics --2008 update: *Circulation*. 2008;117:e25-146
2. Task Force on the management of stable CAD of the ESC. *Eur Heart J*. 2013;34:2949-3003
3. Yang EH, et al: Current and future treatment strategies for refractory angina. *Mayo Clin Proc*. 2004;79:1284-92
4. Serruys PW: Re-appraising the significance of residual angina. *EuroIntervention* 015;10:1253

Chronic angina pectoris refractory to medical and interventional therapies

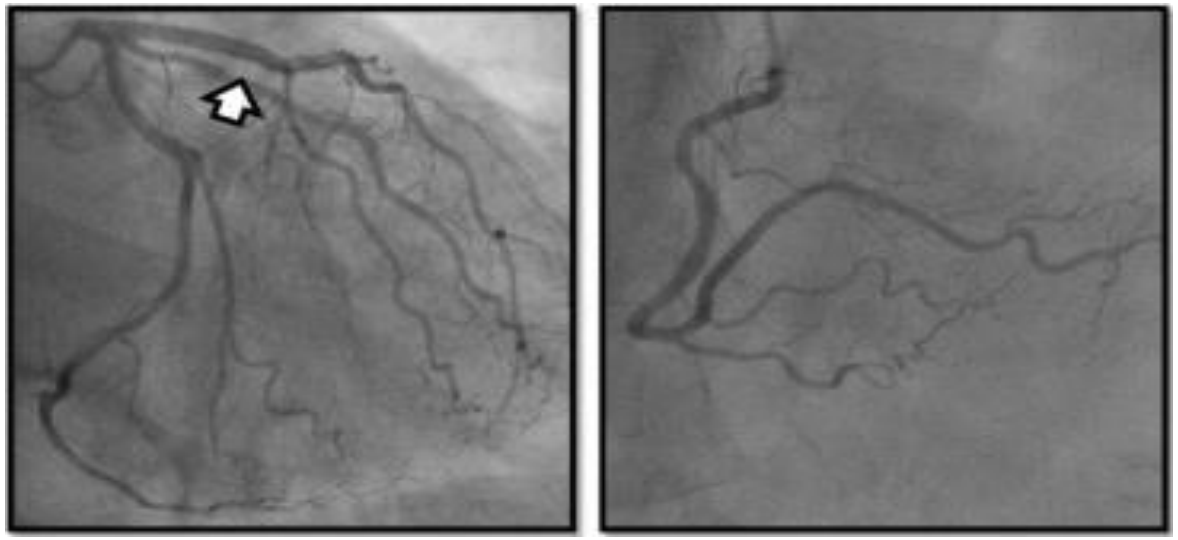
3 main groups of patients:

1. Obstructive CAD who are not good candidates for revascularization
2. Following successful revascularization (25-40%)
3. Non obstructive CAD and microvascular dysfunction (ANOCA)

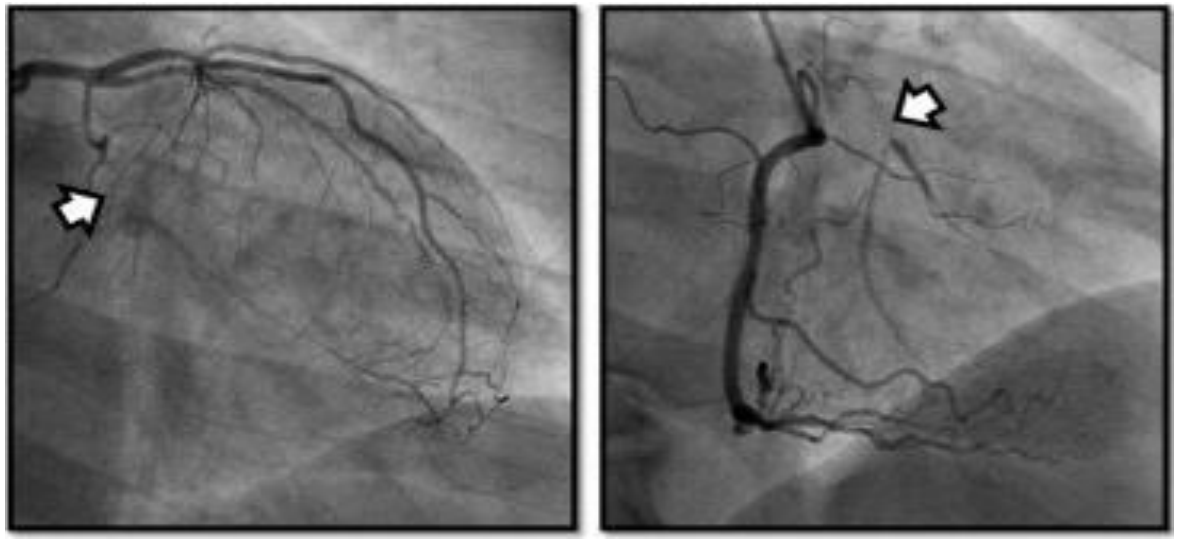
Mannheimer C: The problem of chronic refractory angina. *Eur Heart J* 2002;23:355–370
Nordrehaug JE: Treatment of chronic refractory angina pectoris. *Eur Heart J* 2006;27:1007-1009
DeJongste MJL: Chronic therapeutically refractory angina pectoris. *Heart* 2004;90:225-230
Mukherjee D: DMR—how many patients might be eligible?, *Am J Cardiol* 1999;84:598–600

Coronary angiography in patients with Refractory Angina

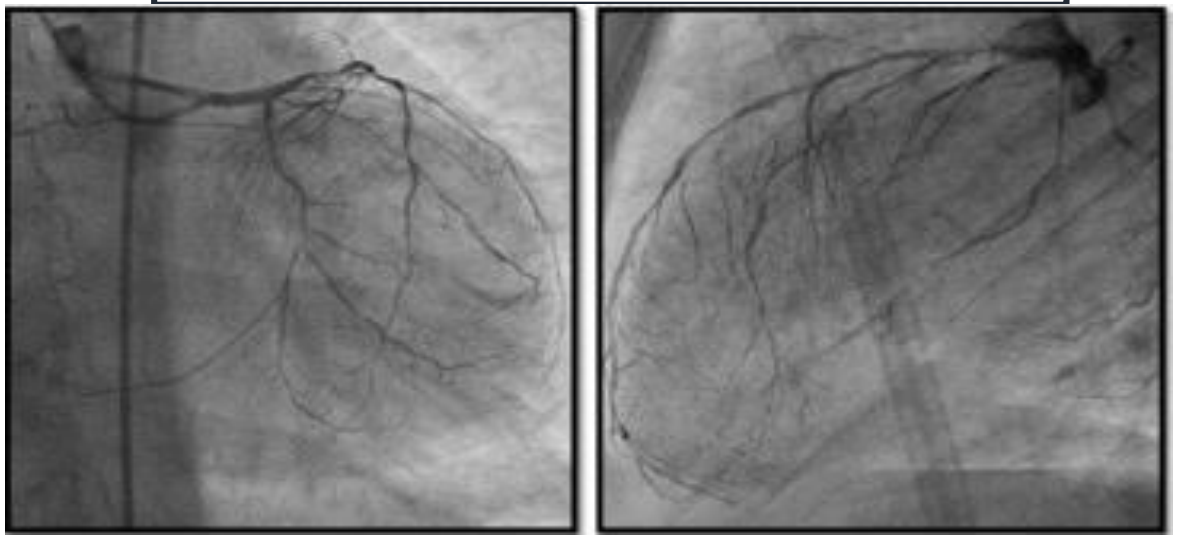
Microvascular angina



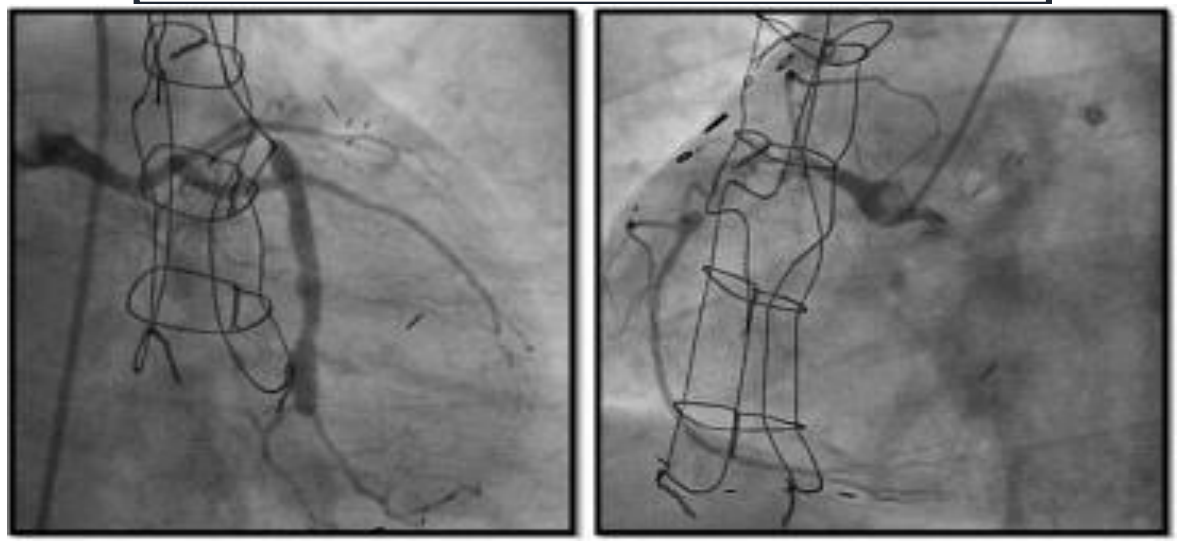
Limited territory at risk/ CTO



Diffuse thread-like atherosclerosis



End-stage CAD



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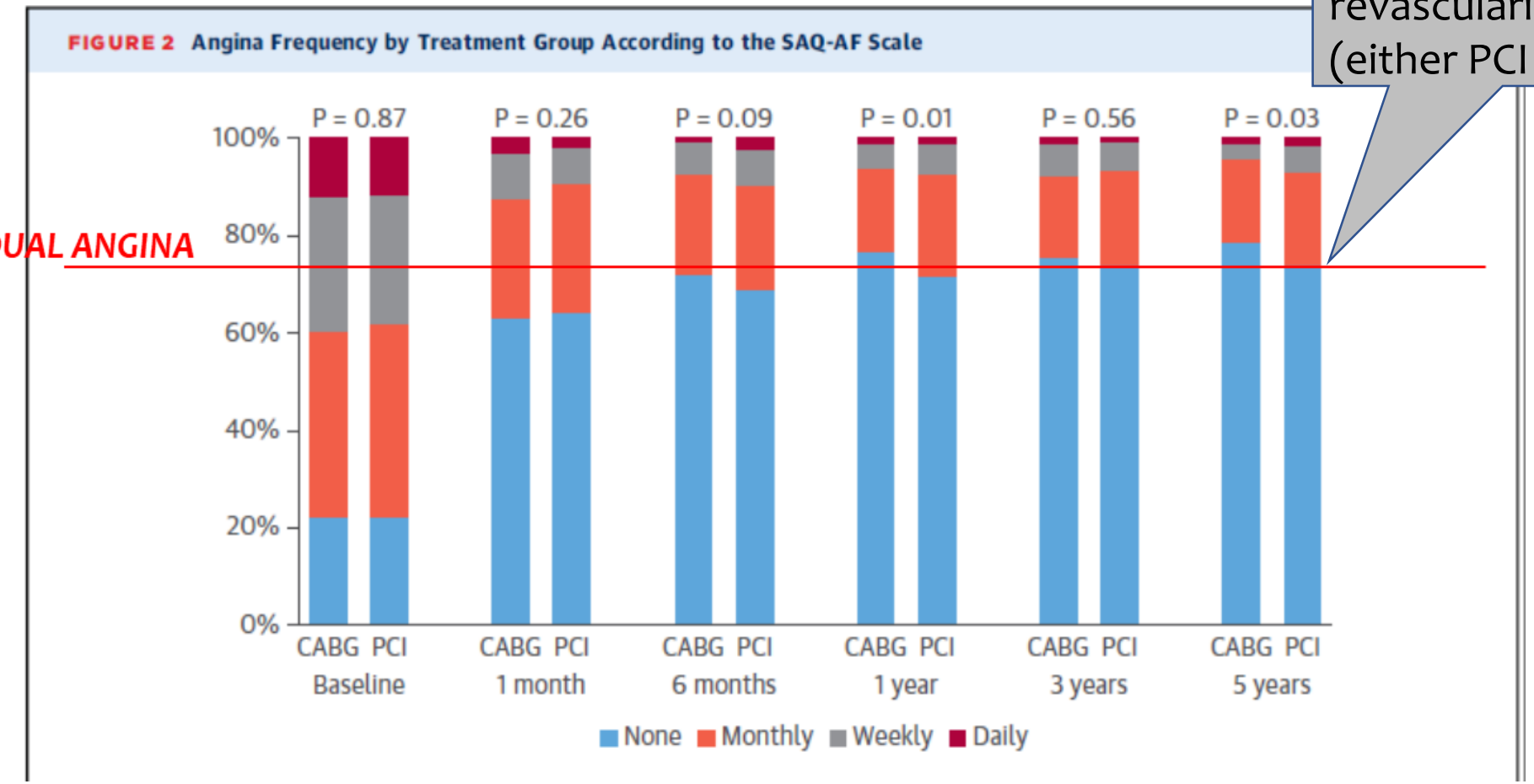
http://dx.doi.org/10.1016/j.jacc.2017.02.031

Quality of Life After Surgery or DES in Patients With 3-Vessel or Left Main Disease

Mouin S. Abdallah, MD, MSc,[a] Kaijun Wang, PhD,[b] Elizabeth A. Magnuson, ScD,[b,c] Ruben L. Osnabrugge, MSc,[d] A. Pieter Kappetein, MD, PhD,[d] Marie-Claude Morice, MD,[e] Friedrich A. Mohr, MD, PhD,[f] Patrick W. Serruys, MD, PhD,[d] David J. Cohen, MD, MSc,[b,c] on behalf of the SYNTAX Trial Investigators

More than 25% of patients continue to suffer from angina pectoris following revascularization (either PCI or CABG)

FIGURE 2 Angina Frequency by Treatment Group According to the SAQ-AF Scale



Mouin S. Abdallah: *J Am Coll Cardiol* 2017;69:2039–50

The concept of Coronary sinus (CS) narrowing for the treatment of chronic angina

SCIENTIFIC BASIS FOR THE SURGICAL TREATMENT OF CORONARY ARTERY DISEASE

Claude S. Beck, M.D.
and
David S. Leighninger, M.D., Cleveland

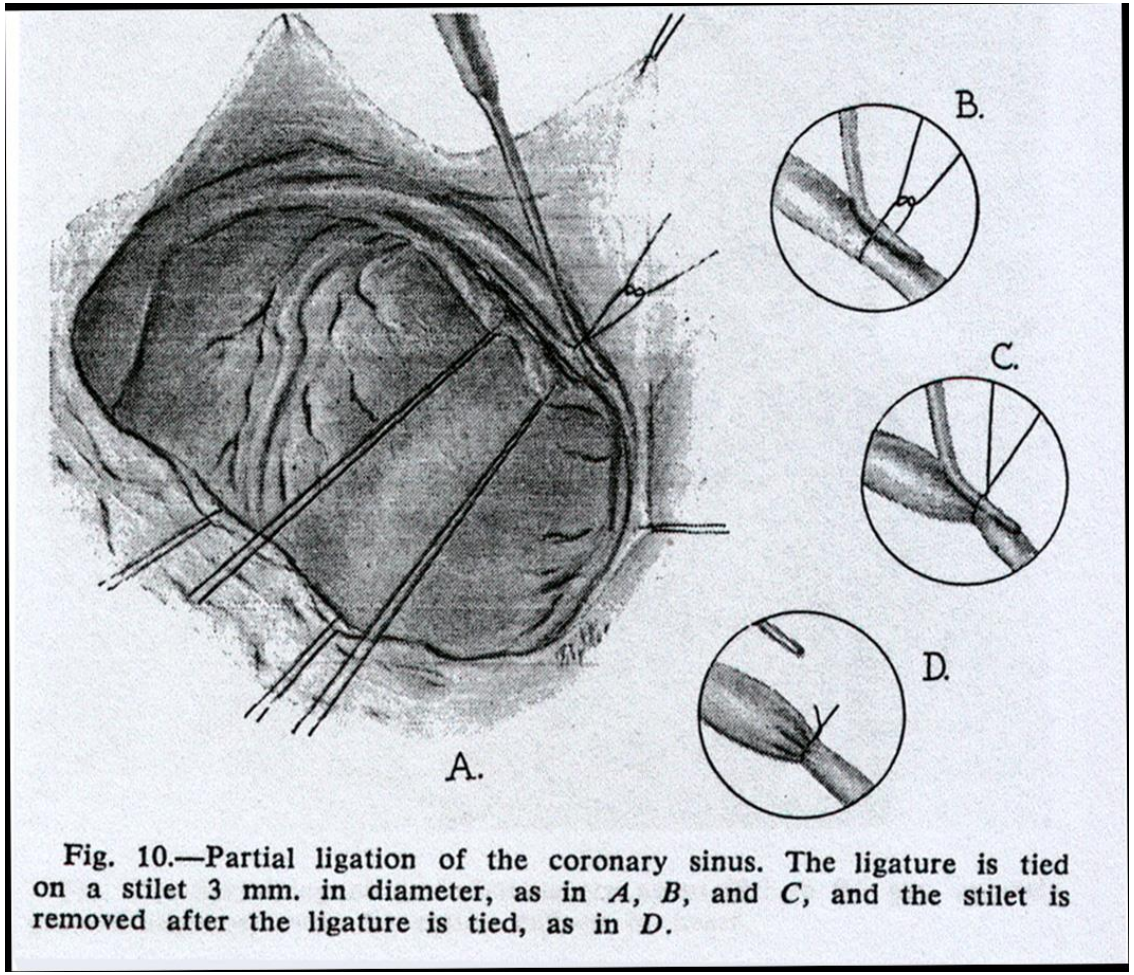


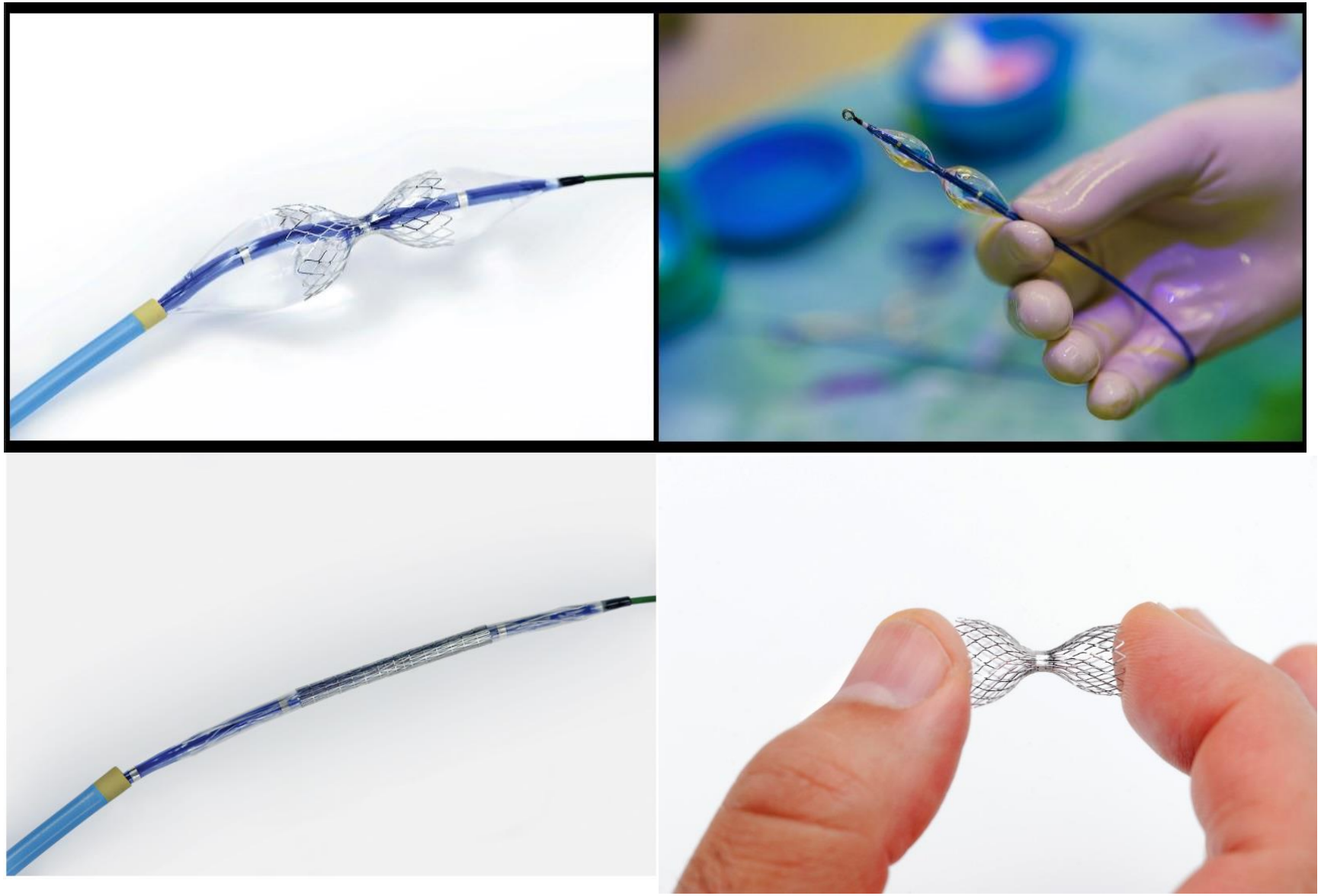
Fig. 10.—Partial ligation of the coronary sinus. The ligature is tied on a stilet 3 mm. in diameter, as in *A*, *B*, and *C*, and the stilet is removed after the ligature is tied, as in *D*.

JAMA 1955,159 (13):1264-1271

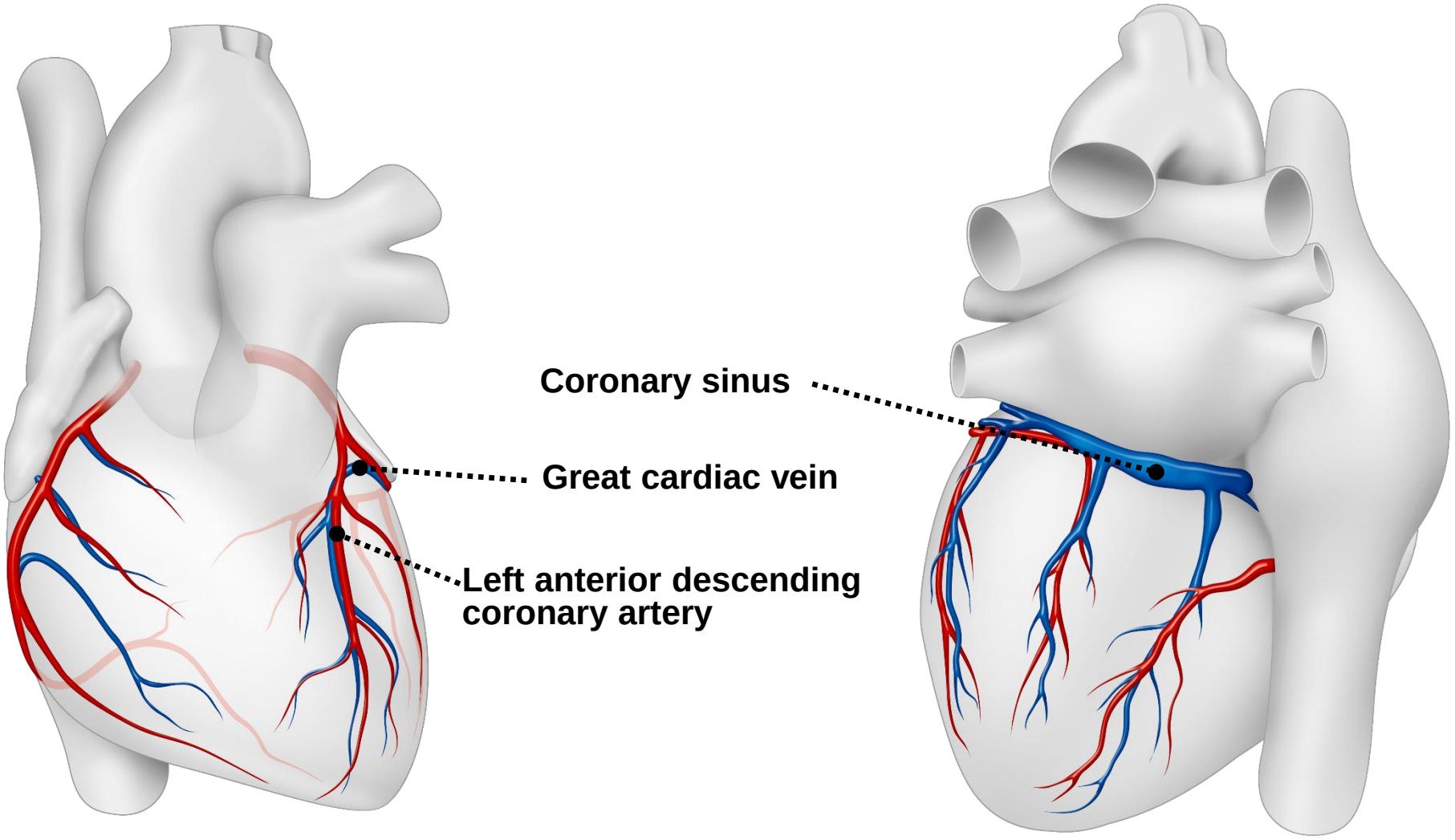
Claude Schaeffer Beck
Western Reserve University
Cleveland Ohio

- From 1948 to 1964 he treated with this procedure more than 1000 patients with coronary heart disease
- In 1952, he became the first to receive the title of professor of cardiovascular surgery in the United States

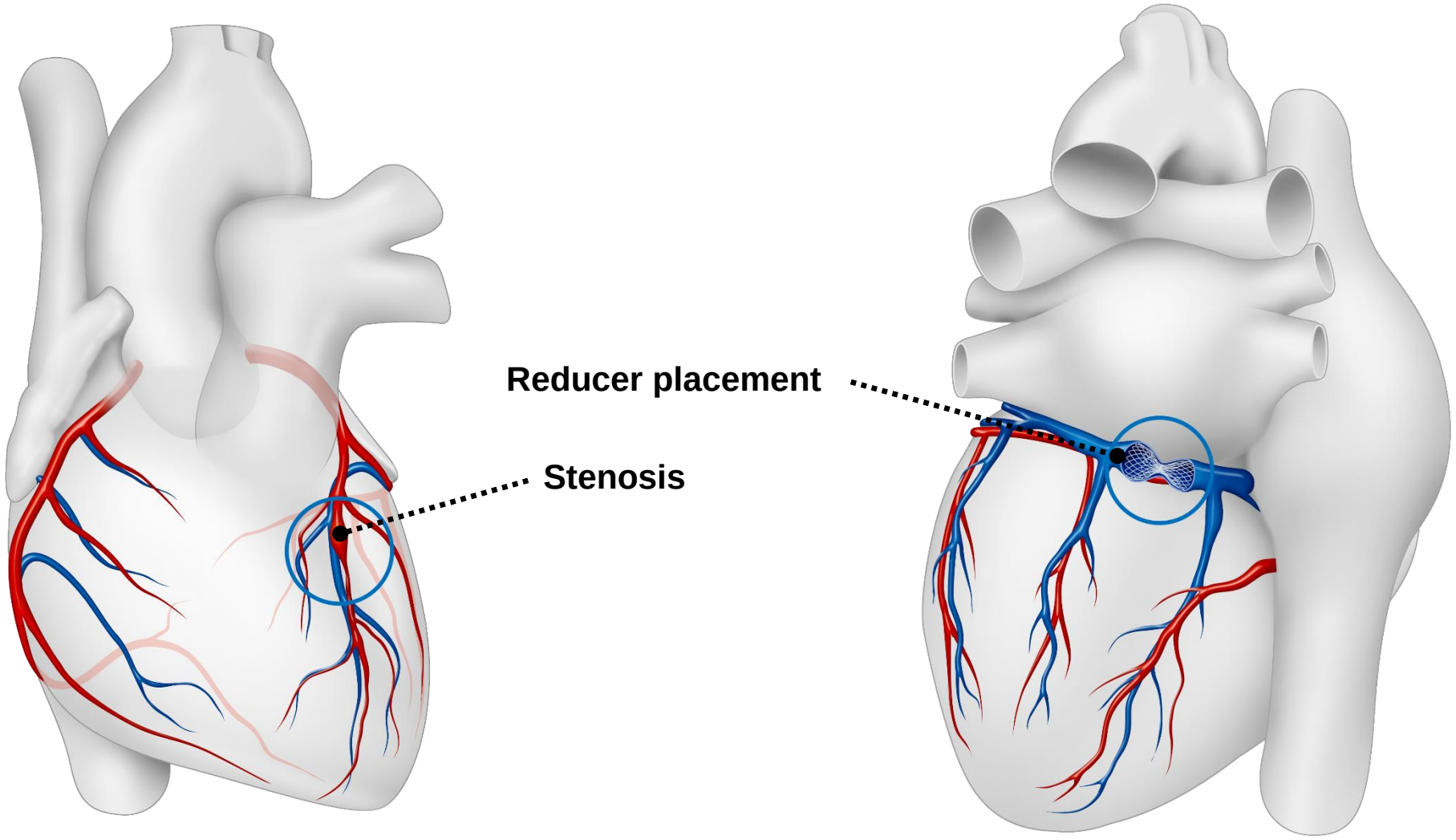
The CS Reducer
A stainless steel, balloon expandable device



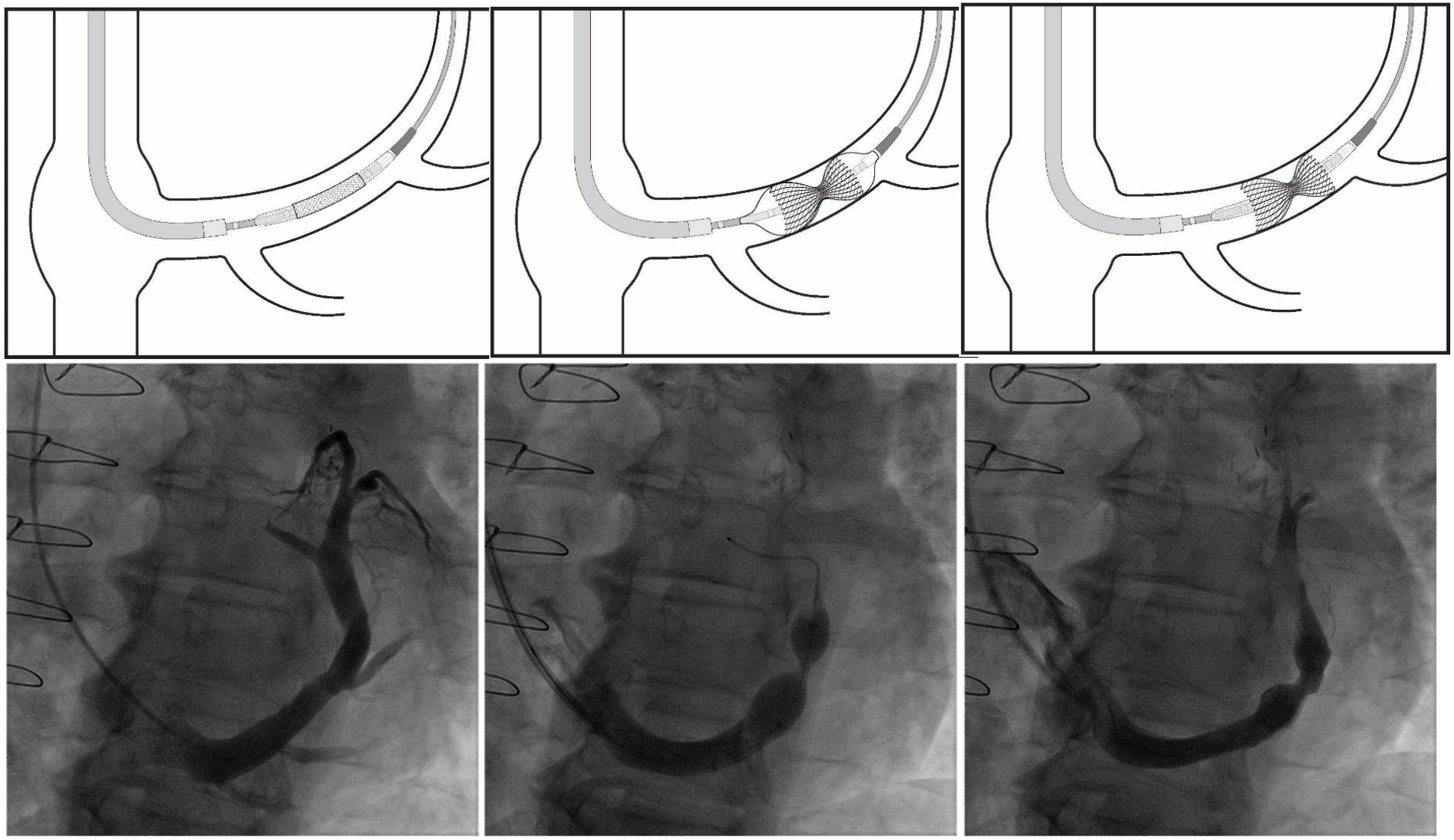
Healthy Heart, Major Vessels



Coronary sinus Reducer



The coronary Sinus Reducer
A device-based therapy for refractory angina



Clinical Evaluation

Reducer Therapy Published Clinical Evidence

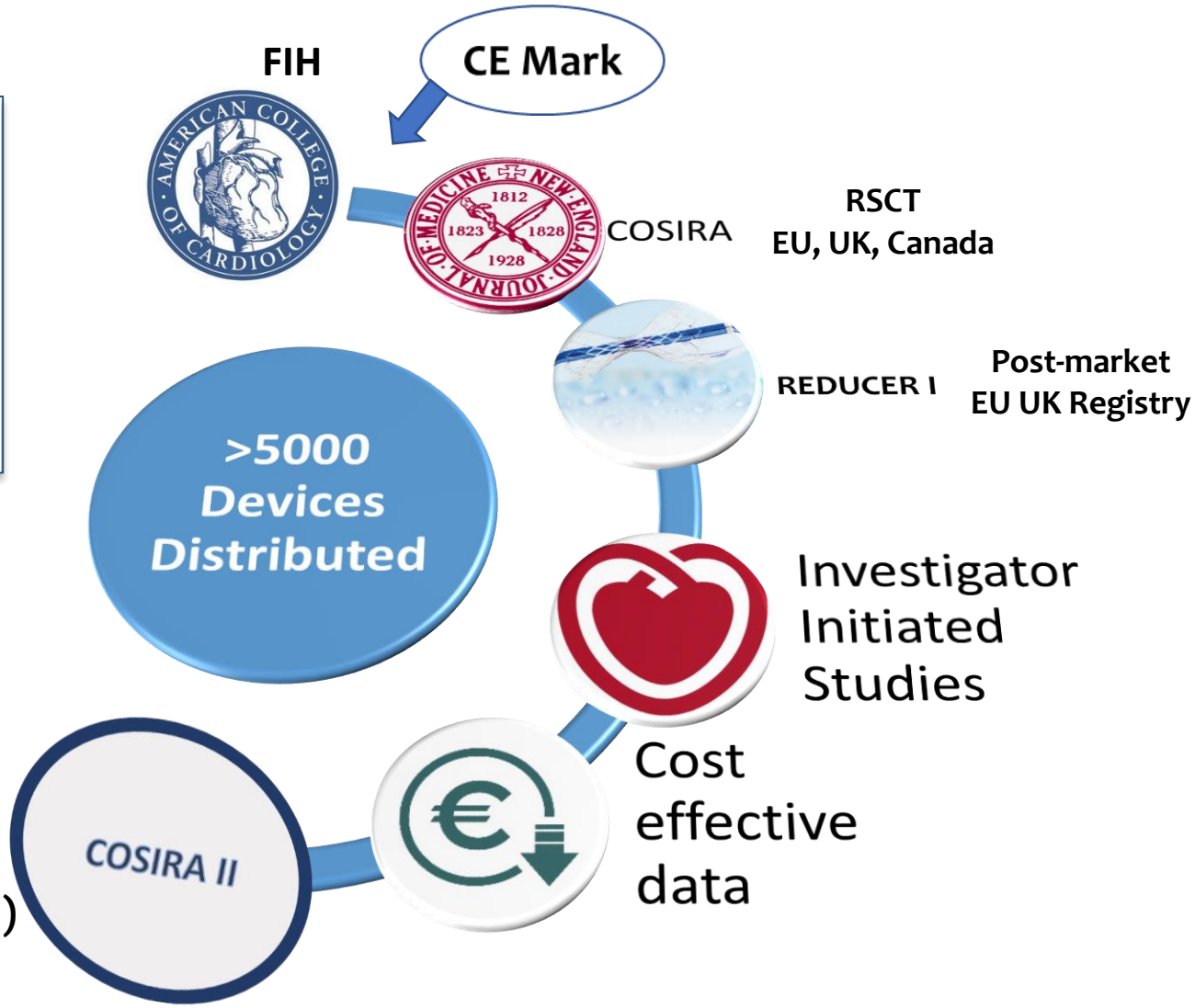
ESC European Society of Cardiology
European Heart Journal (2019) 00, 1–71
doi:10.1093/eurheartj/ehz425

ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)

Class[a]	Level[b]
IIb	B



First In Man

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ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2007.01.061

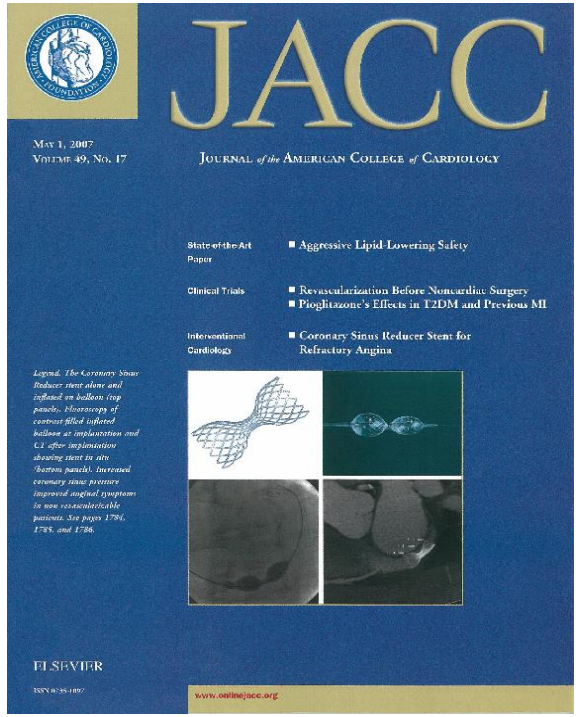
Interventional Cardiology

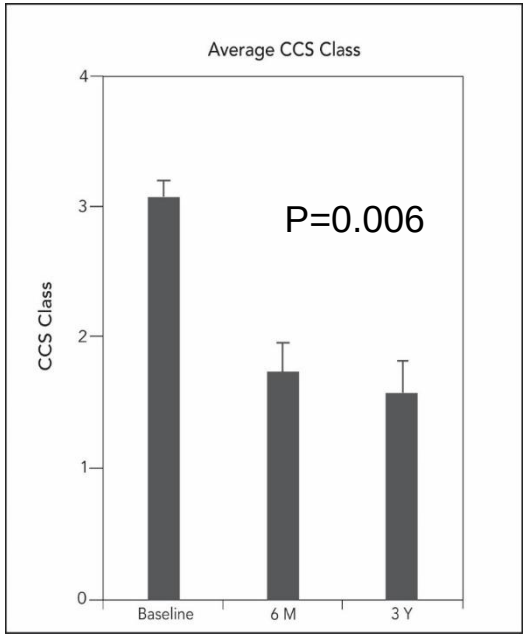
Coronary Sinus Reducer Stent for the Treatment of Chronic Refractory Angina Pectoris

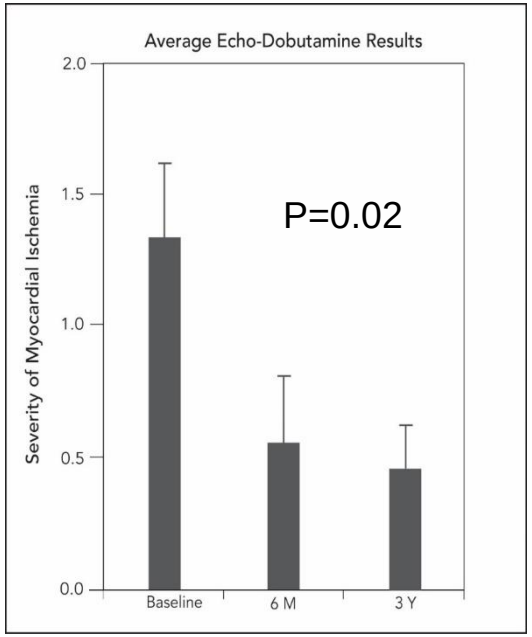
A Prospective, Open-Label, Multicenter, Safety Feasibility First-in-Man Study

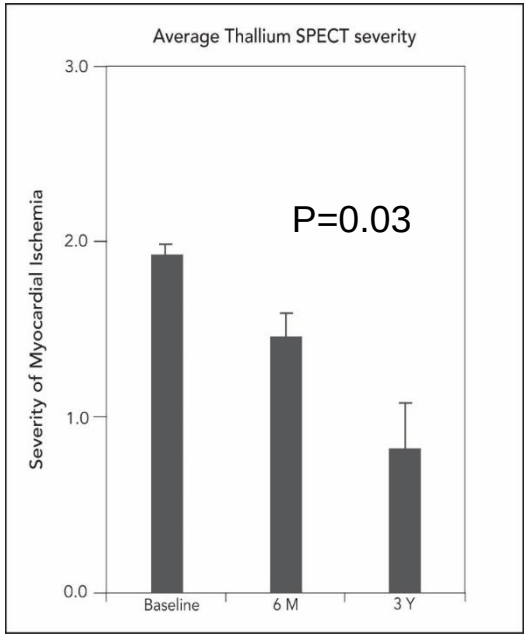
Shmuel Banai, MD,* Shmuel Ben Muvhar,† Keyur H. Parikh, MD,‡ Aharon Medina, MD,§ Horst Sievert, MD,‖ Ashok Seth, MD,¶ Jonathan Tsehori, MD,* Yoav Paz, MD,* Ami Sheinfeld, MD,# Gad Keren, MD*

Tel Aviv, Or Yehuda, Jerusalem, and Ramat Gan, Israel; Ahmedabad and New Delhi, India; and Frankfurt, Germany





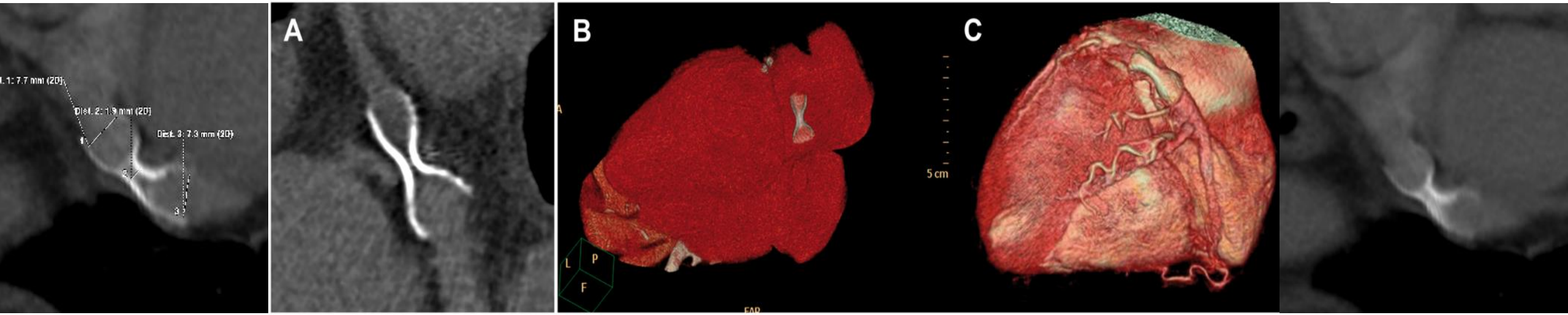




Banai S et al: JACC 2007;49:1783

First-in-Human Use of CS Reducer in Patients with Refractory Angina: 12 Years Anatomical and Clinical Outcomes

Long-term structural, anatomical and clinical durability of the Reducer:
All 7 Reducers were patent at 12 years, with no strut fractures, dislocation, thrombosis or migration

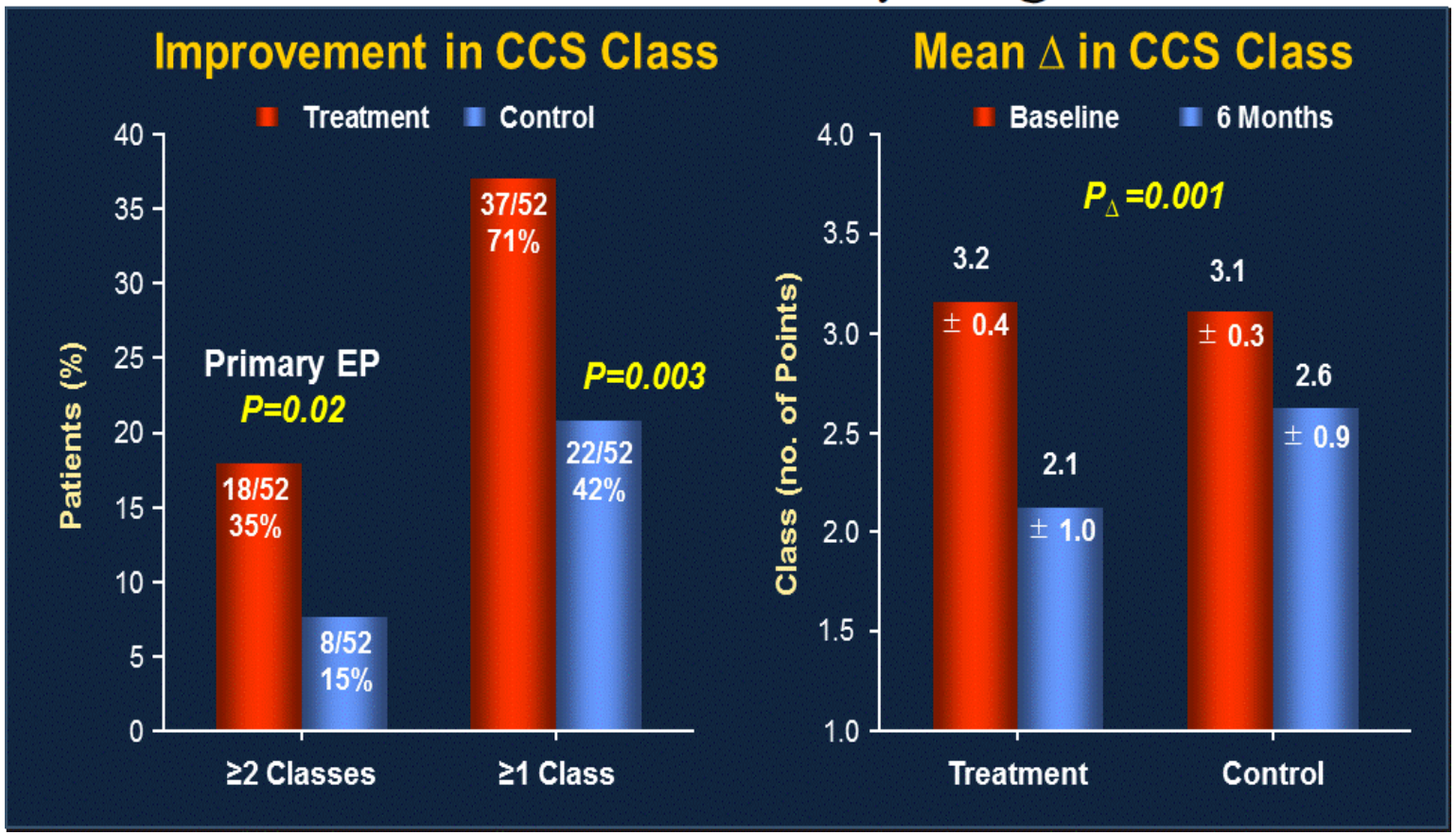


Parikh P, Banai S: *J Am Coll Cardiol*. 2018 Dec 18;72(24):3227-3228

The NEW ENGLAND JOURNAL of MEDICINE

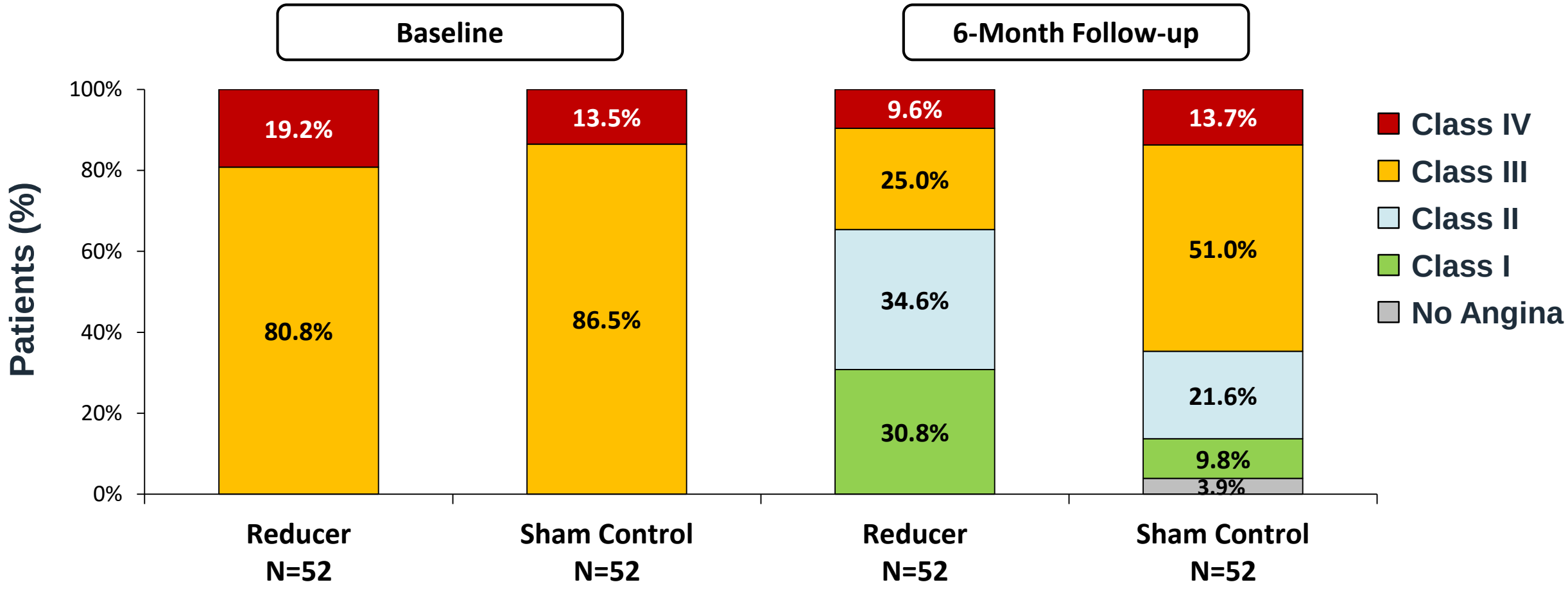
ORIGINAL ARTICLE

Efficacy of a Device to Narrow the Coronary Sinus in Refractory Angina



Verheye S, Banai S, et al. NEJM 2015;372:519

COSIRA: CCS Class Change from Baseline to 6-Months



Verheye S, Banai S, et al. NEJM 2015;372:519

REDUCER-I

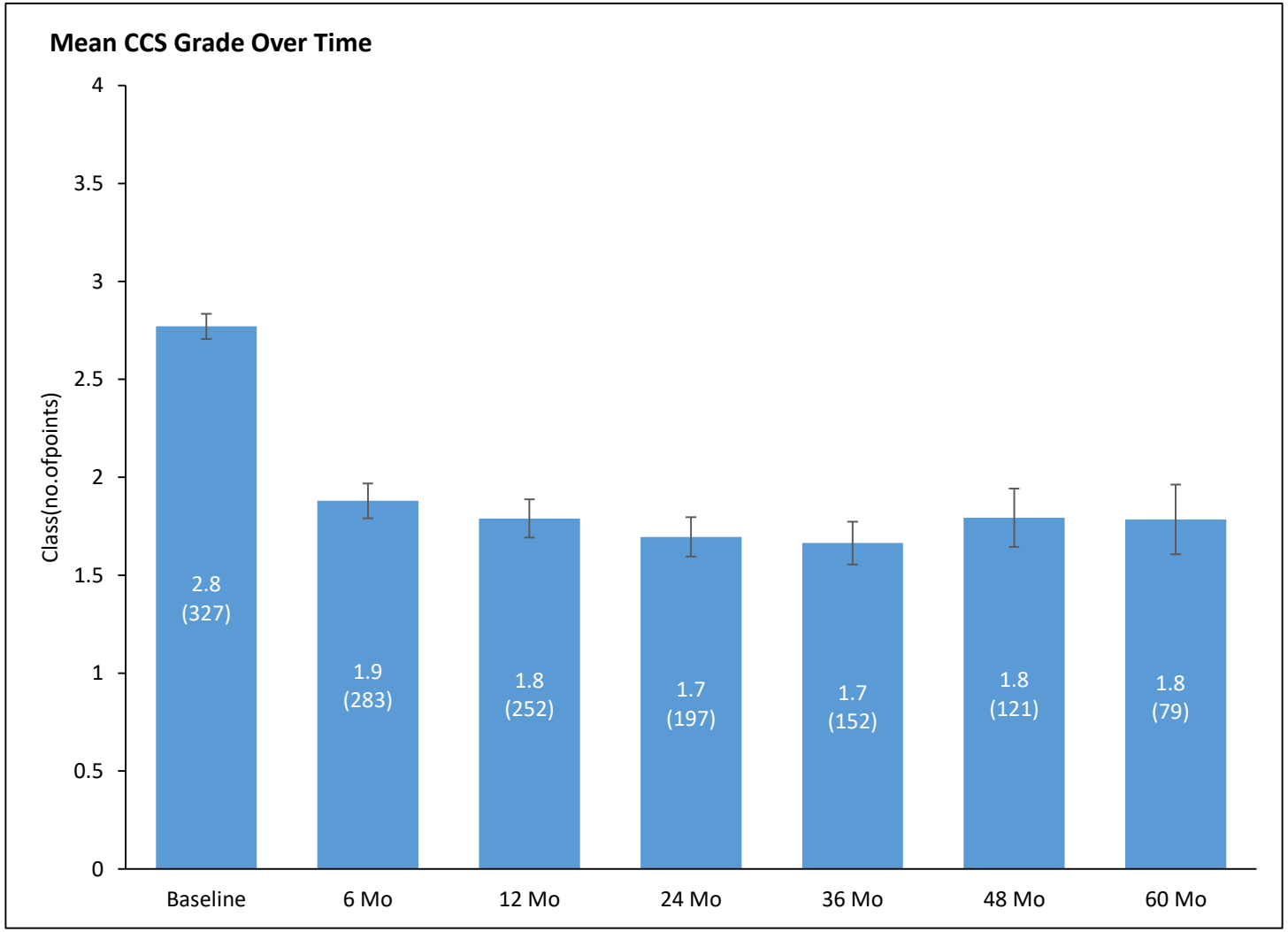
Multicenter, EU, UK, post market, observational study

- ❑ Up to 400 subjects will be enrolled
- ❑ In 22 medical centers in Europe, UK
- ❑ 362 patients have been enrolled (as of Oct, 2022)

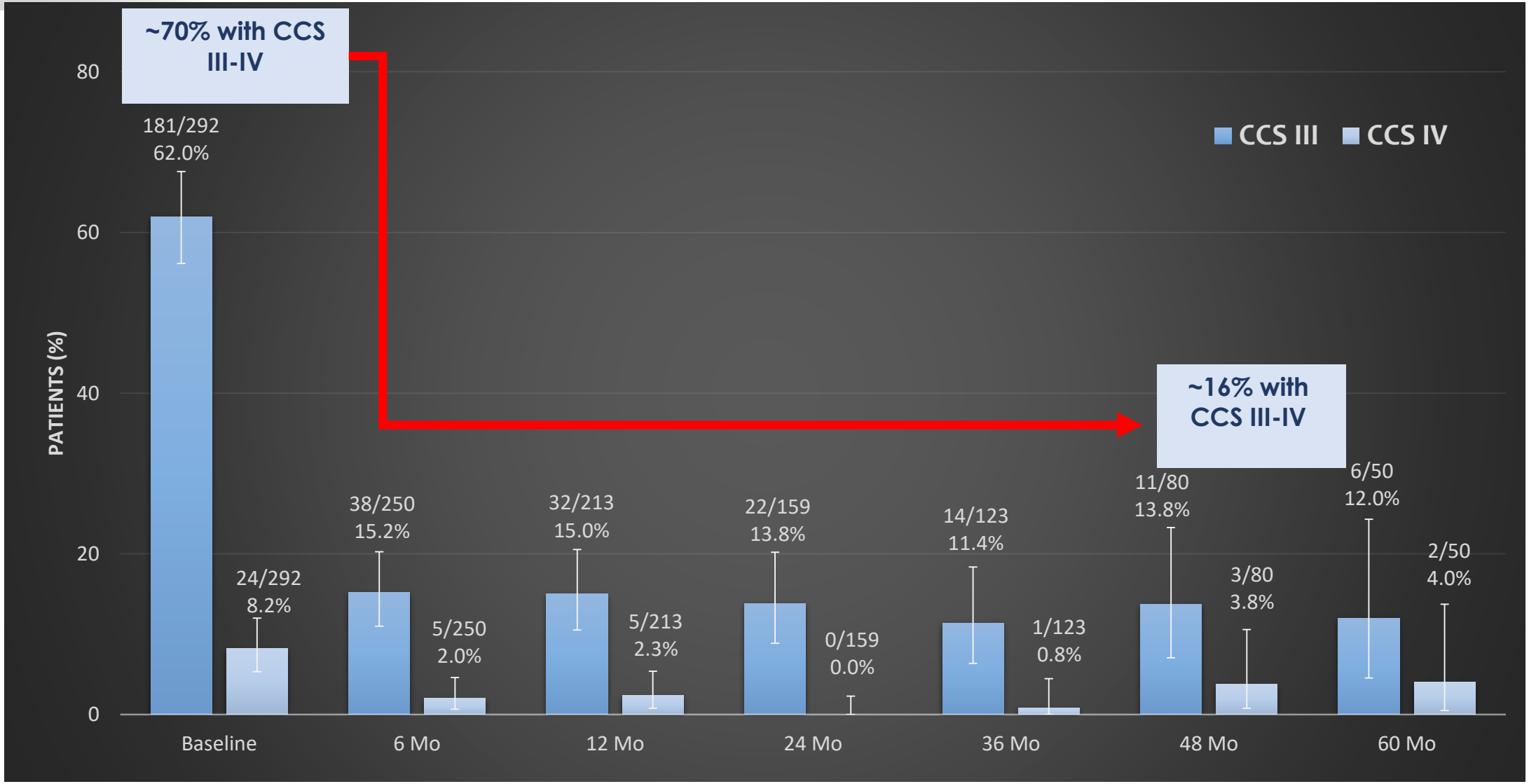
REDUCER-I Post Market Study
Top Enrolling Centers (Updated 9.9.2022)

Principal Investigator	Site Name	Country	Last Enrollment	Arm 1	Arm 2	Arm 3	Total Enrollment
Verheye	ZNA Middelheim	BE	31May2022	53	4	5	**62**
van Kuijk	St. Antonius Ziekenhuis	NL	24March2021	34	0	0	**34**
Vlachojannis	UMC Utrecht	NL	5Sep2022	35	0	5	**40**
De Silva	Royal Brompton Hospital	UK	15June2022	30	0	0	**30**
Montorfano	San Raffaele Hospital	IT	11July2018	20	0	4	**24**
Byrne	King's College Hospital	UK	15Aug2022	16	2	4	**22**
Dupont	ZOL Hospital	BE	01Aug2022	12	0	7	**19**
Linke	Herzzentrum Dresden Clinic	DE	15June2022	17	0	0	**17**
Patterson	St. Thomas Hospital	UK	20Oct2021	16	0	0	**16**
Pasotti	Fondazione Cardiocentro Ticino	CH	2June2022	14	0	0	**14**
Schmitz	Elisabeth Krankenhaus Essen	DE	13Nov2018	6	0	**7**	**13**
Lindsay	Bradford Royal Infirmary	UK	20Oct2020	10	0	3	**13**
Haas	Kerckhoff-Klinik	DE	19Feb2021	10	0	1	**11**
Buschmann	Graz	AT	26July2022	15	0	0	**15**
		REDUCER-I Totals		**304**	**11**	**39**	**354**

Mean CCS Class over time, all cohort, May 2002



REDUCER-I
Patients with Angina CCS Class 3-4



Am J Cardiology 2021;139:22-27

Usefulness of Coronary Sinus Reducer Implantation for the Treatment of Chronic Refractory Angina Pectoris

Gianpiero D'Amico, MD[a], Francesco Giannini, MD[b], Mauro Massussi, MD[a], Matteo Tebaldi, MD[c], Alessandro Cafaro, MD[d], Alfonso Ielasi, MD[e], Fabio Sgura, MD[f], Federico De Marco, MD, PhD[g], Giulio G Stefanini, MD, PhD[h], Marco Ciardetti, MD[i], Francesco Versaci, MD[j], Roberto A Latini, MD[k], Salvatore Saccà, MD[l], Sergio Ghiringhelli, MD[m], Andrea Picchi, MD[n], Marco Cerrito, MD, PhD[o], Achille Gaspardone, MD[p], and Giuseppe Tarantini, MD, PhD[a,*]

Italian National Registry

- 16 medical centers
- 187 patients
- Median follow-up: 18.4 m

The American Journal of Cardiology®

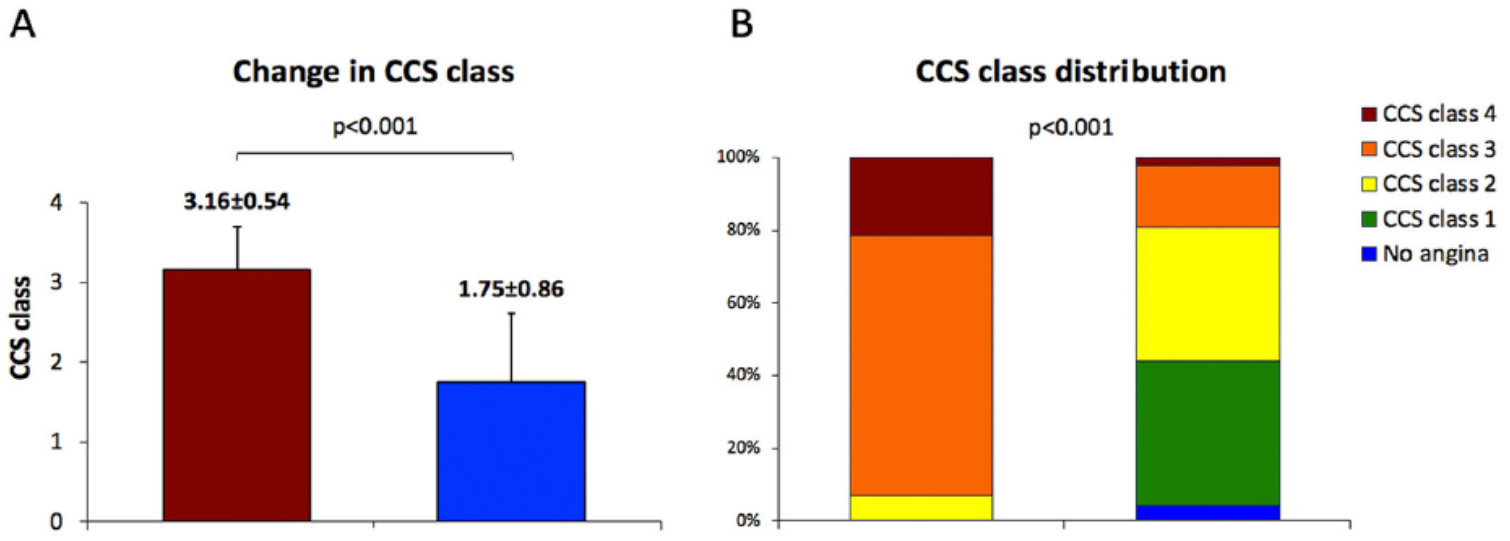
2021;139:22-27

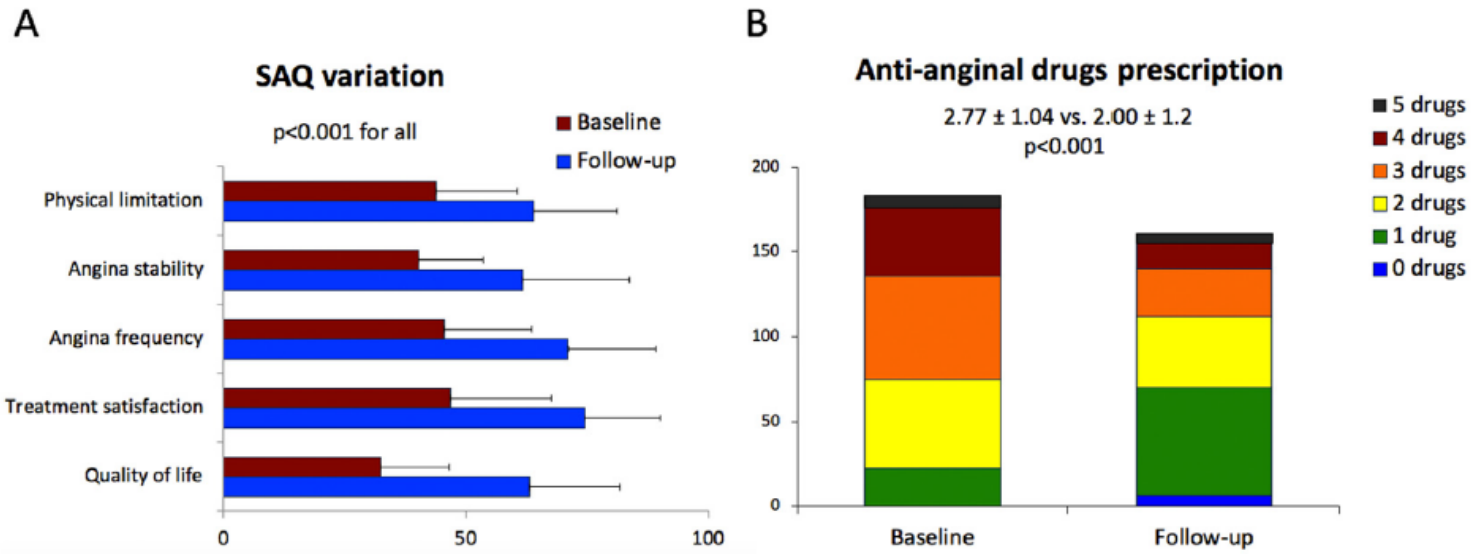
Am J Cardiology 2021;139:22-27

Usefulness of Coronary Sinus Reducer Implantation for the Treatment of Chronic Refractory Angina Pectoris

Conclusions:

In this multicenter, country-level study, Reducer therapy was safe and effective in reducing angina and improving QOL





International Journal of Cardiology 337 (2021) 29–37

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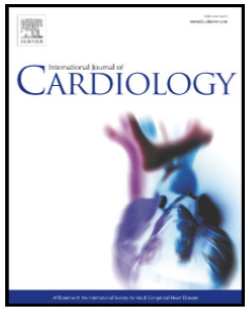


Safety and efficacy of coronary sinus narrowing in chronic refractory angina: Insights from the RESOURCE study

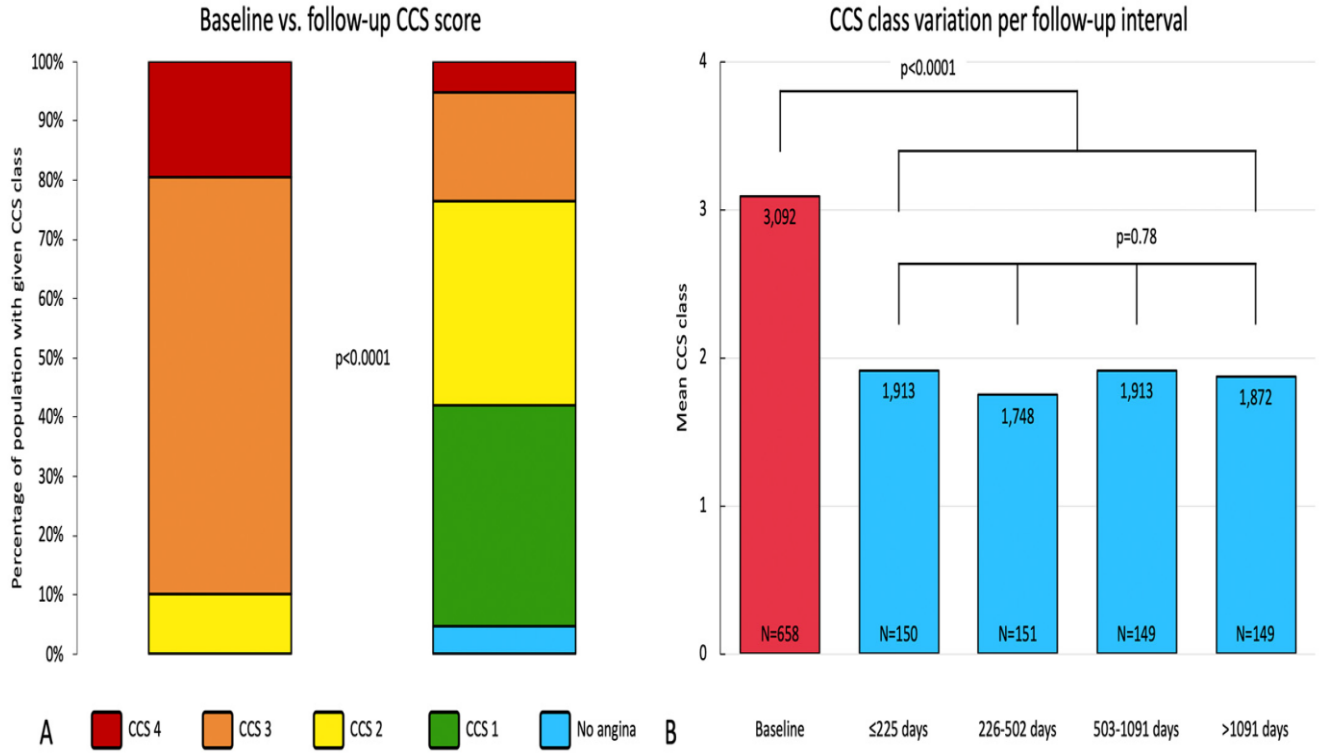
RESOURCE Study:

- Observational, multi-center retrospective registry
- 658 patients with RA from 20 centers in EU, UK, and Israel
- Endpoints: anginal symptoms (CCS score), procedural success rate, and MACEs
- Median follow-up of 502 days (IQR 225–1091)

RESOURCE Study - Results

Efficacy:

Improved by ≥2 CCS classes	39.7%
Improved by ≥1 class	76%
Procedural success rate	96.7%
Any complication	5.7%



Safety:

- Any complication occurred in 5.7% of procedures, but never required bailout surgery nor resulted in intra- or periprocedural death or myocardial infarction
- One patient developed periprocedural stroke after inadvertent carotid artery puncture

Ponticelli F. et al: *Int J Cardiol* . 2021 Aug 15;337:29-37

Reducer therapy and its effect on objective evidence of myocardial ischemia

Coronary Sinus Reducer Implantation improves Angina and Objective Evidence of Myocardial Ischemia

EuroIntervention

Konigstein M, Banai S: *EuroIntervention*. 2018 Jul 20;14(4):e452-e458

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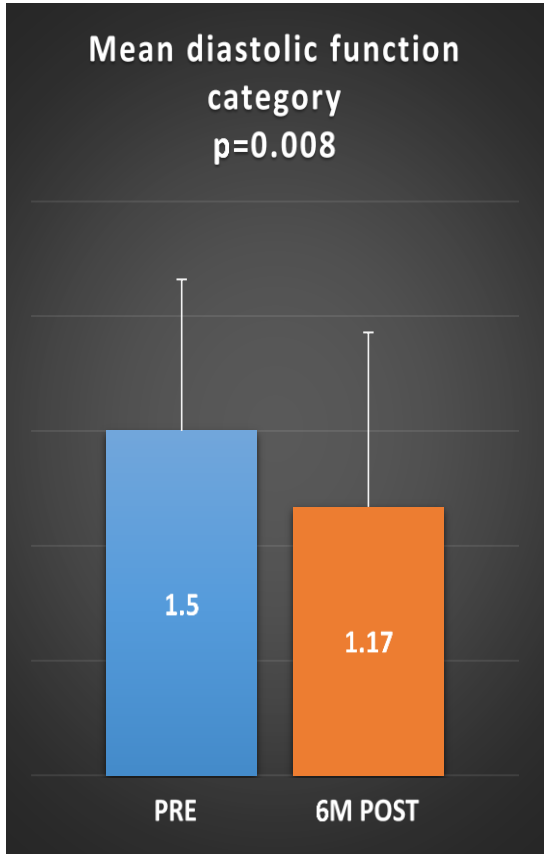
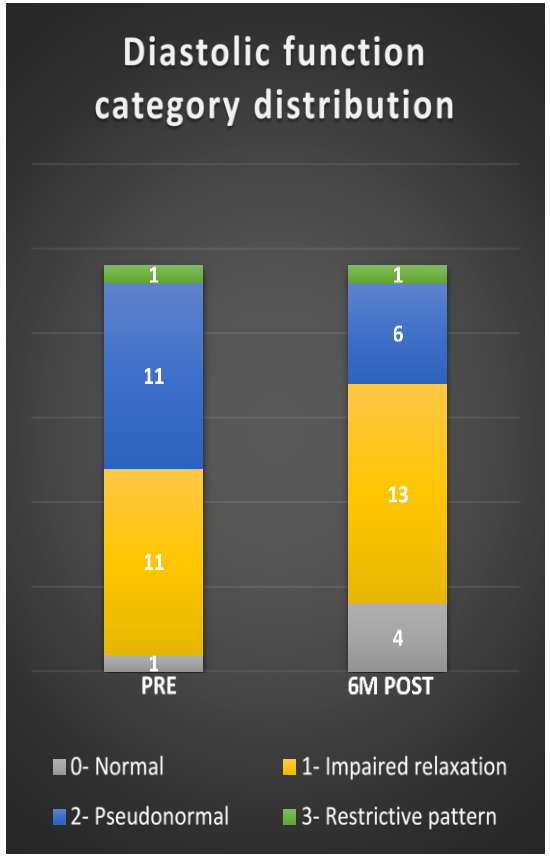
The impact of coronary sinus narrowing on LV diastolic function





CS narrowing improves diastolic function
in patients with myocardial ischemia and angina

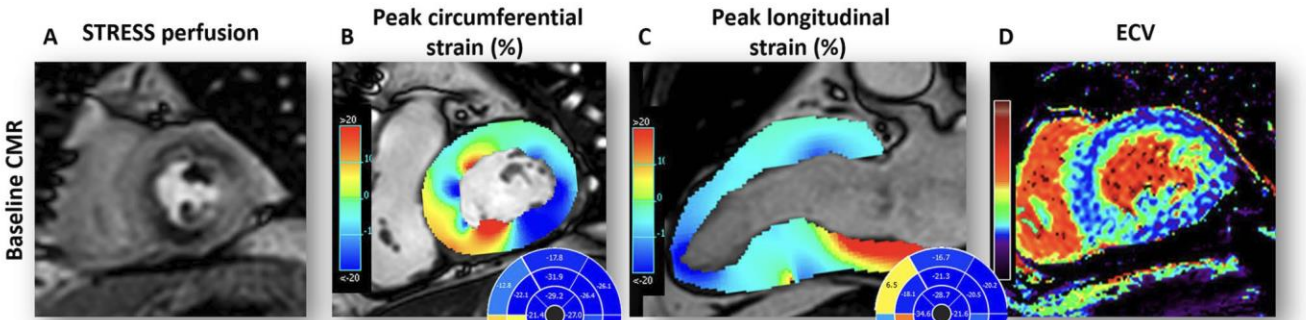
Szekely Y, Banai S: *Intern J Cardiol*. 2019 Sep 15;291:8-12

The International Journal of Cardiovascular Imaging
https://doi.org/10.1007/s10554-020-01964-9

ORIGINAL PAPER

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

Anna Palmisano[1,2] · Francesco Giannini[3,4] · Paola Rancoita[5] · Guglielmo Gallone[3,6] · Giulia Benedetti[1,7] · Luca Baldetti[3] · Georgios Tzanis[3] · Davide Vignale[1,2] · Caterina Monti[8] · Francesco Ponticelli[4] · Marco Ancona[3] · Matteo Montorfano[3] · Alessandro Del Maschio[1] · Francesco De Cobelli[1,2] · Antonio Colombo[4] · Antonio Esposito[1,2]



20 consecutive patients with refractory angina underwent multiparametric stress CMR before and 4m after Reducer implantation

Results:

- Reducer improved myocardial contractility (EF rose from 61 to 67%; p = 0.0079)
- Improves myocardial longitudinal and circumferential strain
- Reduced ischemic burden
- Improved intramural perfusion balance in segments with baseline ischemia

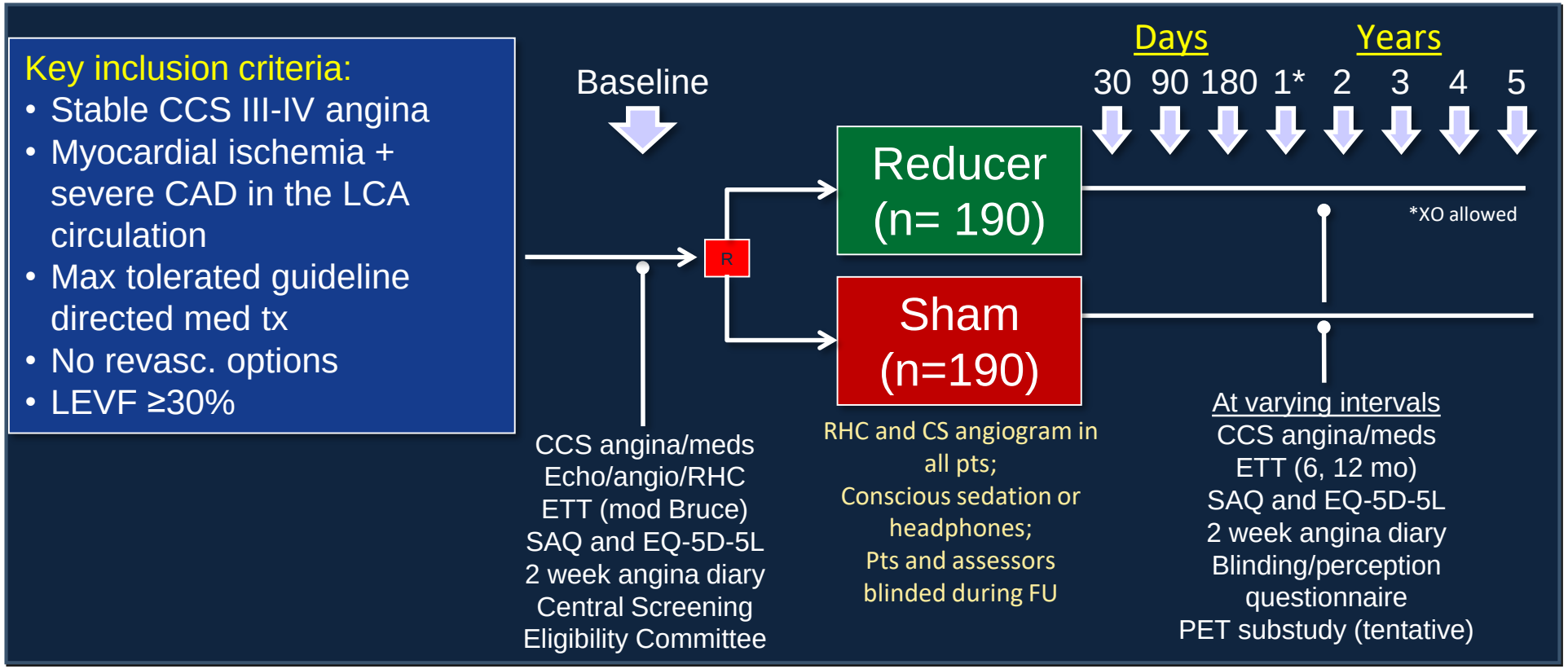
COSIRA II:

Efficacy of the COronary SInus Reducer in Patients with Refractory Angina II

2022-2024

Prospective, randomized, double-blind, sham-controlled trial
~380 patients, up to 50 centers in North America

PIs: Timothy D. Henry and Gregg W. Stone



The CS Reducer as a potential therapy for microvascular angina

The potential beneficial effect on microvascular coronary blood flow is currently being evaluated in several clinical trials:

- Tommaso Gori, University Medical Center Mainz, Germany
- Amir Lerman, Mayo Clinic, Rochester MN, USA
- Ranil De Silva, Royal Brompton, London, UK
- George J Vlachojannis, Peter Damman, UMC Utrecht, The Netherlands
- Dr Rasha Al-Lamee, Hammersmith Hospital, London UK
- Julien ADJEDJ, Saint Laurent du Var, France
- Maayan Konigstein, Tel Aviv Medical Center, Israel

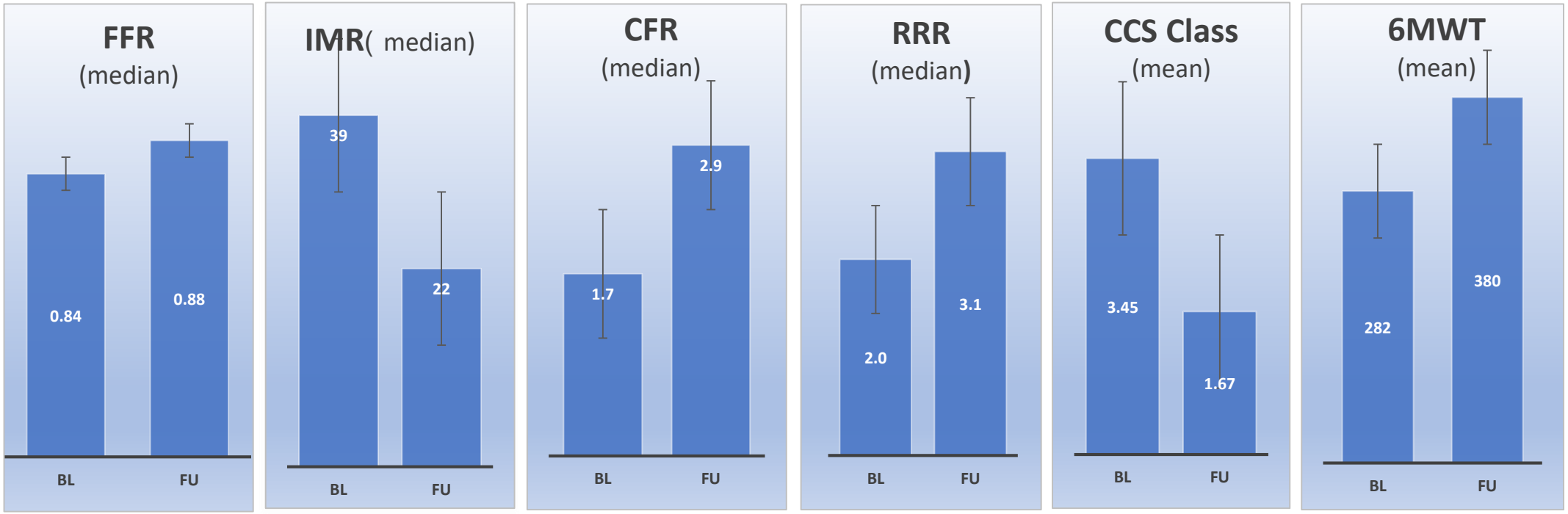
Patients with ANOCA and MVD treated with Reducer

Preliminary results from the TLV medical center prospective trial

n=11

Patients with ANOCA despite maximal medical therapy and documented MVD are treated with Reducer

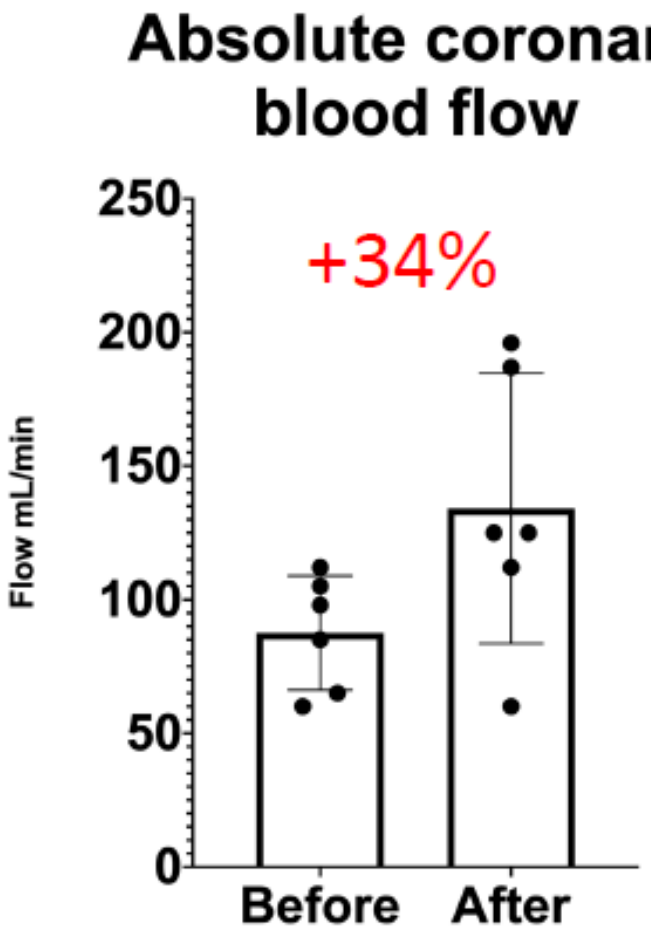
Invasive coronary physiology evaluation performed at baseline and 6M post Reducer implantation



Retour sur le mécanisme

Flux absolu par Thermodilution coronaire

n=6



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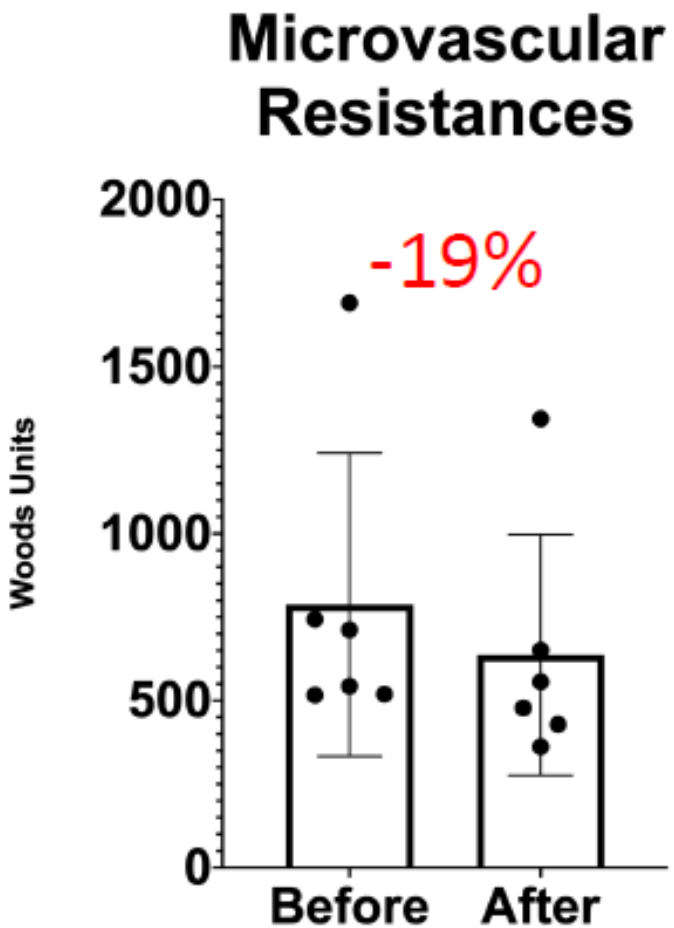

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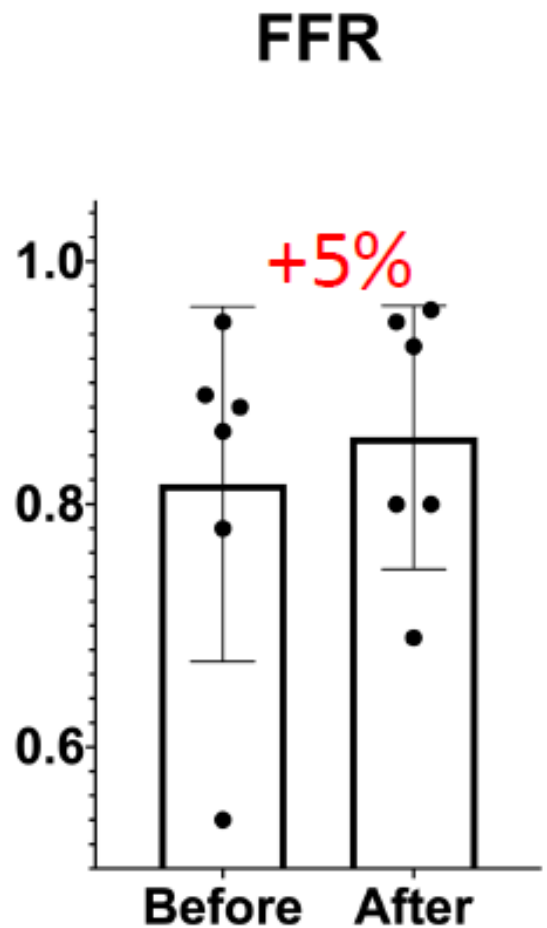

P=0.30

Conclusions

- The clinical efficacy of Reducer on reducing angina burden is apparent
- Reducer therapy is safe and effective in patients with obstructive CAD
- Preliminary data suggest that the Reducer might also be an effective therapy for coronary microvascular dysfunction (ANOCA/INOCA)

Thank You