When all fails, just reduce the symptoms & ischemia!

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Metropolitan General
EAPCI young ambassador

Disclosures

- *No conflicts of interest*

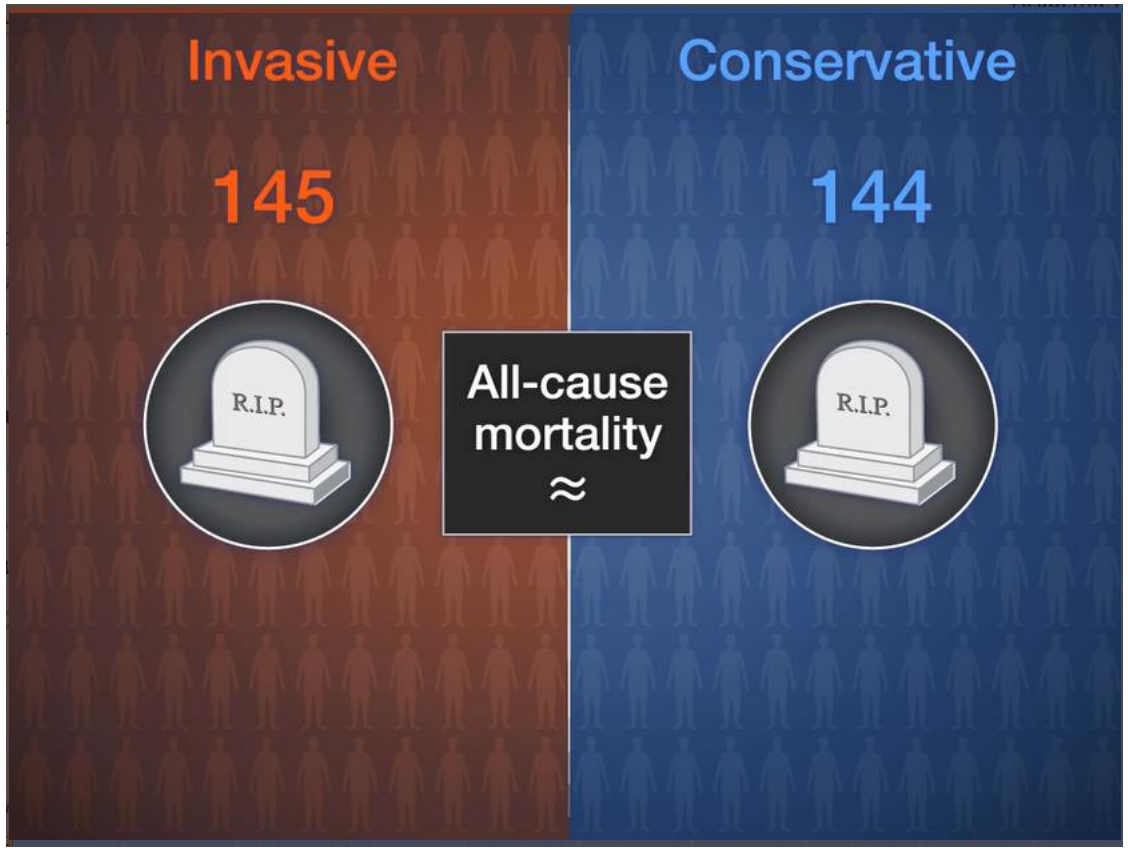
Why Do We Revascularize in Stable Ischemic Heart Disease?

- **To improve survival (???)**

Impact of Revascularization on Mortality in Contemporary SIHD Trials

- COURAGE: No difference
- BARI 2D: No difference
- FAME 2: No difference

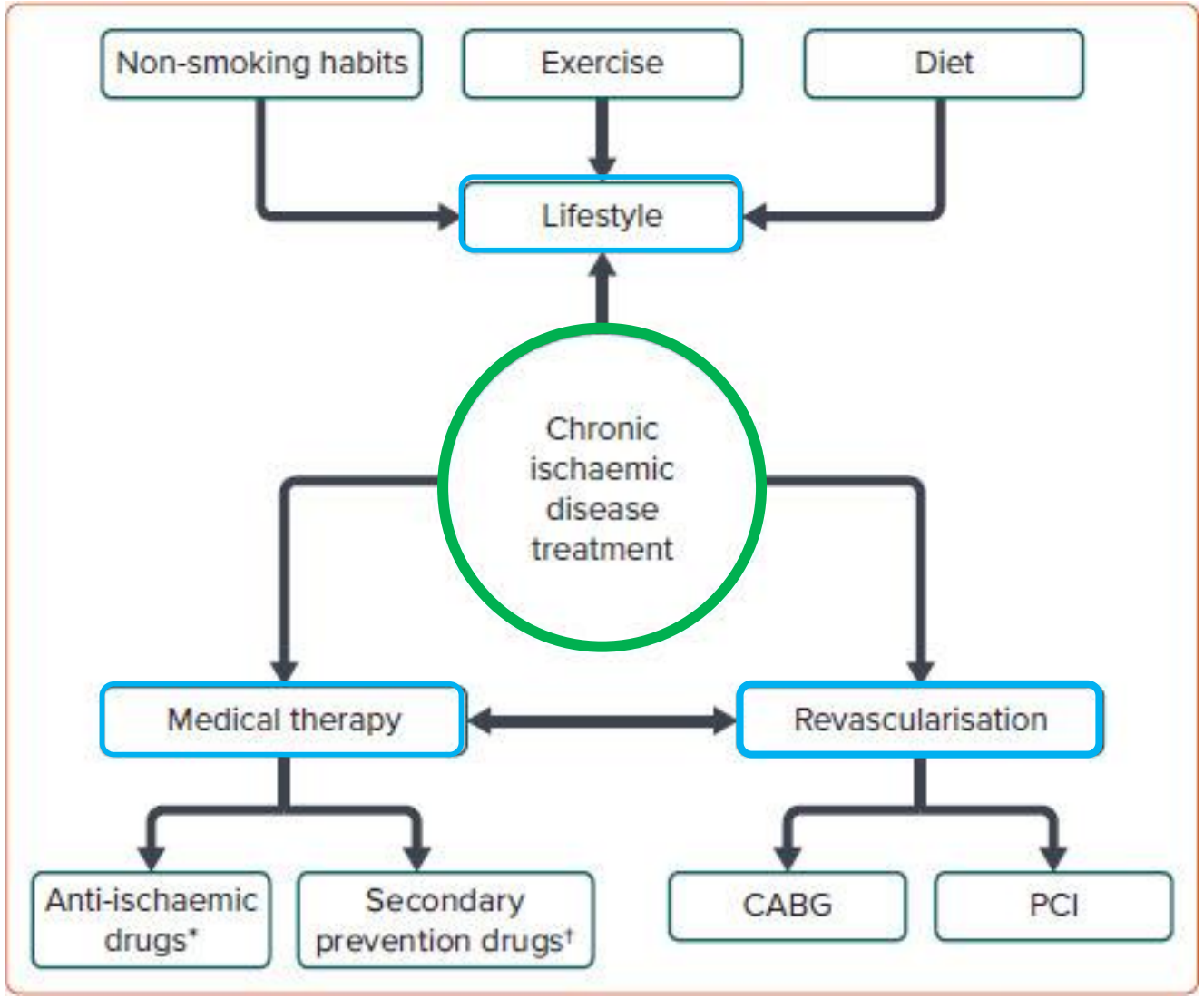
Ischemia TRIAL



* Pts with severe refractory angina & LM pts **excluded**

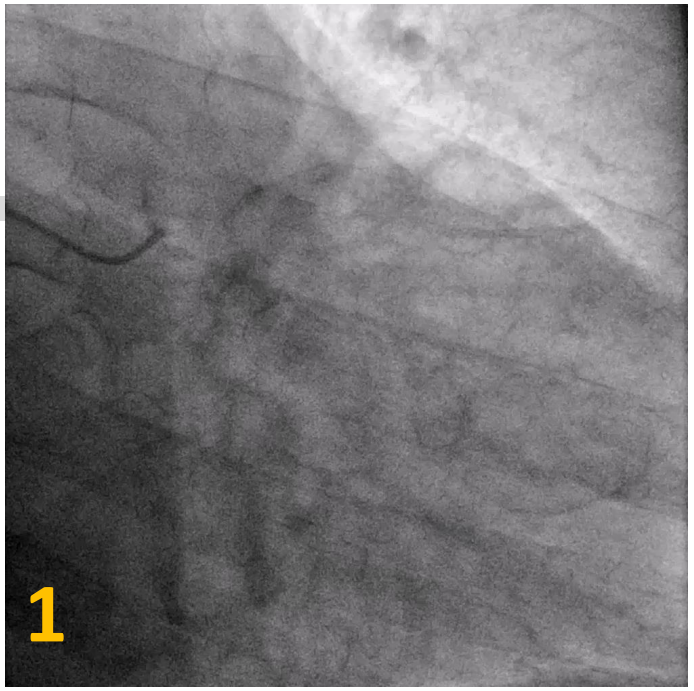
Why Do We Revascularize in Stable Ischemic Heart Disease?

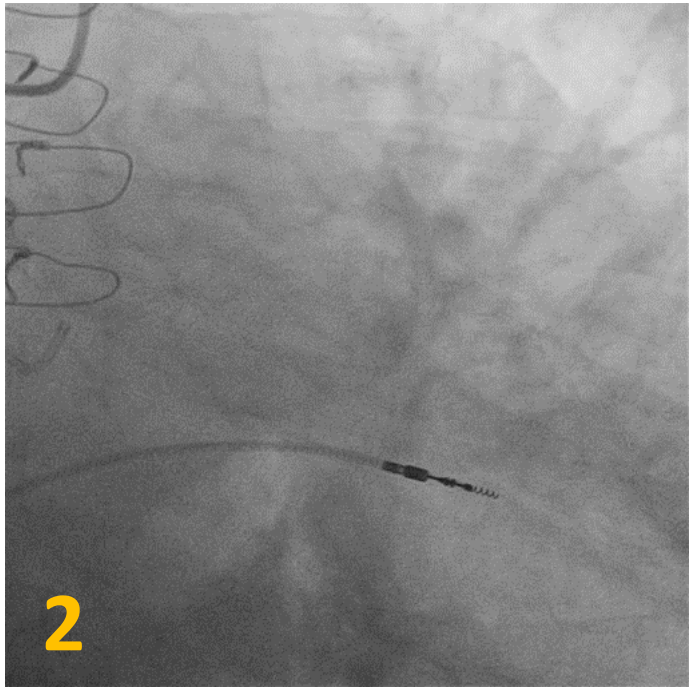
- Only **To improve symptoms (?)**

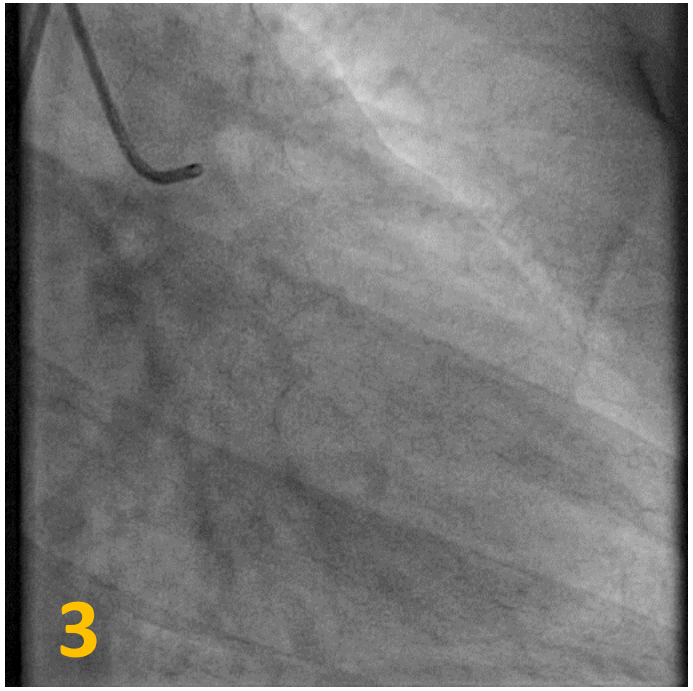


STABLE ANGINA

clinical cases



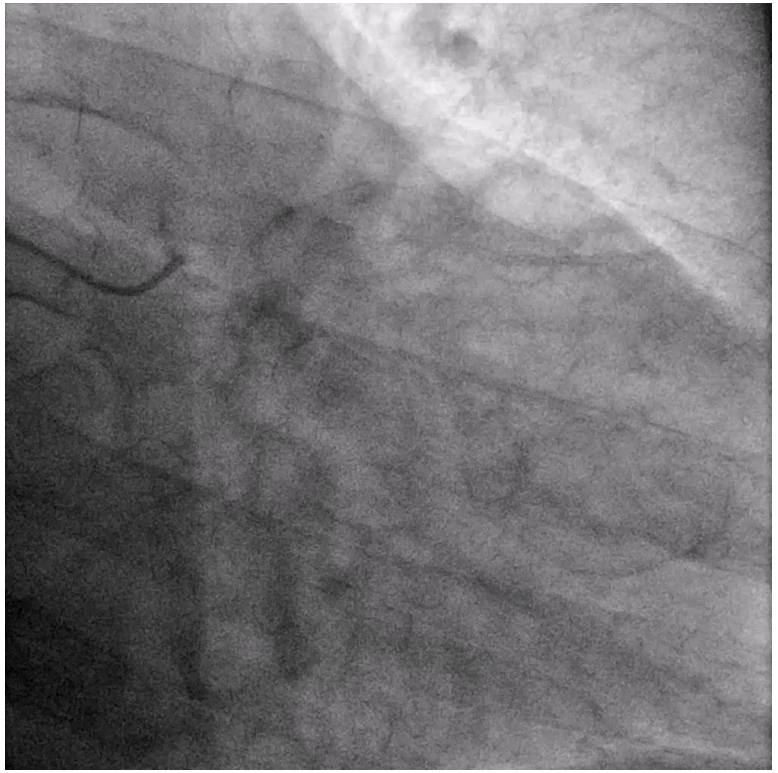


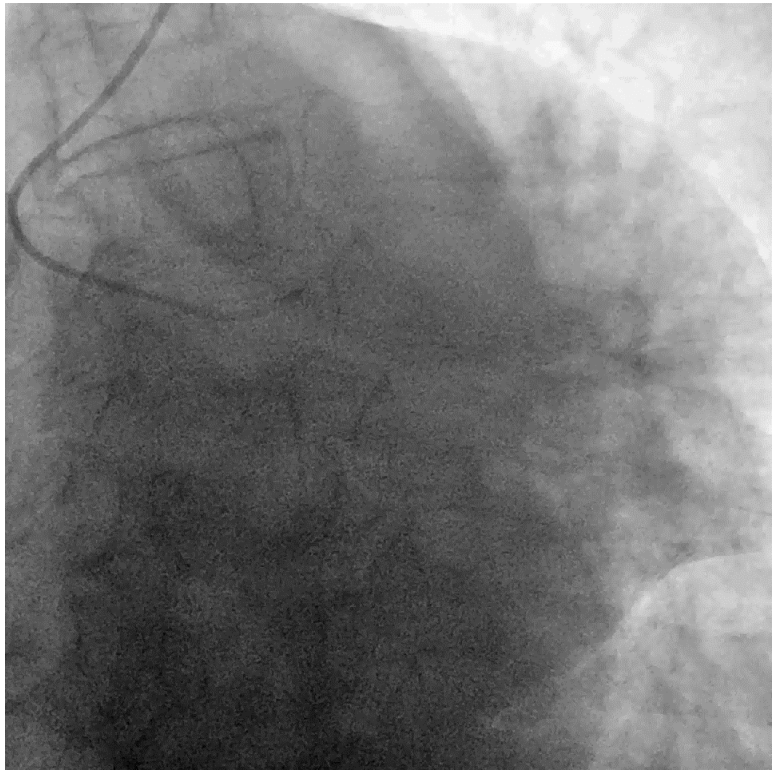


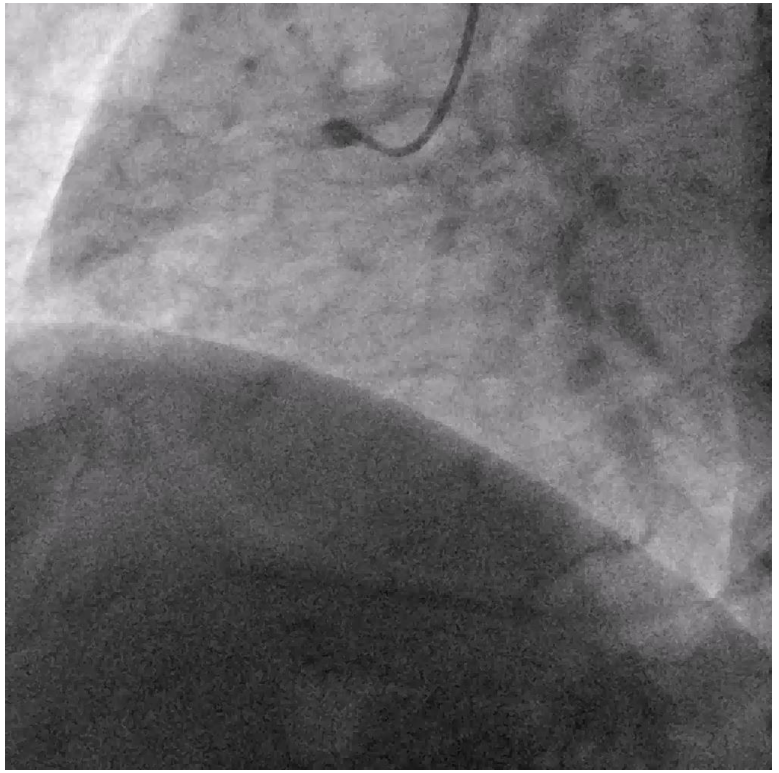
Refractory angina cases
(CCS angina class>=III)

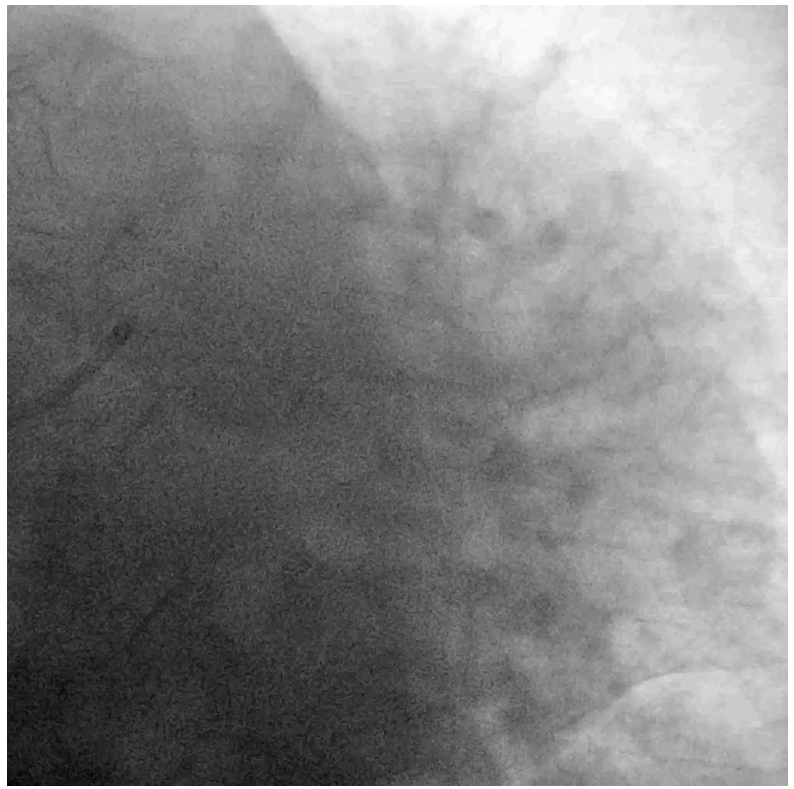
1st Case

- 77-year ♂ EF: 45 %
- Chronic angina: CCS III *(OMT: b-blocker, Ca antag., ranolazine)*
- SPECT: **scar (no viability inferior wall)**

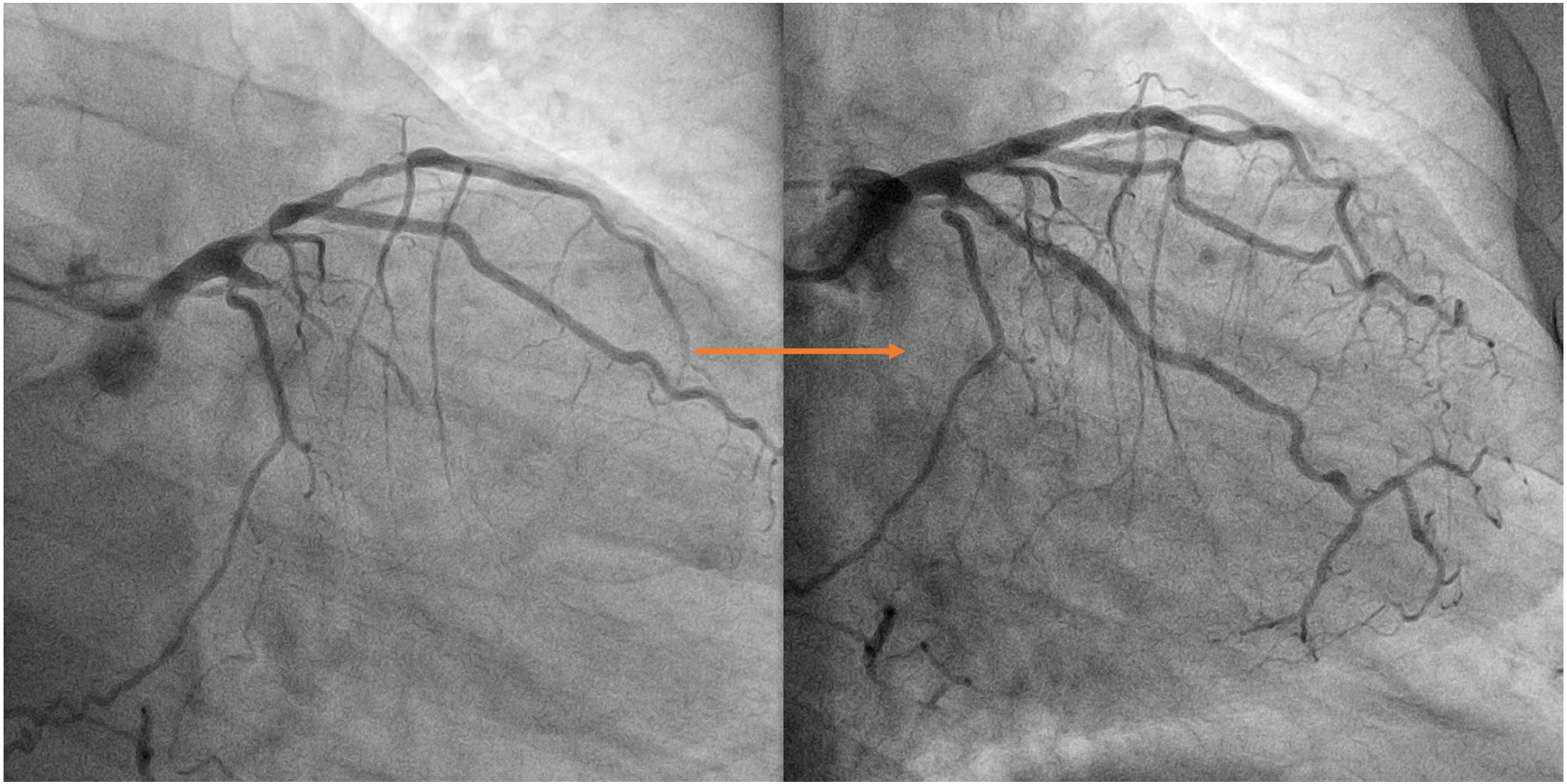








- EF: 45 % →55-60%
- Angina free: CCS III → I
- Stop Ranolazine



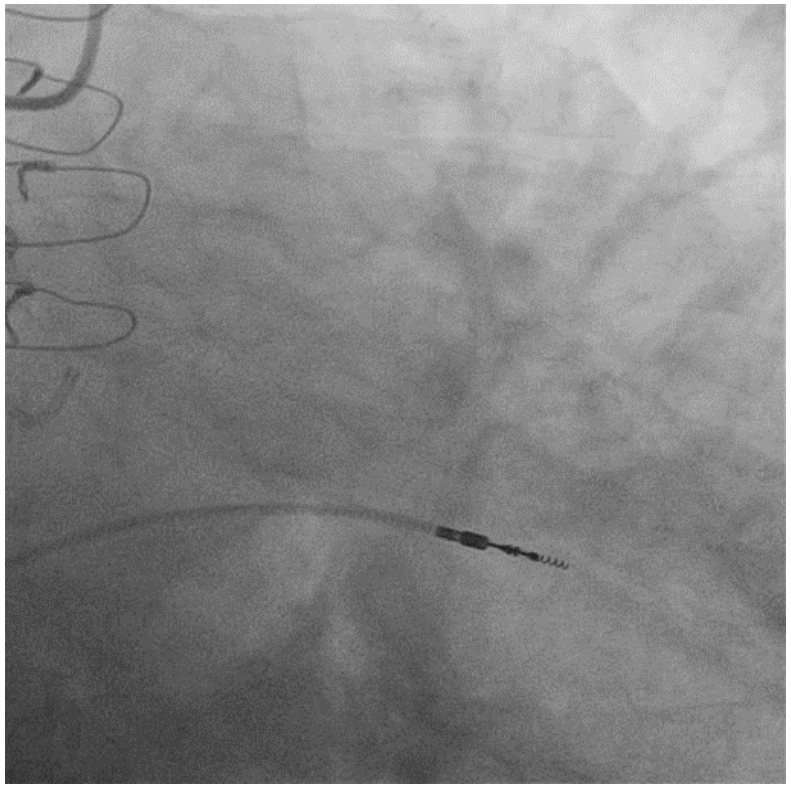
2nd Case – Refractory angina no option pt

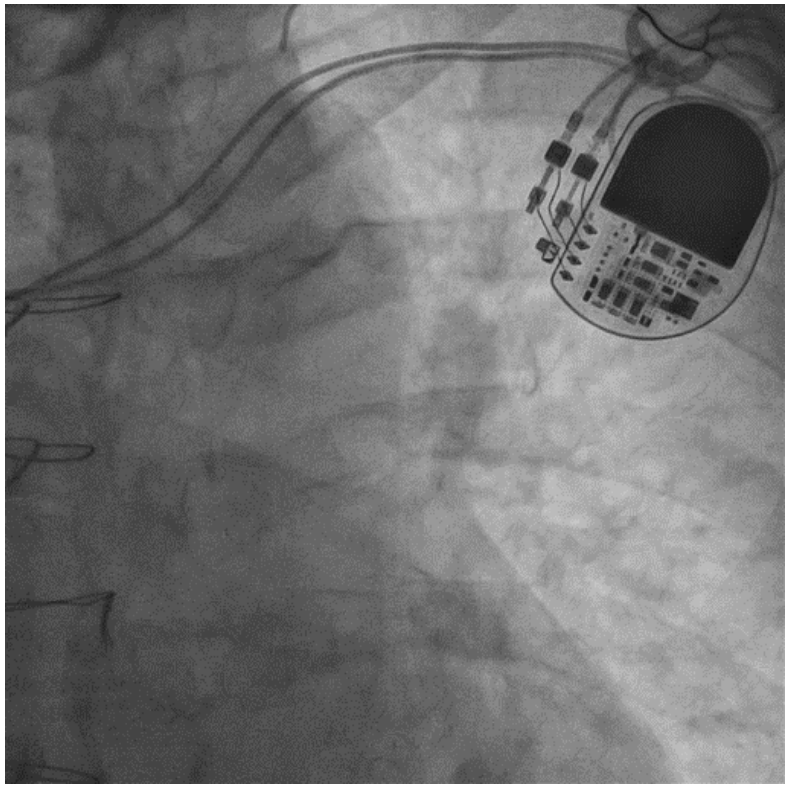
- 77-year ♂
- ΣN: CABG (1998)→ SVG closed

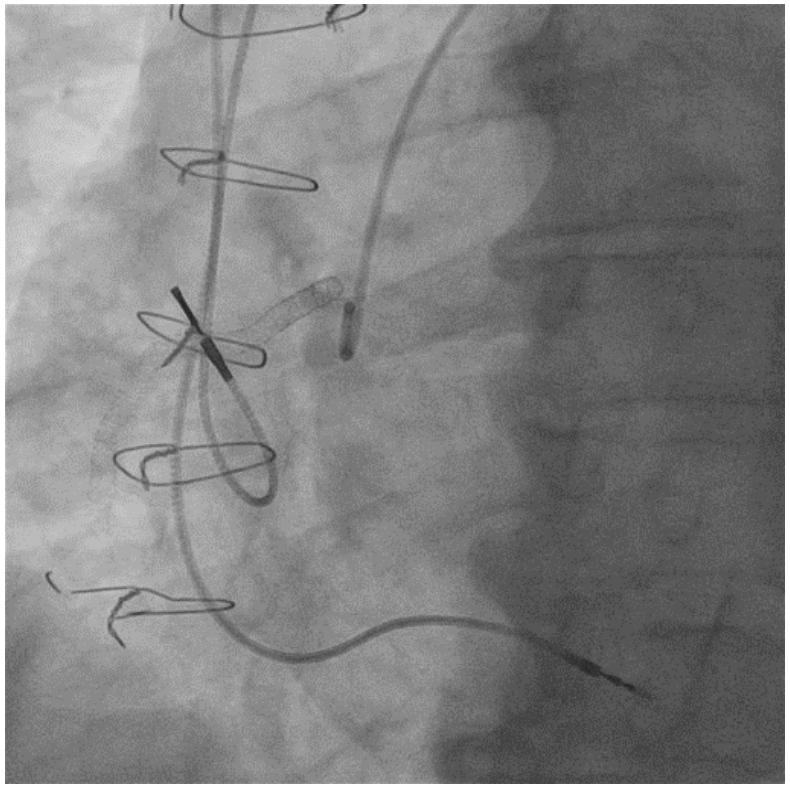
  *__5 PCI__ in RCA (multiple restenosis)
- DM, CKD (Cr 1,8), HP, EF: 45 %
- **Refractory angina** CCS III-IV *(OMT: bisoprolol, amlodipin, ranolazin, nitrates)*

- SPECT: large **reversible ischemia infero-lateral wall** *CATH:* - *LIMA → LAD*

  *- **CTO**: prox. Ram, LCX (SVGs closed)*



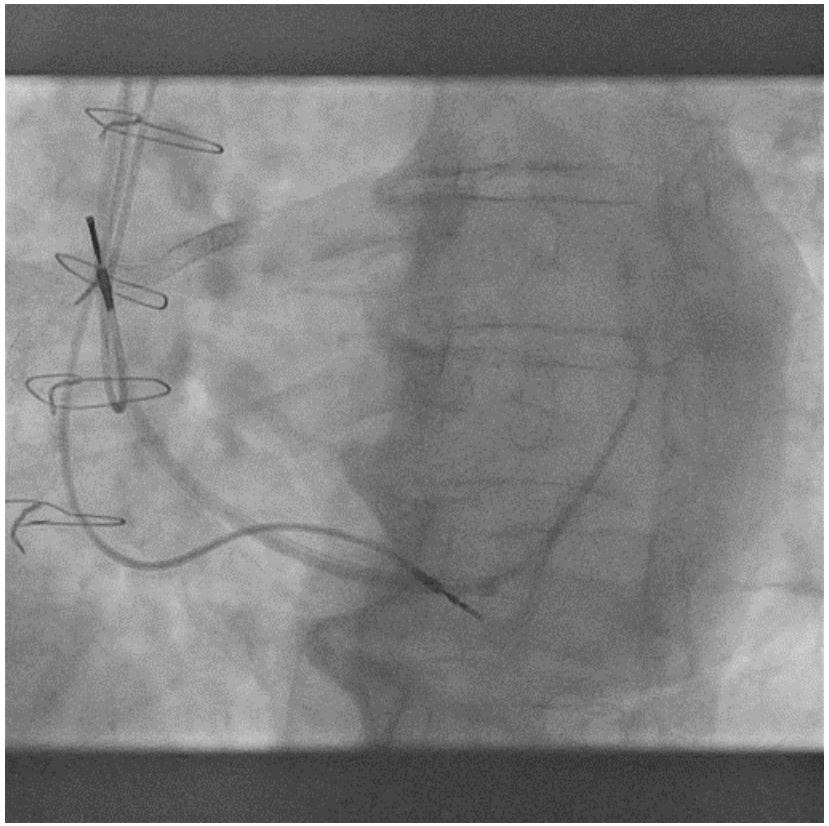


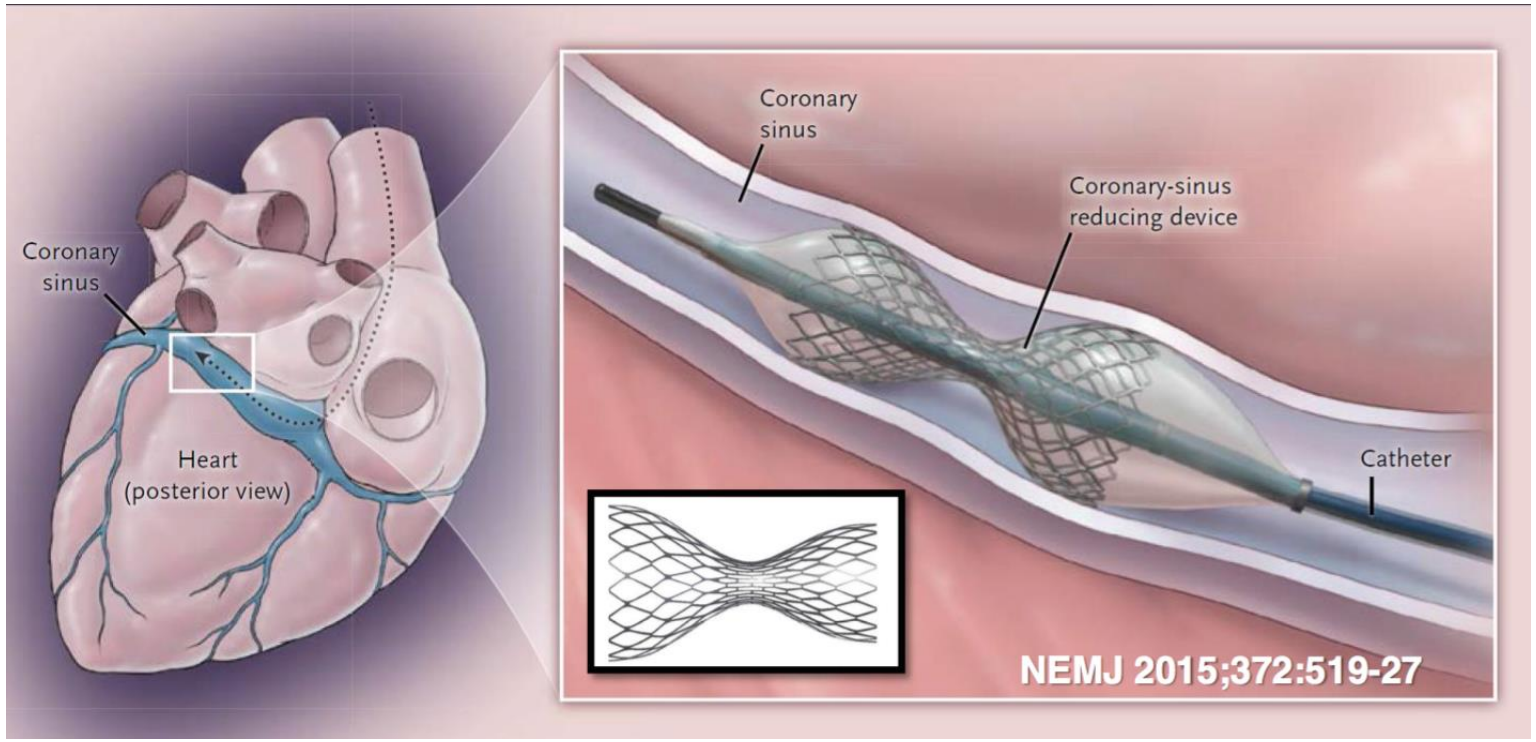


Problems

1. Targets
2. CKD (contrast for CTO)
3. 5 previous restenosis with PCI

Coronary Sinus Reducer





Technical aspects in Coronary Sinus Reducer implantation

Giannini F. - Tzanis G, Ponticelli F, Baldetti L, Demir O, Mitomo S, Gallone G, Banai S, Colombo A.

EuroIntervention. 2019. pii: EIJ-D-18-01180

3rd Case

CS REDUCER

for Symptomatic Coronary Microvascular Dysfunction ???

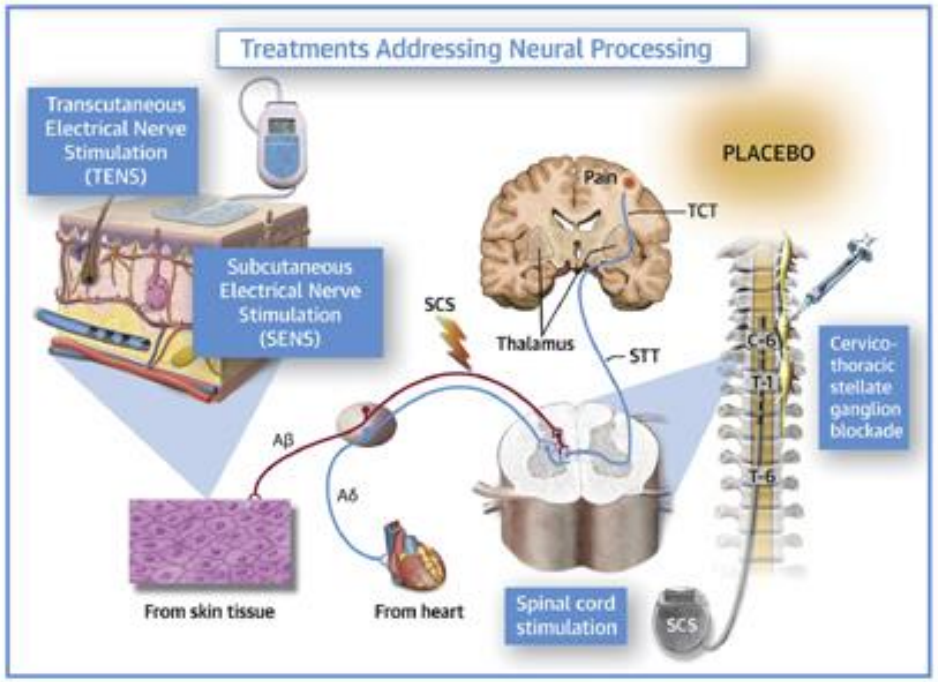
ANOCA

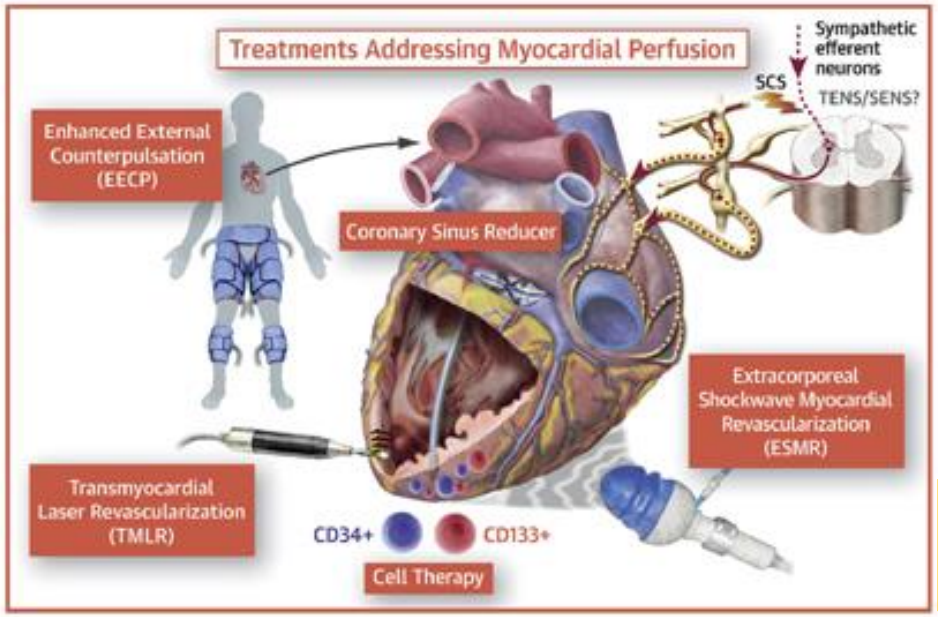
3rd Case- INOCA

- 42-year ♂
- ΣΝ: PCI σε LCx
- **Refractory angina** :

CCSIII

CENTRAL ILLUSTRATION: New Therapeutic Nonpharmacological Technologies in Refractory Angina





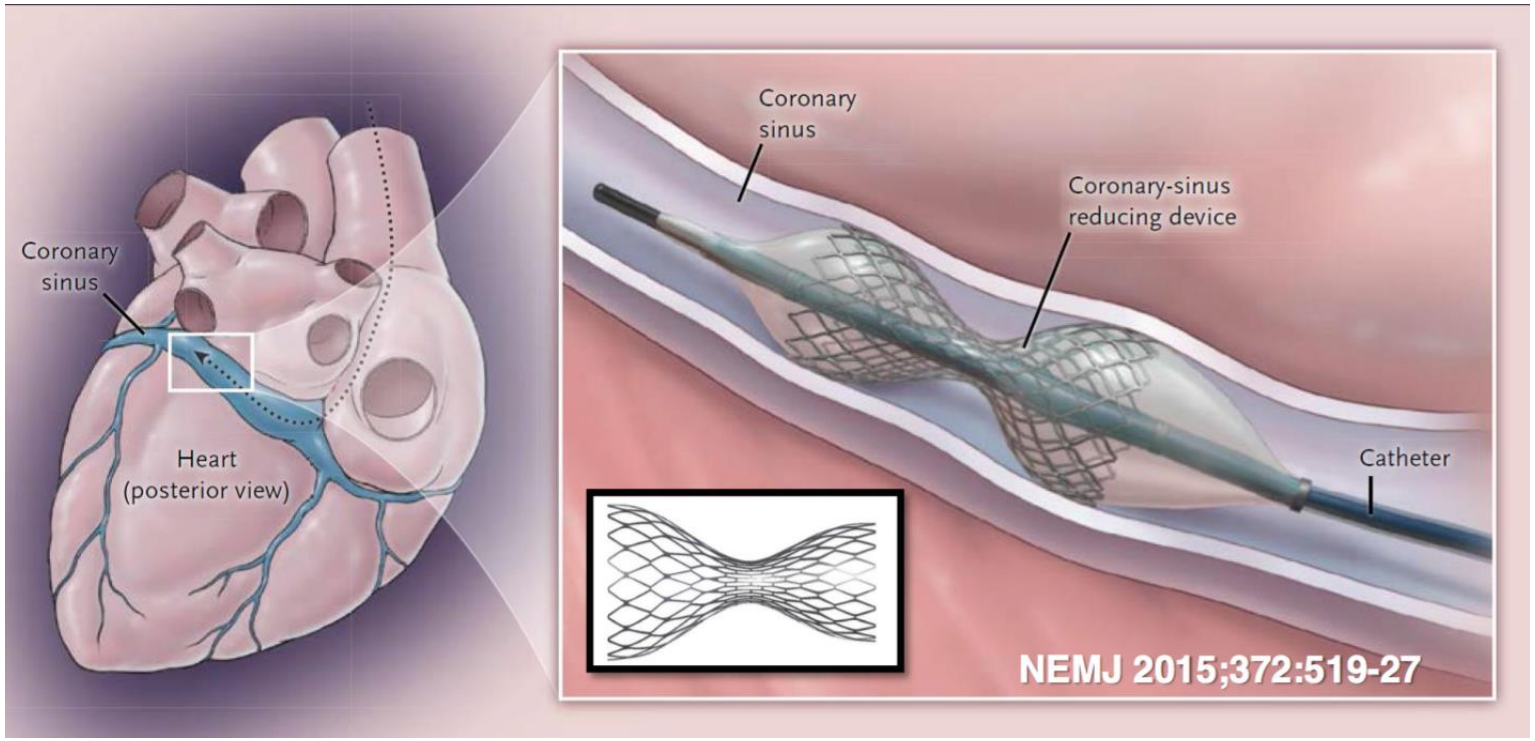
Device for Refractory angina

- Refractory angina may be prevalent in **5**%-**10**% of stable CAD patients.
- **Prevalence increases**→: *aging* & *life expectancy* of ischemia heart disease

- These "no-option" patients experience severe angina despite OMT

*G. Gallone, L. Baldetti, **G. Tzanis**, A. Colombo, T.Henry, F. Giannini. **JACC Int** 2020;13(1)*

Coronary Sinus Reducer

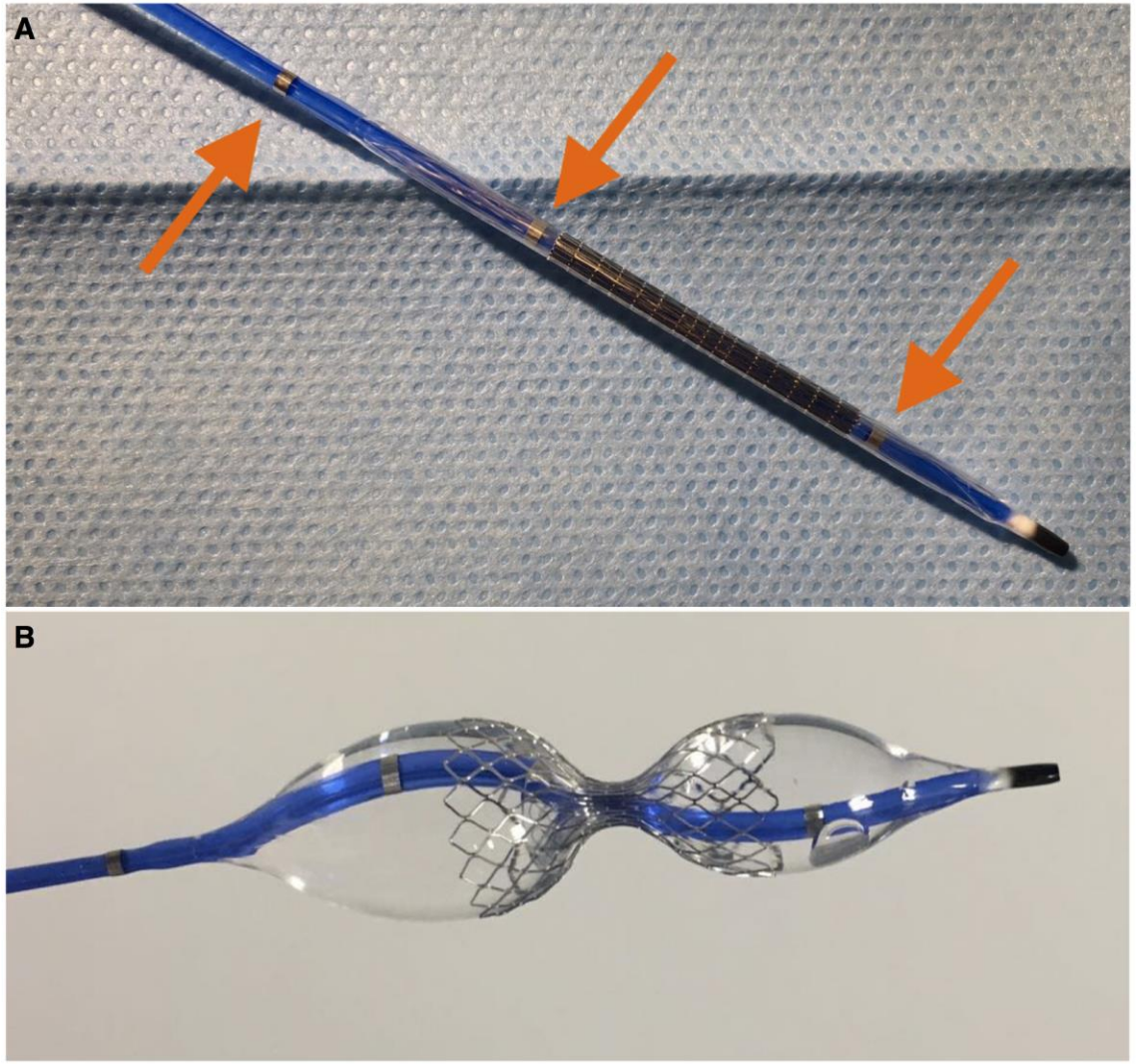


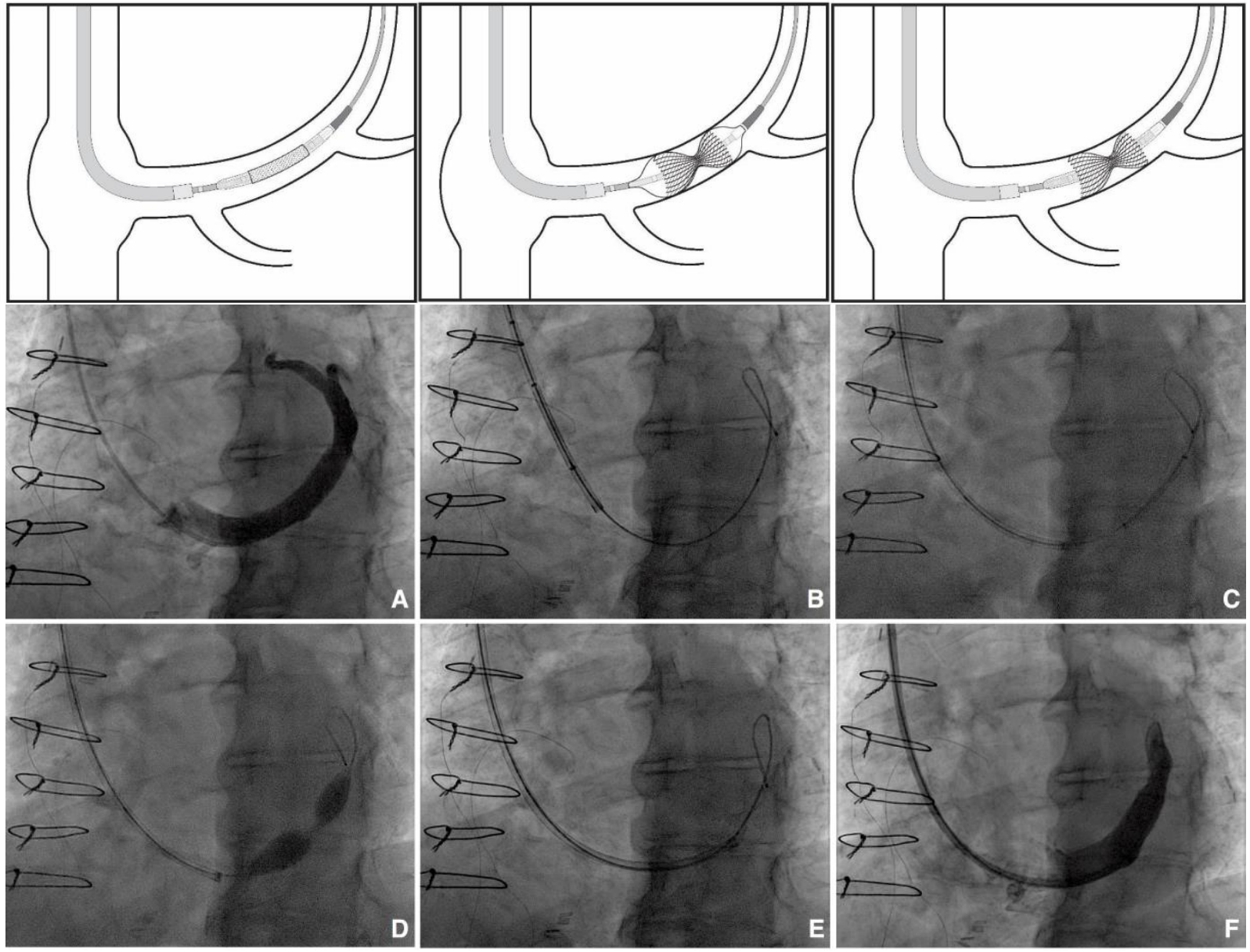
- ✓ The device is implanted in the coronary sinus (CS)
- ✓ Creates narrowing → modulate flow → increase CS pressure
- ✓ CS pressure elevation increases perfusion → providing relief of ischemia & angina

Coronary Sinus Reducer

A stainless steel
balloon-expandable device

Expansion:
Hour-glass shaped balloon





Technical aspects in Coronary Sinus Reducer implantation

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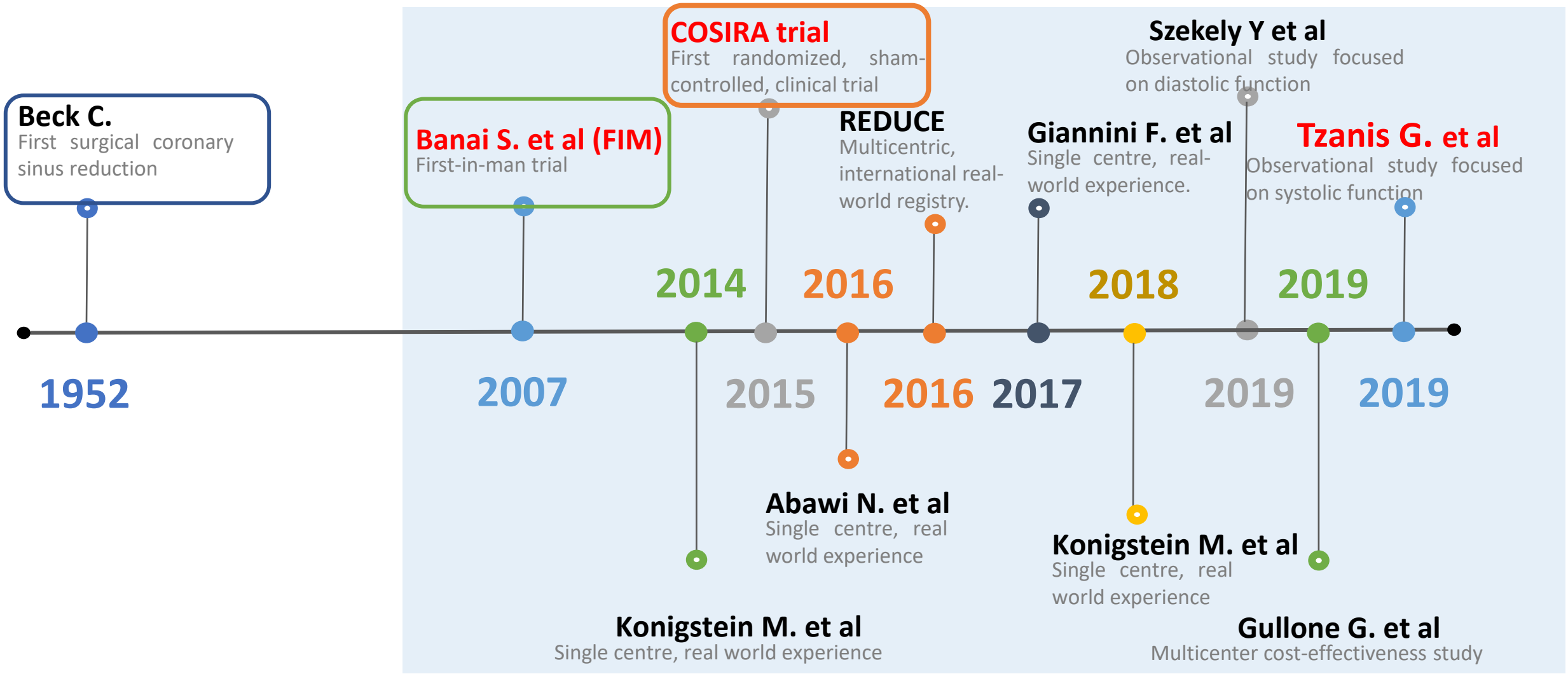
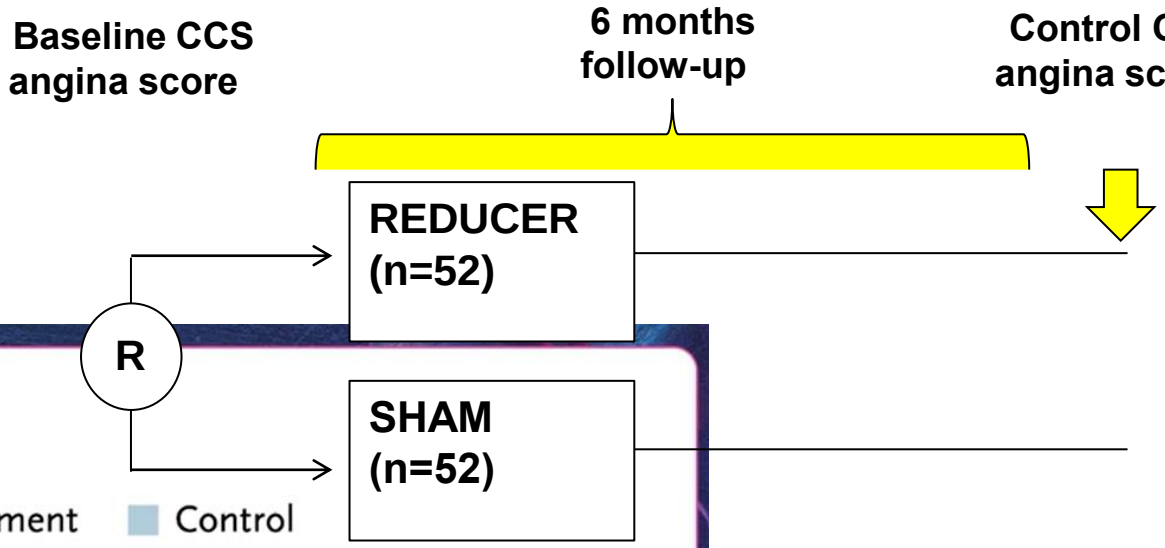
EuroIntervention. 2019. pii: EIJ-D-18-01180

CLINICAL INDICATIONS (ESTABLISHED)

refractory angina

REDUCER – CS Reducer Timeline





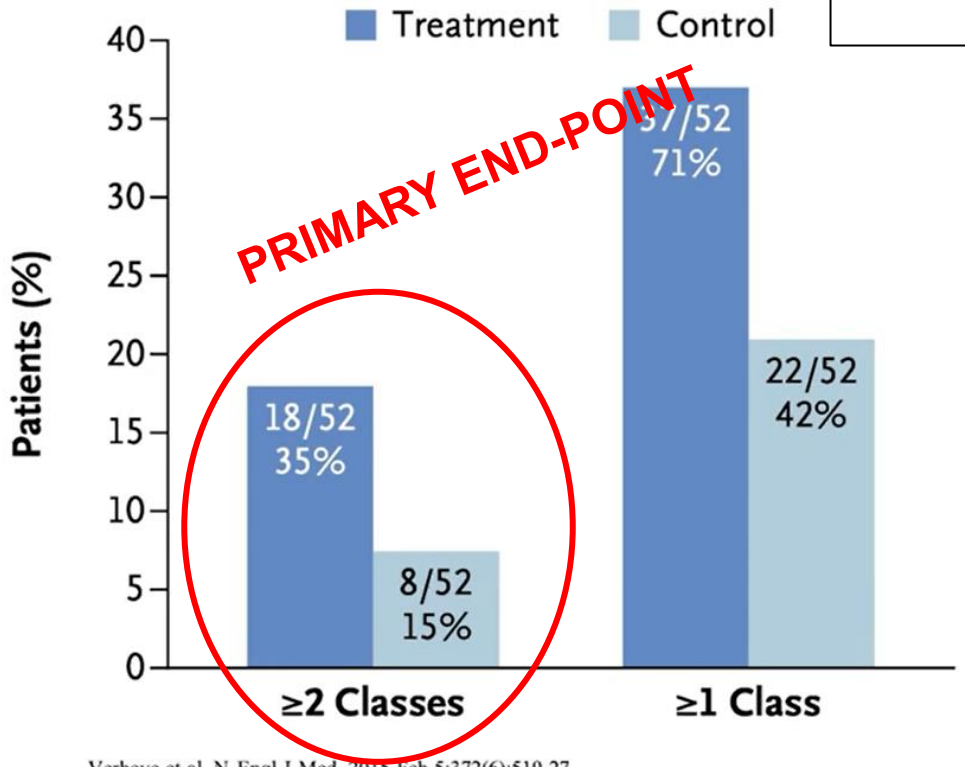
The COSIRA trial

Primary endpoint improvement in ≥2 Canadian Cardiovascular Society classes

CSR group 18/52 (35%)

Placebo group 8/52 (15%)

p=0.02



Verheye et al. N Engl J Med. 2015 Feb 5;372(6):519-27

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)

Recommendations for treatment options for refractory angina

Recommendations	Class[a]	Level[b]
Enhanced external counterpulsation may be considered for symptom relief in patients with debilitating angina refractory to optimal medical and revascularization strategies.[524]	IIb	B
A reducer device for coronary sinus constriction may be considered to ameliorate symptoms of debilitating angina refractory to optimal medical and revascularization strategies.[525]	IIb	B
Spinal cord stimulation may be considered to ameliorate symptoms and quality of life in patients with debilitating angina refractory to optimal medical and revascularization strategies.[526]	IIb	B
Transmyocardial revascularization is not recommended in patients with debilitating angina refractory to optimal medical and revascularization strategies.[529]	III	A

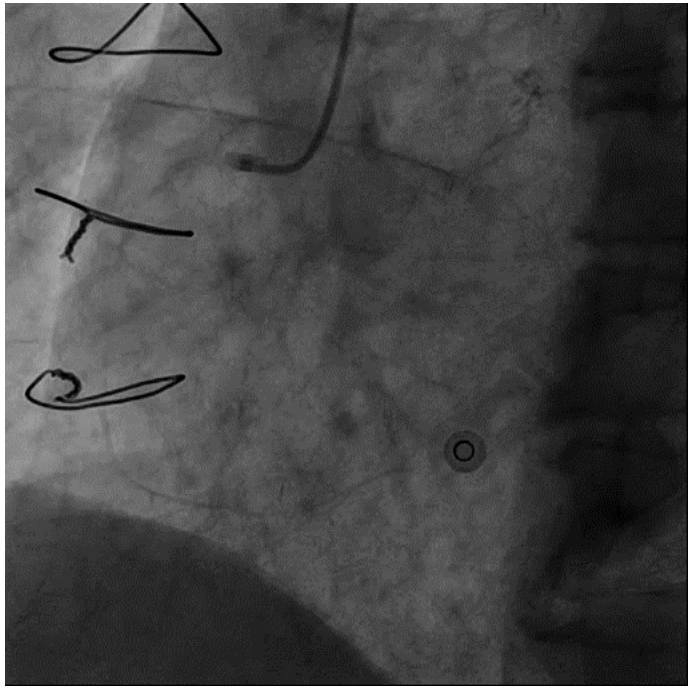
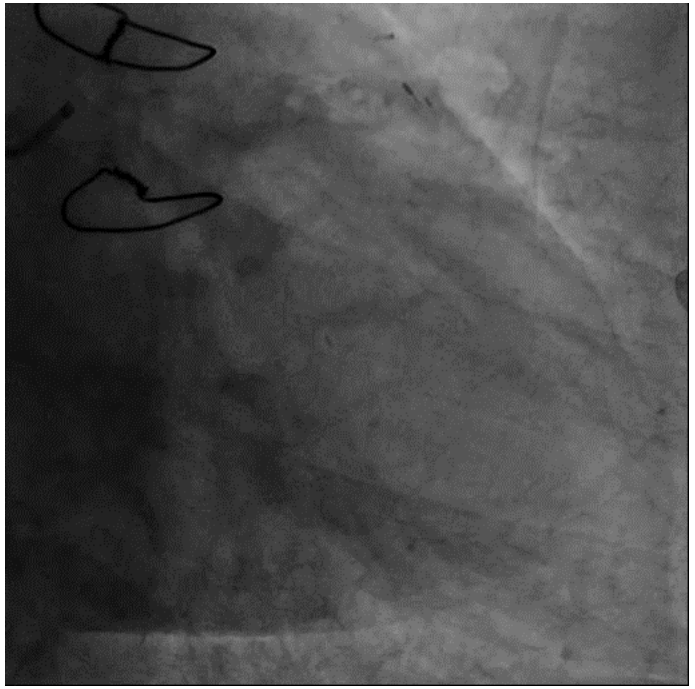
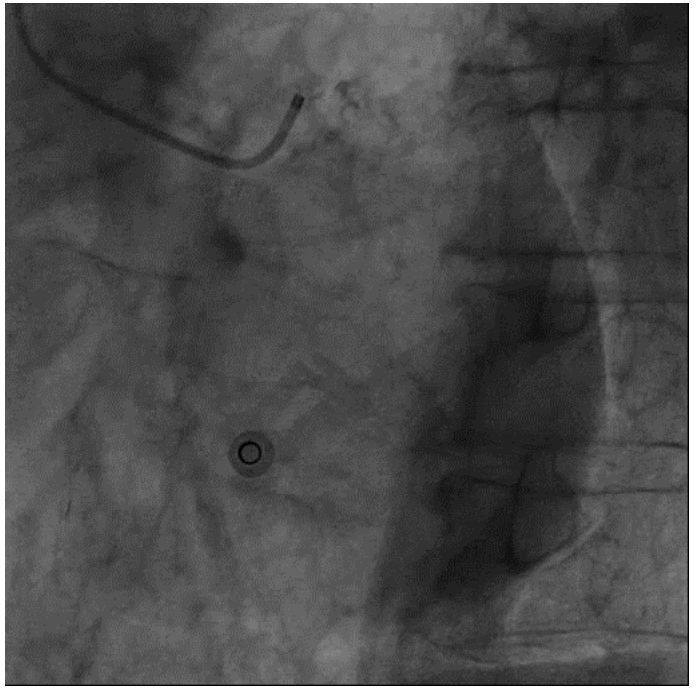
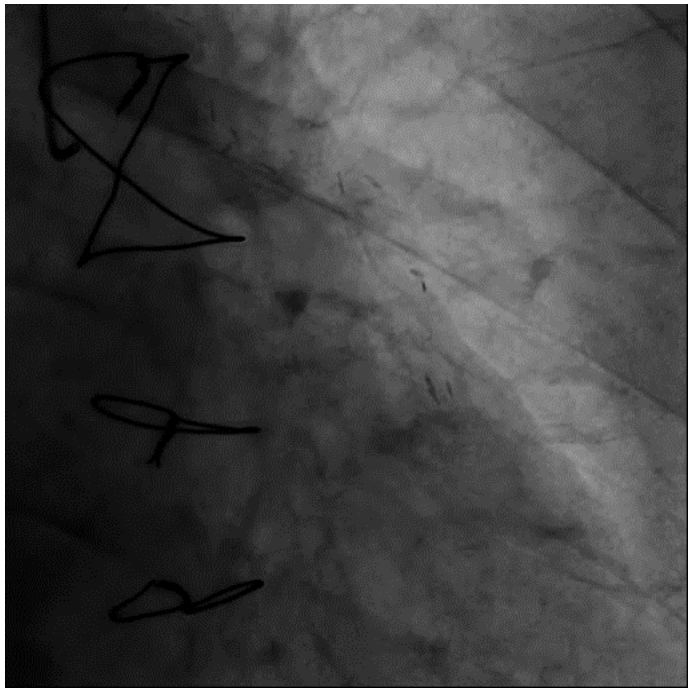
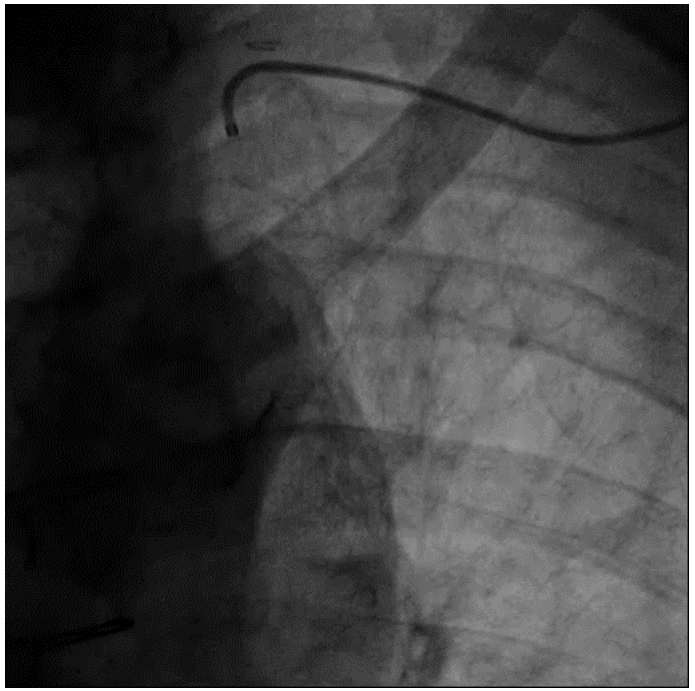
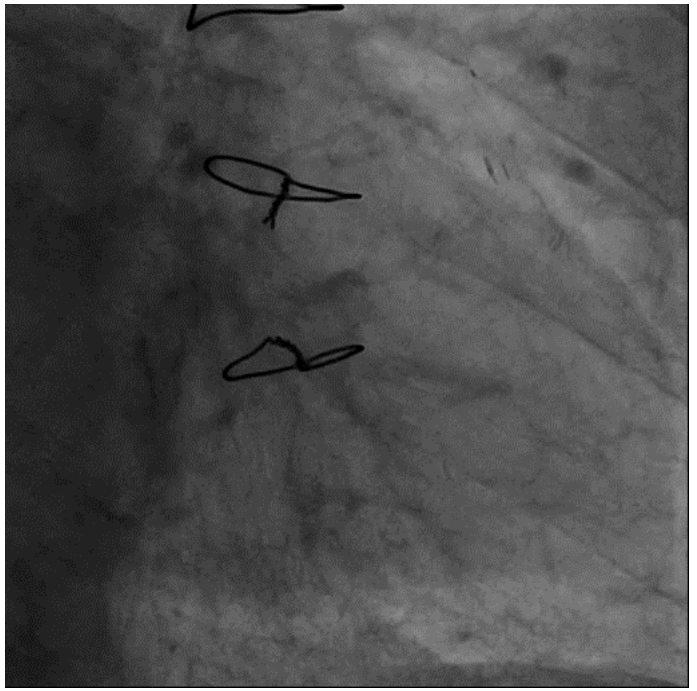
CS REDUCER

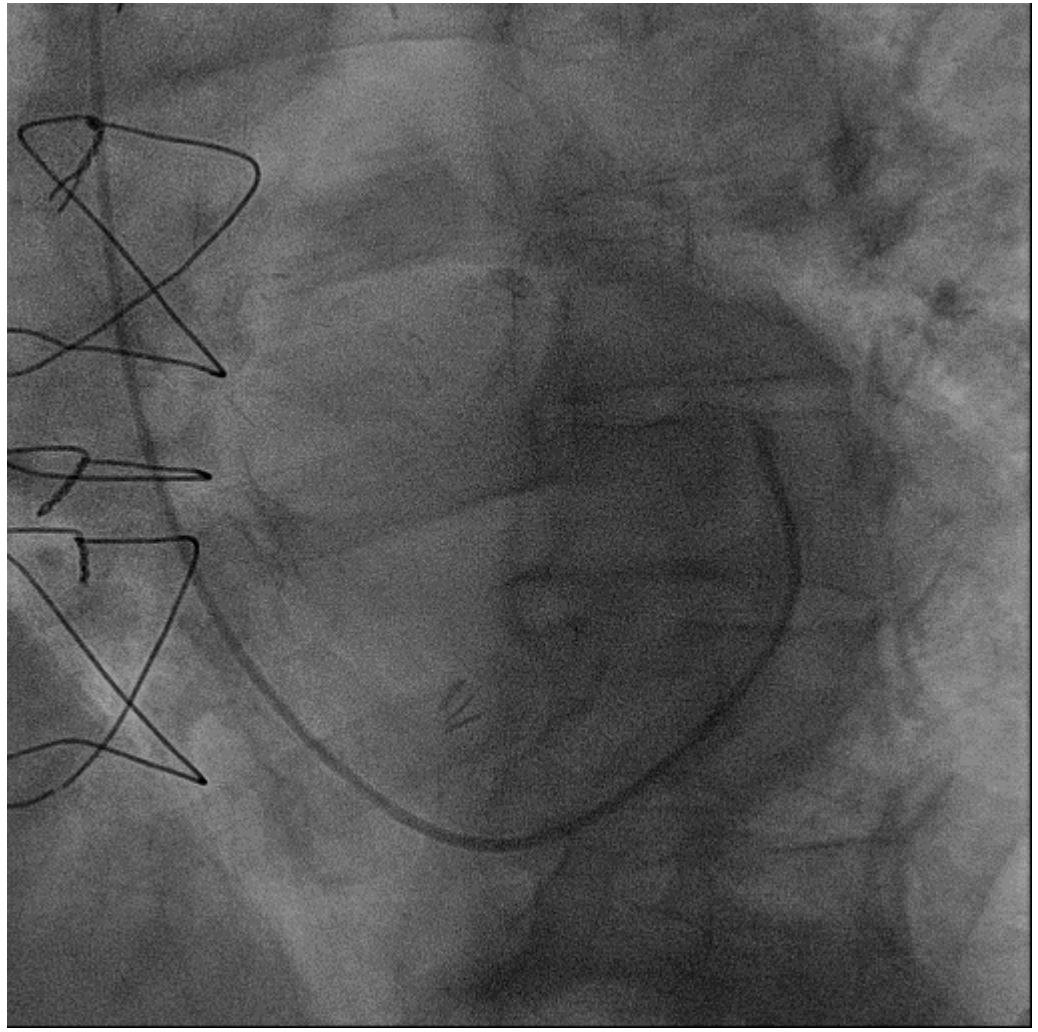
apart from symptoms →

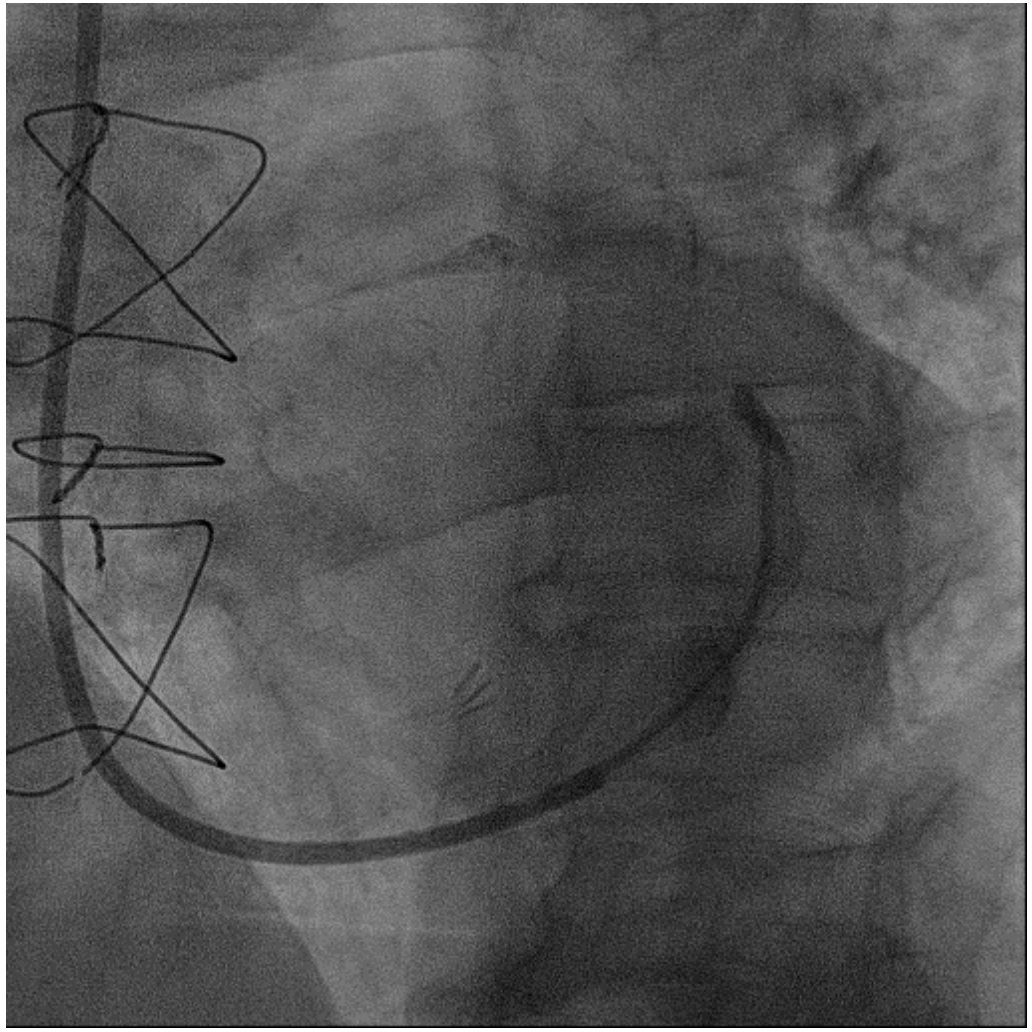
Ischemia

CSR & Ischemia - case report

- 82-year ♂
- CAD: Prior CABG
- Refractory Angina: CCS class III *despite OMT*
- Chronic heart failure (NYHA class II) – EF: 43 %
- *CTO: prox RCA, OM1*

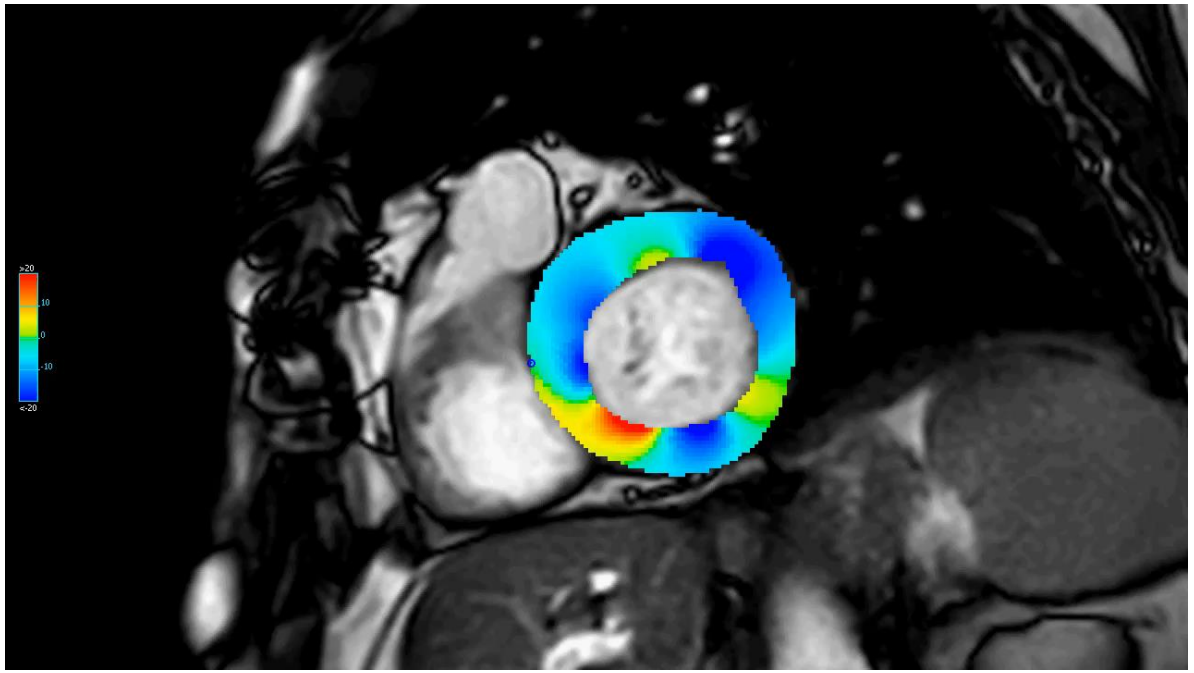







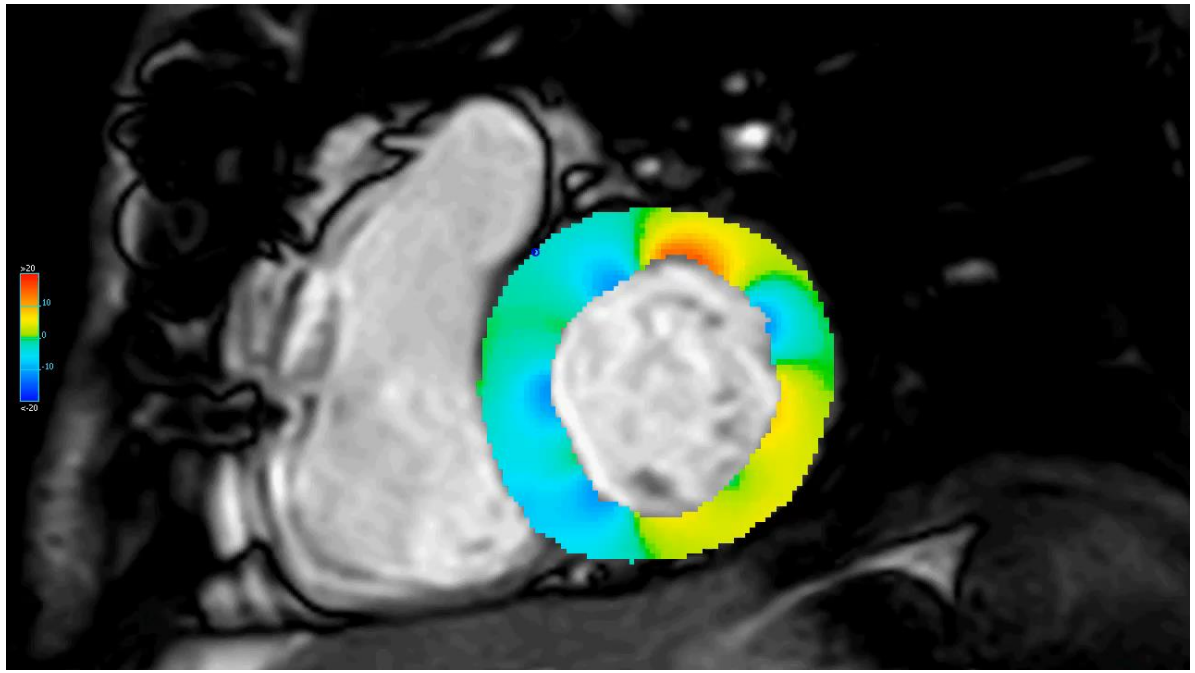




Angina improvement : CCS III → CCS I

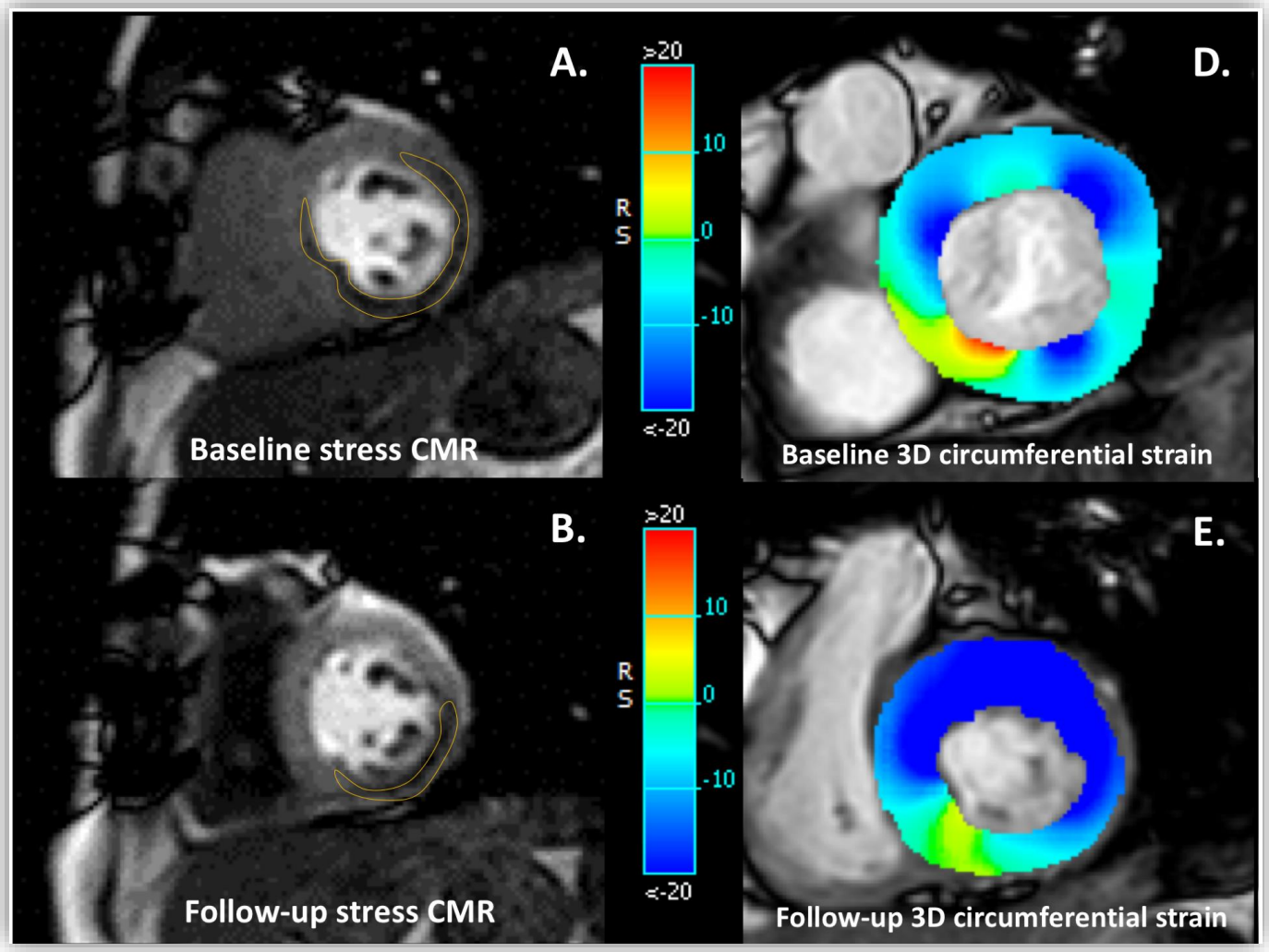
CMR - color coded strain maps





Baseline

4-months after Reducer Implantation

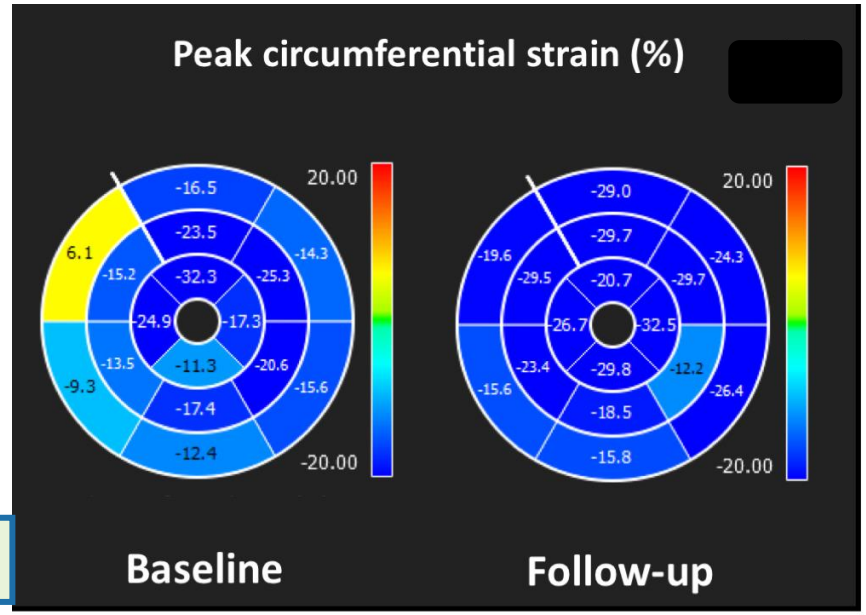


Baseline; (*CCS III – NYHA 2*)

- **MPRI**: 1.03
- **EF:** 43 %

4-months FU; (*No Angina – NYHA 1*)

- improvement in **size** of the inducible perfusion defect
- **MPRI**: 1.31 **EF:** 66 %



Circumferential systolic strain reconstructions of the LV

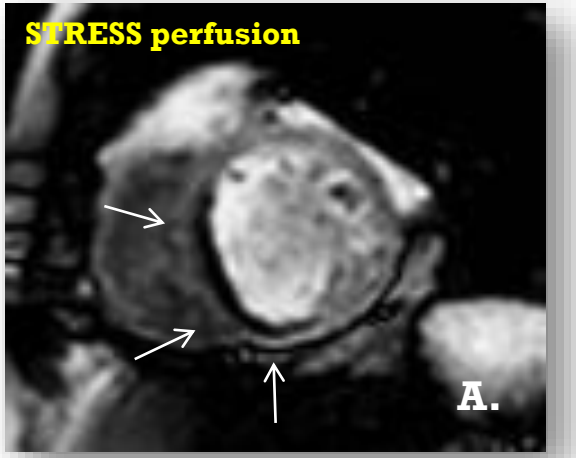
Longitudinal: Base -**14.9**% → 4MFU -**21.6**%

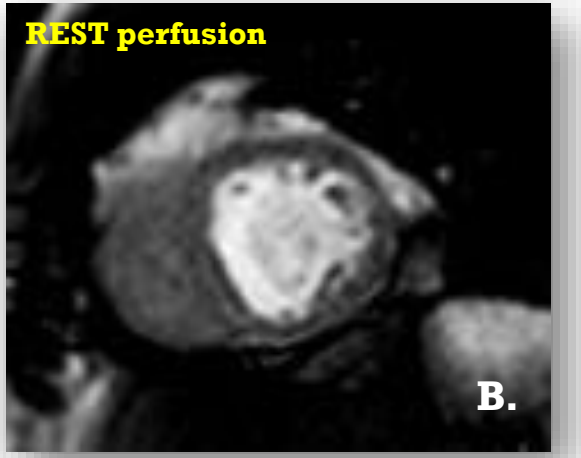
Circumferential: Base -**16.0**%→ 4mfu -**24.4**%

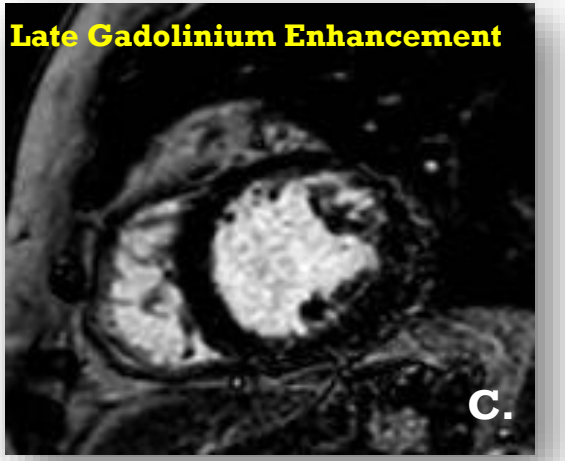
*Gallone,..,**Tzanis G**, Colombo A, Giannini F. **Can J Cardiol**. 2020;36(4):589*

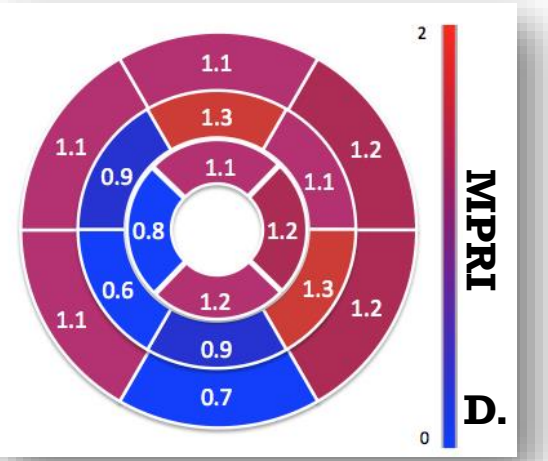
An example

Baseline CMR

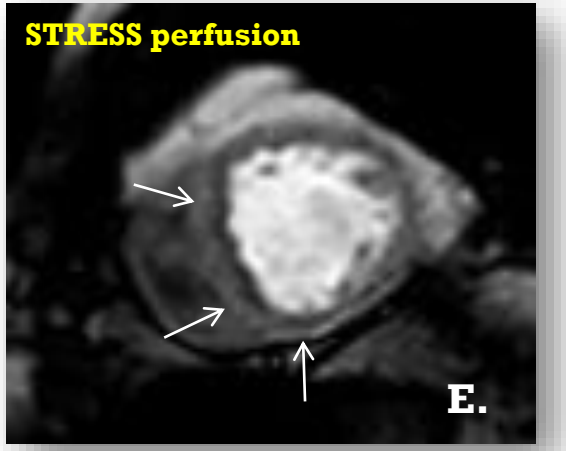


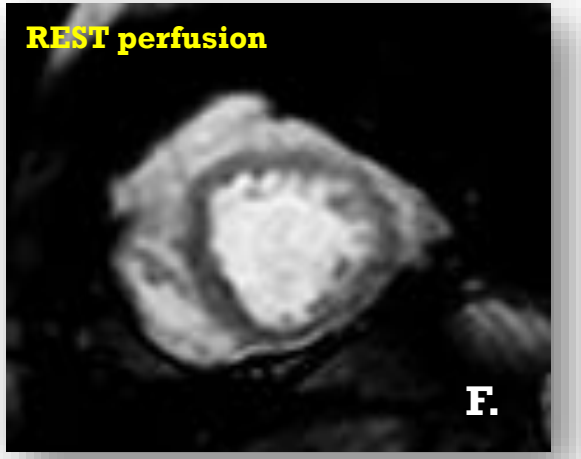


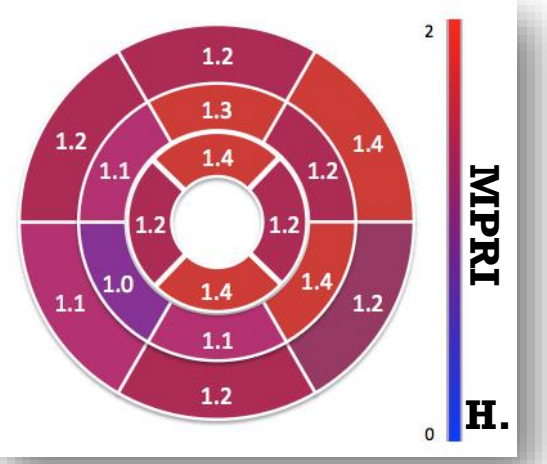




4 months CMR

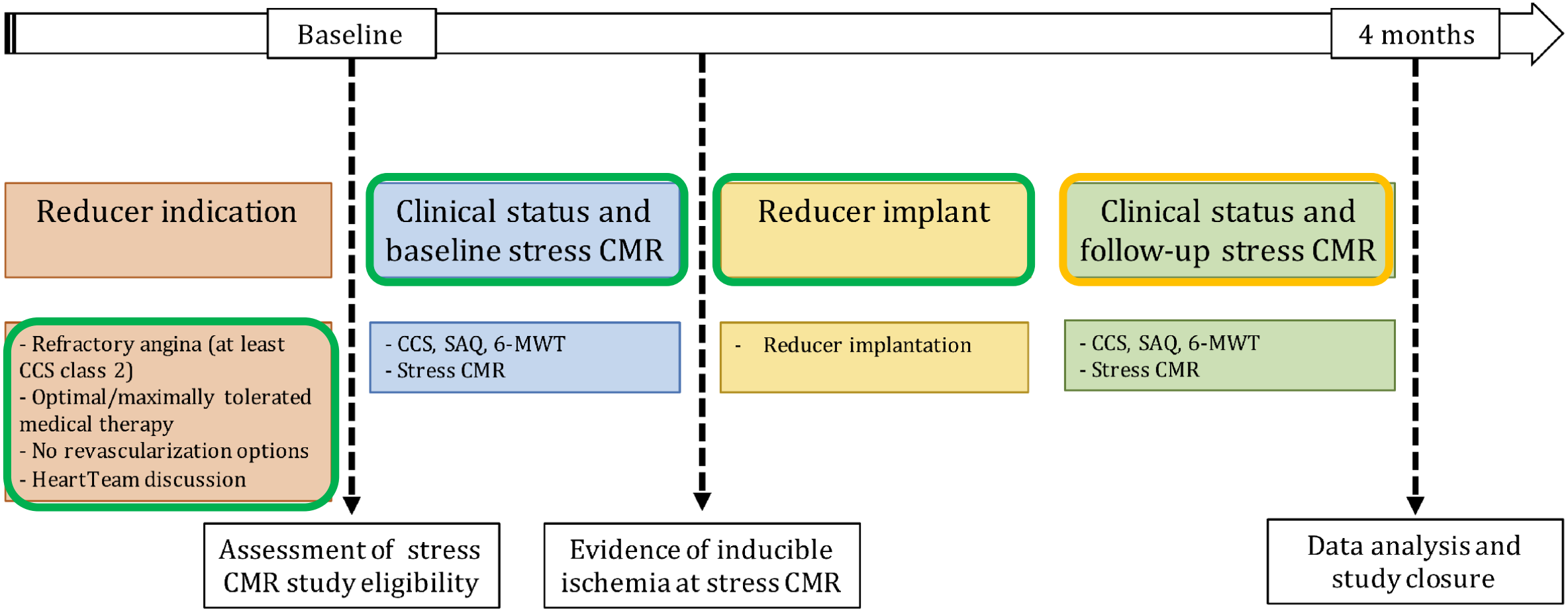






CS Reducer & ischemia reduction study protocol

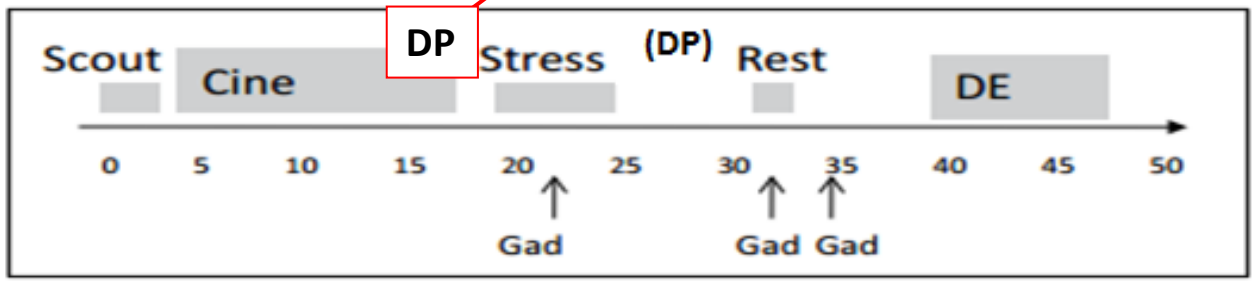
- **Non-randomized**, single-center experience (San Raffaele Hospital, Milan, Italy)
- **15 patients (93% CABG):** CCS class 3 refractory angina with no revascularization options

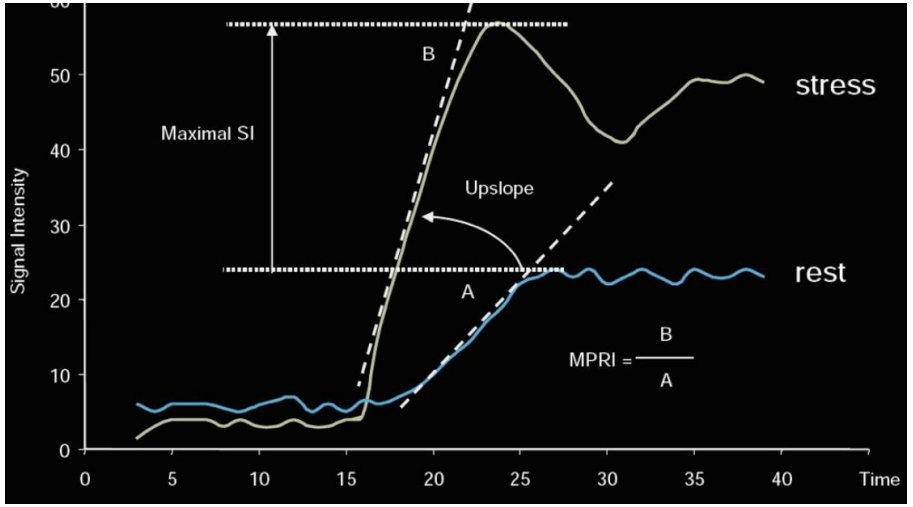


STRESS CARDIAC MAGNETIC RESONANCE PROTOCOL

1.5 T scanner

DYPIRIDAMOLE administered at 0.56 mg/kg ev over a 4-minute period (142 ug/kg/min).





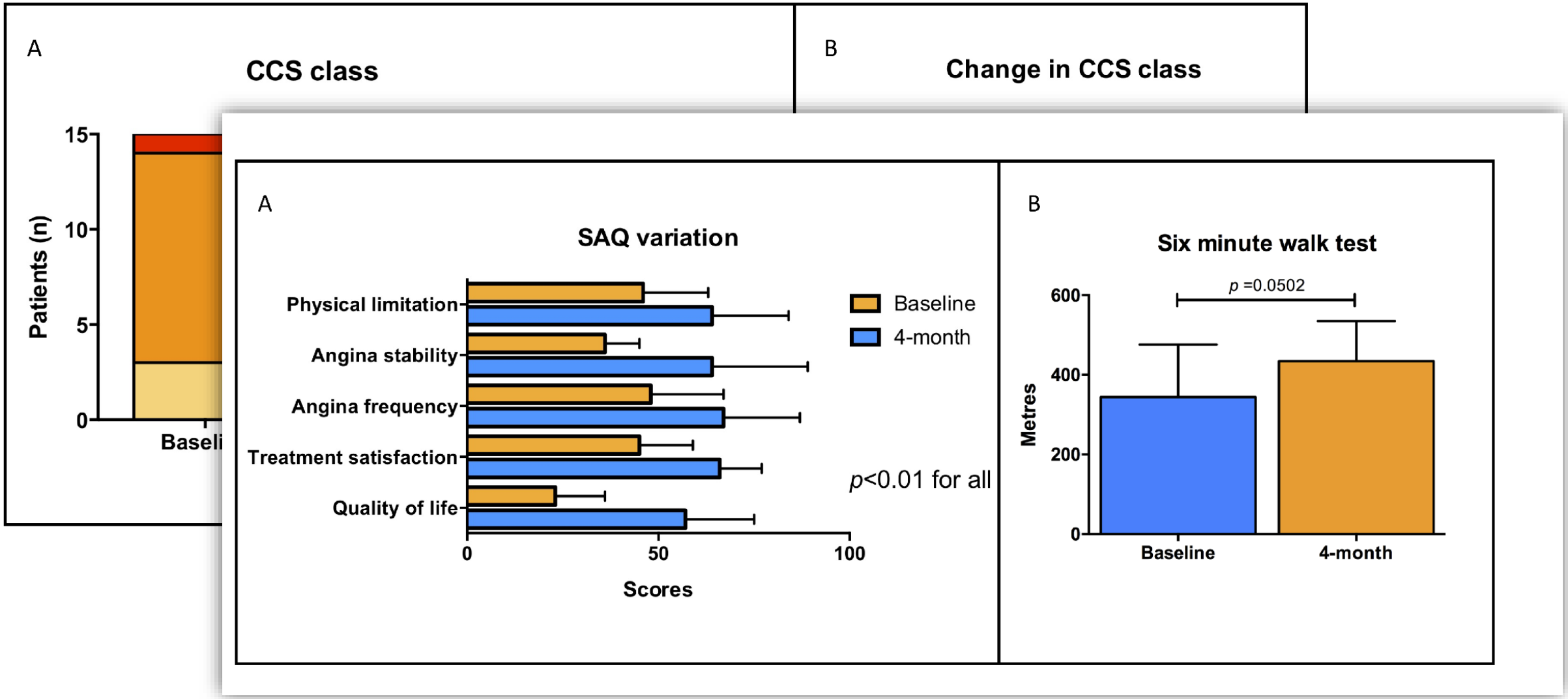
MYOCARDIAL PERFUSION RESERVE INDEX (MPRI)

→ Myocardial BLOOD FLOW

MPRI = RU STRESS/RU REST

RU (relative upslope): ratio between max upslope of first-pass myocardial perfusion time-intensity curve divided by the max upslope of the first-pass lv cavity time-intensity curve

Symptomatic relief & Quality of life



PHYSIOLOGIC EFFICACY

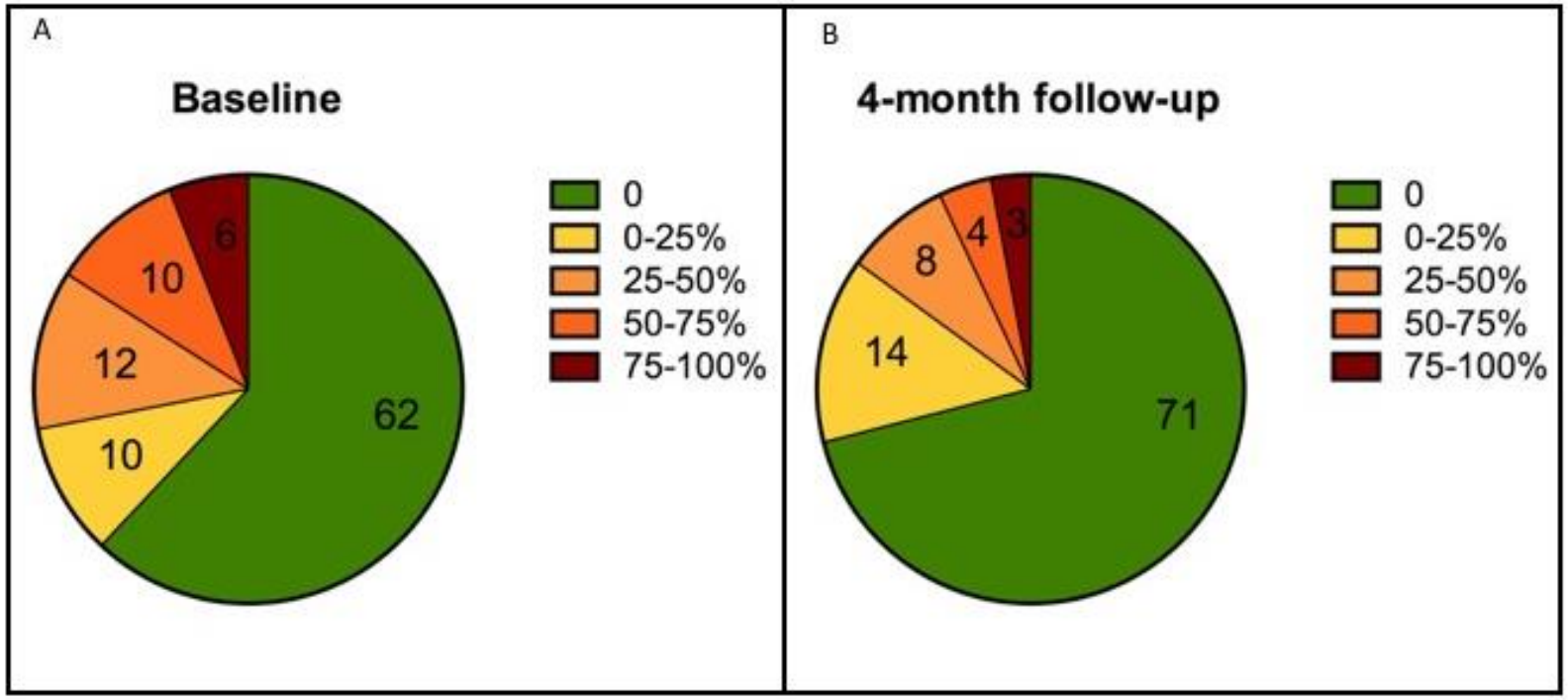
Among 240 myocardial segments:

- 94 (39%) had inducible ischemia at baseline

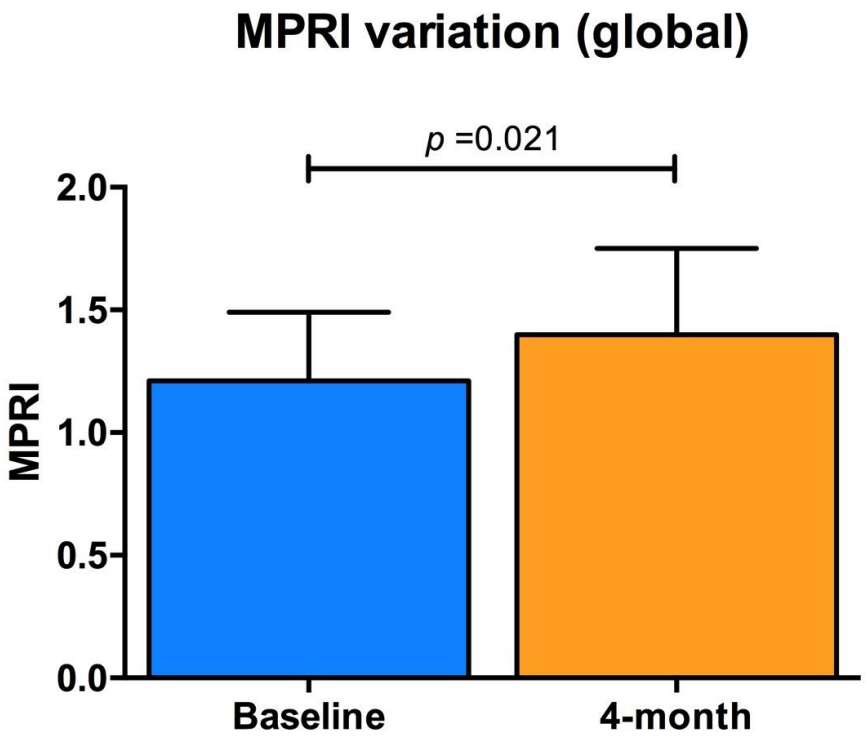
- 65 (27%) had inducible ischemia at 4-month follow-up

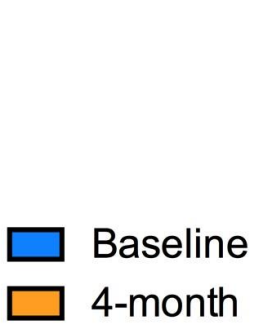
Segments with inducible ischemia

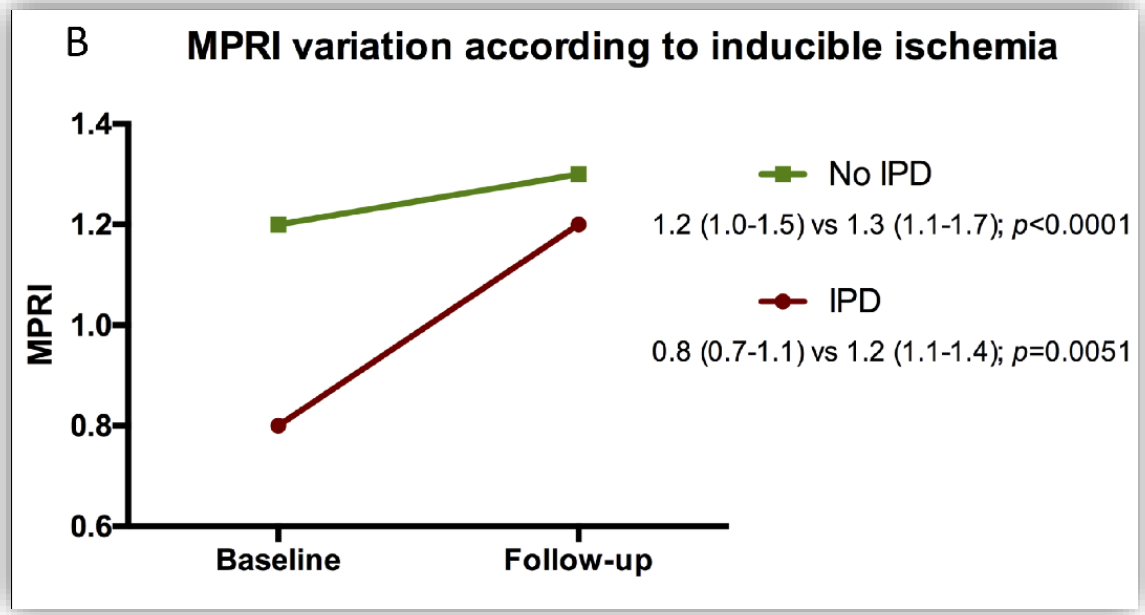
transmurality



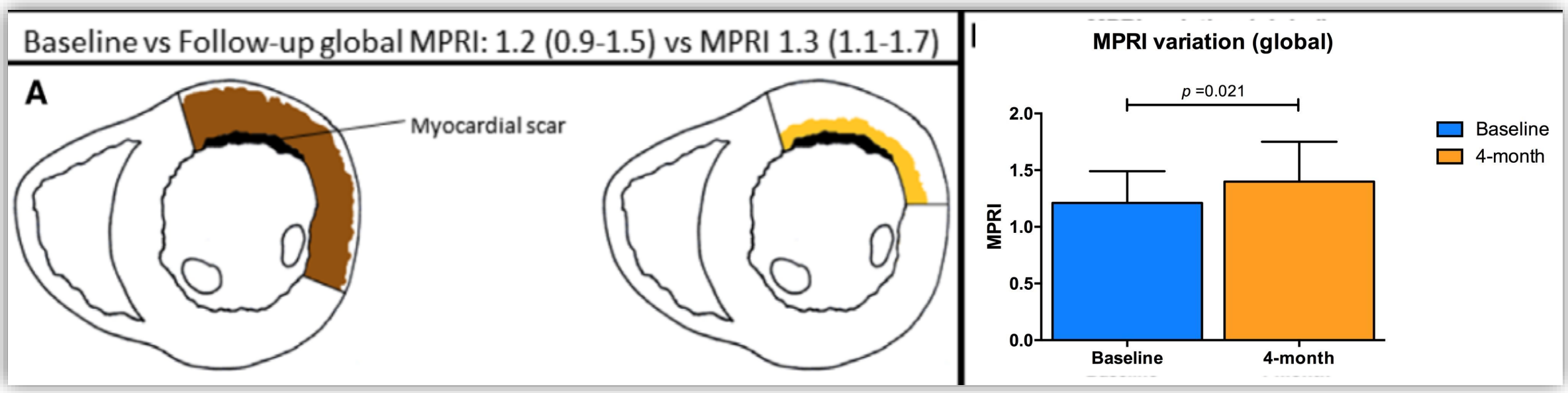
CS Reducer & ischemia reduction



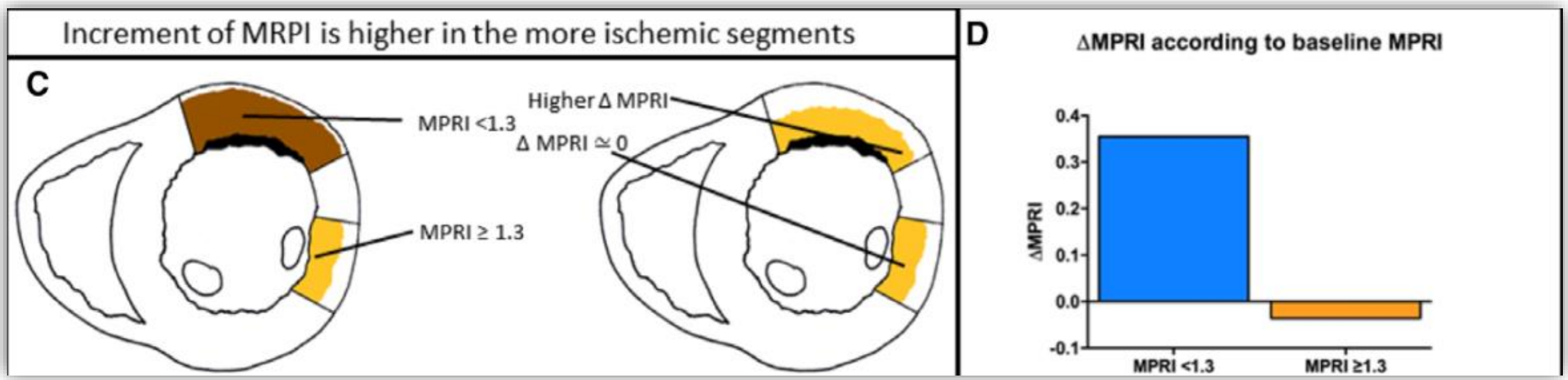




CS Reducer and ischemia reduction



CS Reducer and ischemia reduction



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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

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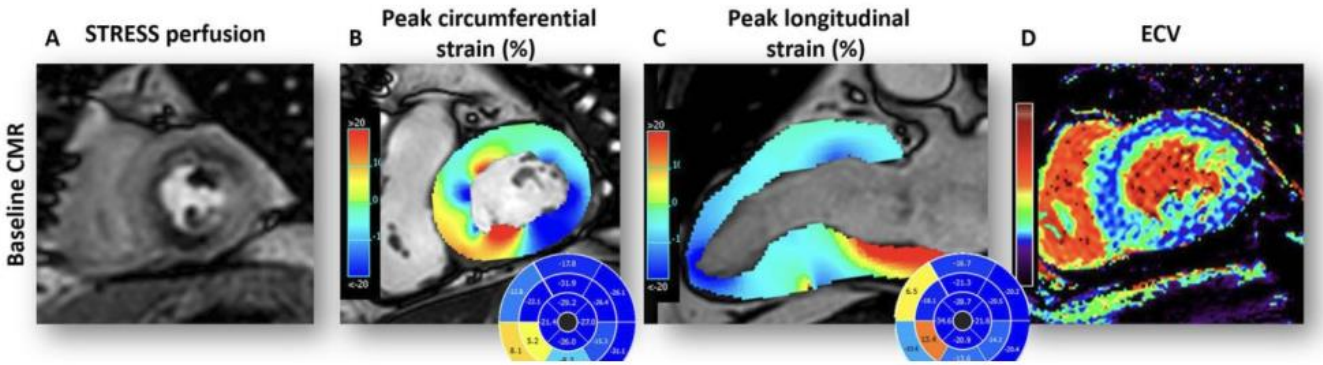


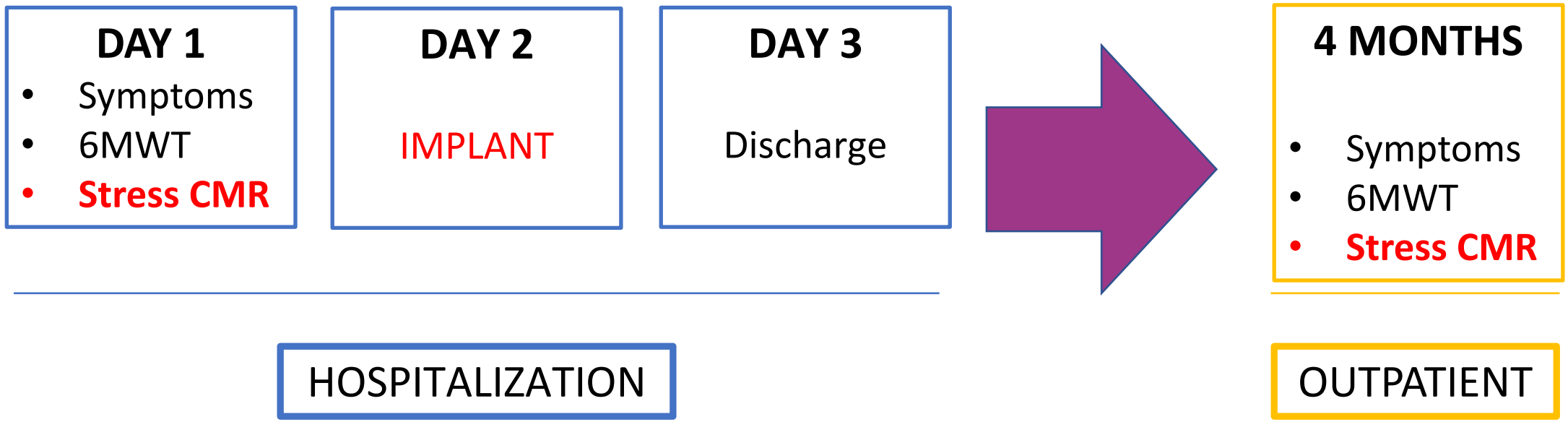
20 consecutive patients with refractory angina underwent multiparametric stress CMR before and 4m after Reducer implantation

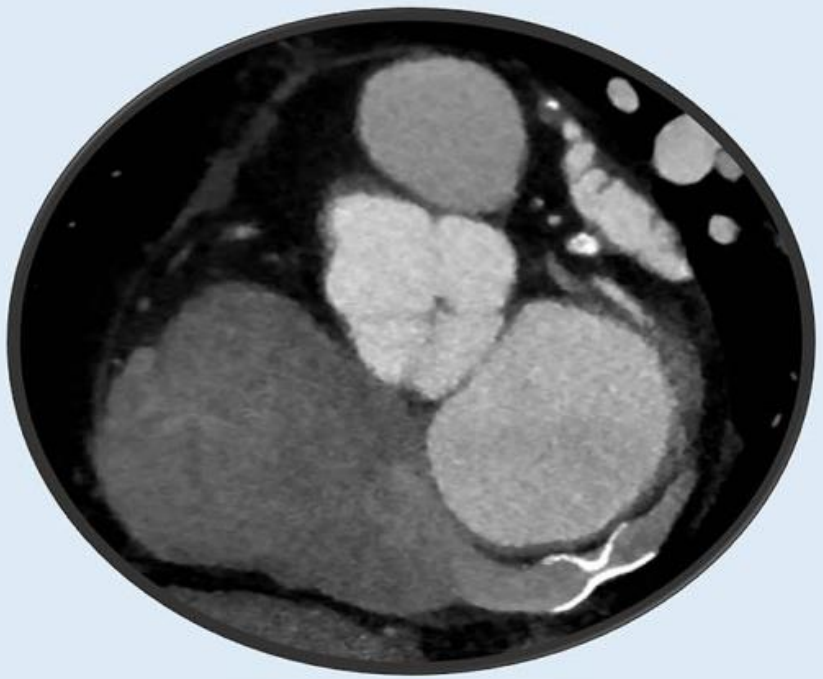
Results:

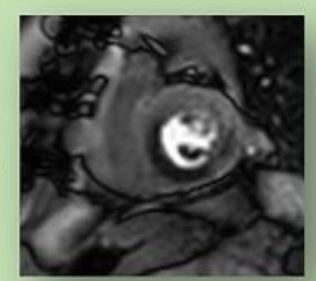
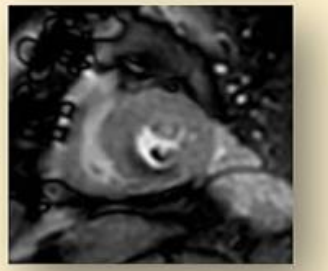
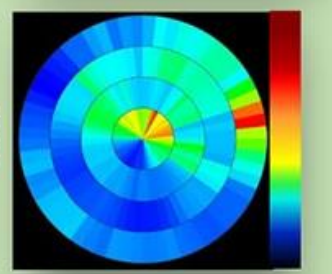
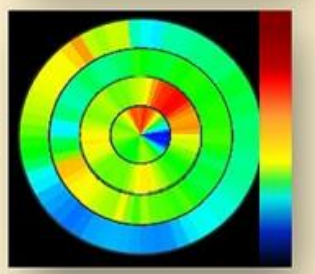
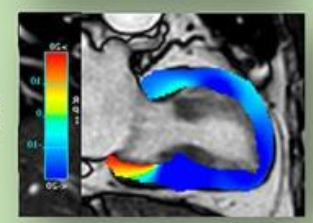
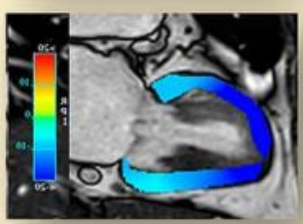
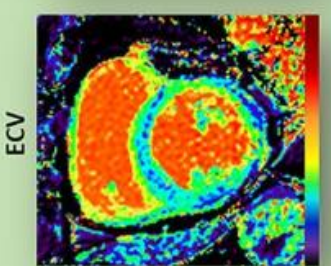
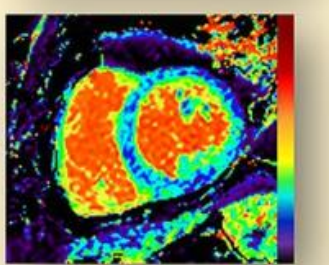
- Reducer improved myocardial contractility (EF rose from 61 to 67%; p = 0.0079)
- Improves myocardial longitudinal and circumferential strain
- Reduced ischemic burden
- Improved intramural perfusion balance in segments with baseline ischemia

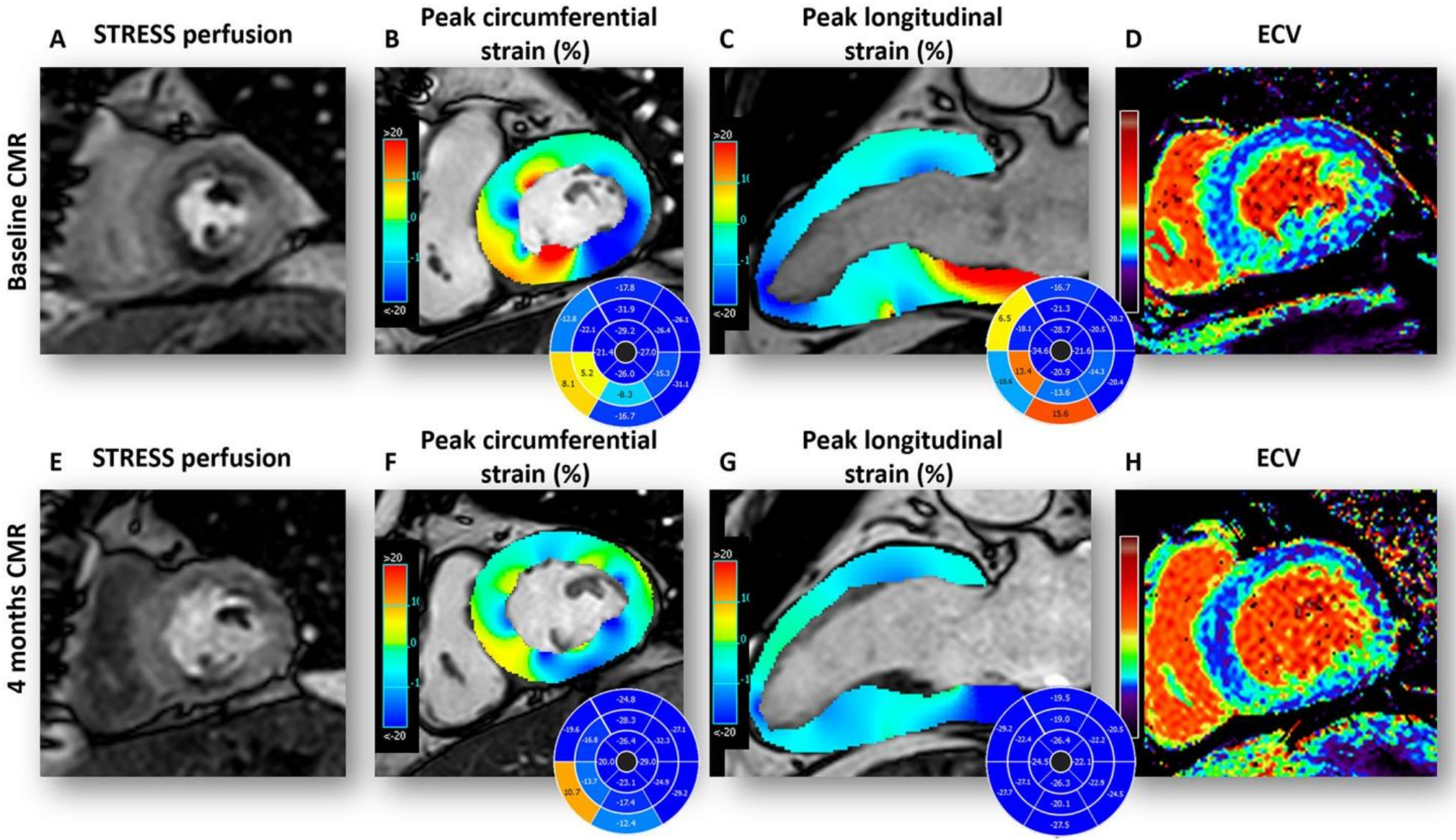
Feature tracking & mapping analysis of myocardial response to improved perfusion reserve in patients with refractory angina

- **20 patients** with CCS class ≥ II, refractory angina under OMT, with no-revascularization options





Effect	Baseline stress-CMR	4 months stress-CMR
↓ Ischemic burden	Stress perfusion 	Stress perfusion 
↑ Myocardial perfusion reserve index	MPRi 	MPRi 
↑ Contractility	GLS 	GLS 
No myocardial remodeling at mapping	ECV 	ECV 



Palmisano A,..,Tzanis G, Colombo A, Esposito A. ***Int J Cardiovasc Imaging.****2021;37(1):291-303*

CS Reducer & systolic function

- **Reduction of ischemic burden (13–11%; p = 0.0135),**
- **Myocardial contractility improved (EF: 61 → 67%;** p = 0.0079)

❑**CS Reducer improves systolic function**

Improvement in longitudinal **Strain** (from - **16** to - **19**%; p = 0.0192) &

Improvement in **circumferential** strain (from - **18** to - **21**%; p = 0.0017)

❑ Recovery of **intramural perfusion balance** in segments with baseline ischemia

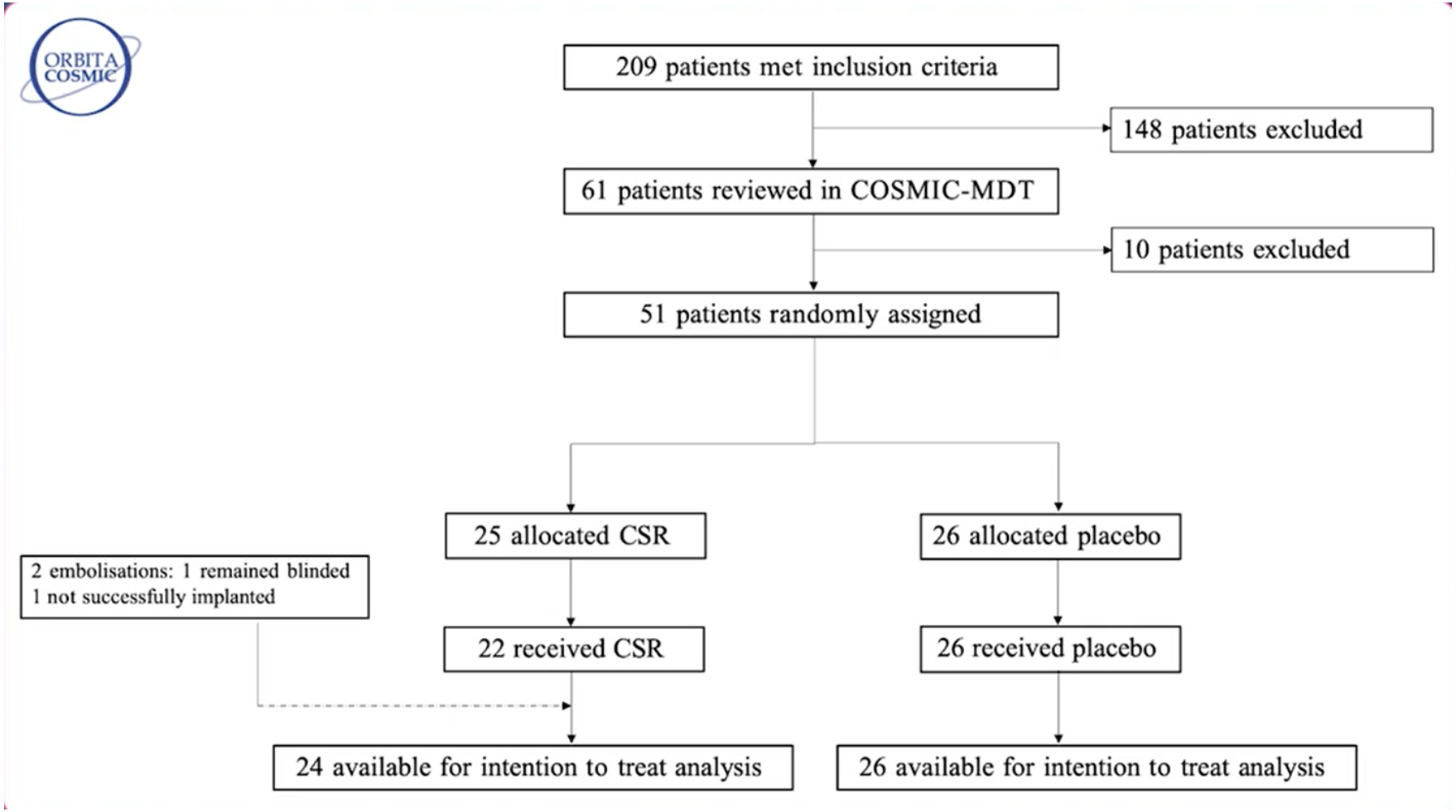
MPRi endocardial/epicardial ratio → **0.67** to **0.96**; p = 0.0107)


radcliffe
ORBITA
COSMIC
ACC 2024

ORBITA-COSMIC is a **double-blind**, **placebo*-controlled** trial of

CSR in patients with **angina, stable coronary artery disease, ischaemia, and no further anti-anginal medication** or **revascularisation options available**

*deep sedation & audio isolation

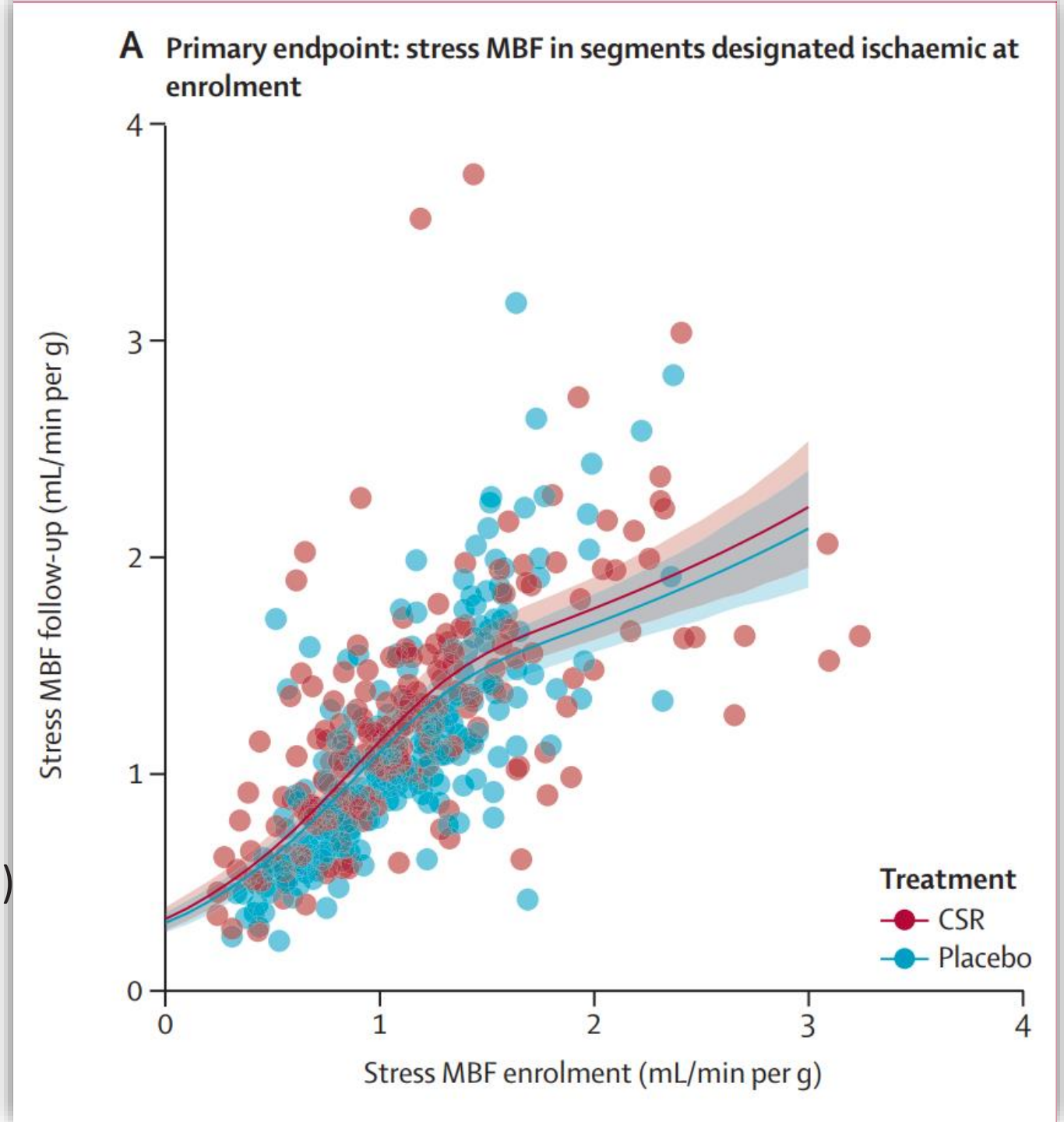


Primary outcome

Myocardial blood flow in ischaemic segments **did not improve** with CSR compared with placebo *(difference 0·06 mL/min per g [95% CrI –0·09 to 0·20]; Pr(Benefit)=78·8%)*

Secondary outcome

evidence of **redistribution** of perfusion from subepicardial → subendocardial myocardium **ischaemic segments**, in the CSR group (0·09 [95% CrI 0·00 to 0·17]; Pr(Benefit)=98·2%)

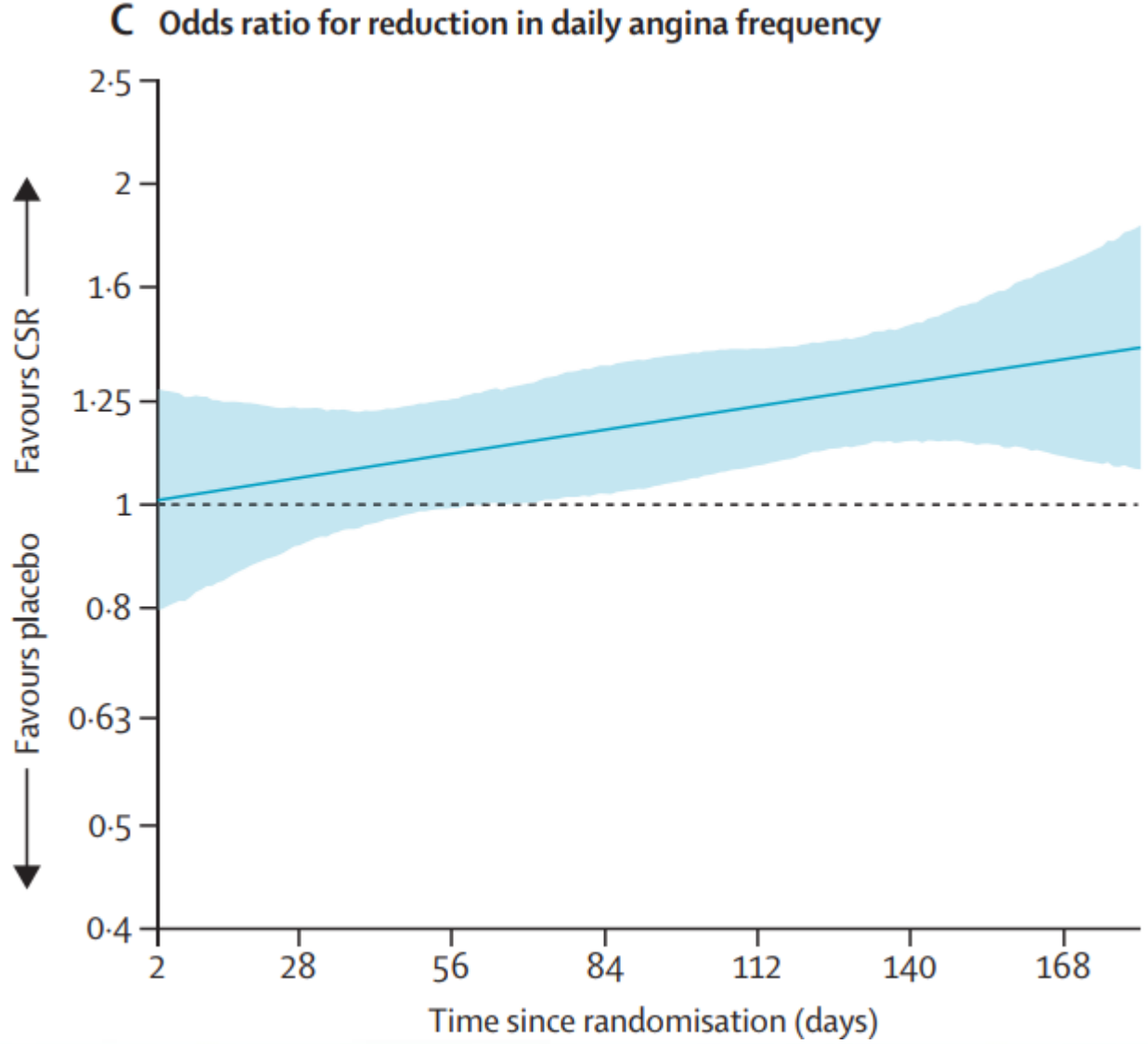


SAQ angina frequency

SAQ angina frequency benefit 16.0

(95% CrI 5.1 to 27.3)

Pr(Benefit)=99.7%



CS Reducer

Take-Home messages

- Refractory angina & ICM: entities with few therapeutic options

- **CS Reducer** can be an option for symptomatic relief for "no-option" chronic angina patients "***Robust DATA***"

- **Improvement to Endo/Epi blood flow ratio after CSR**

- *Further studies should evaluate the mechanism of action & the effect on ischemia*

STABLE ISCHEMIC HEART DISEASE …

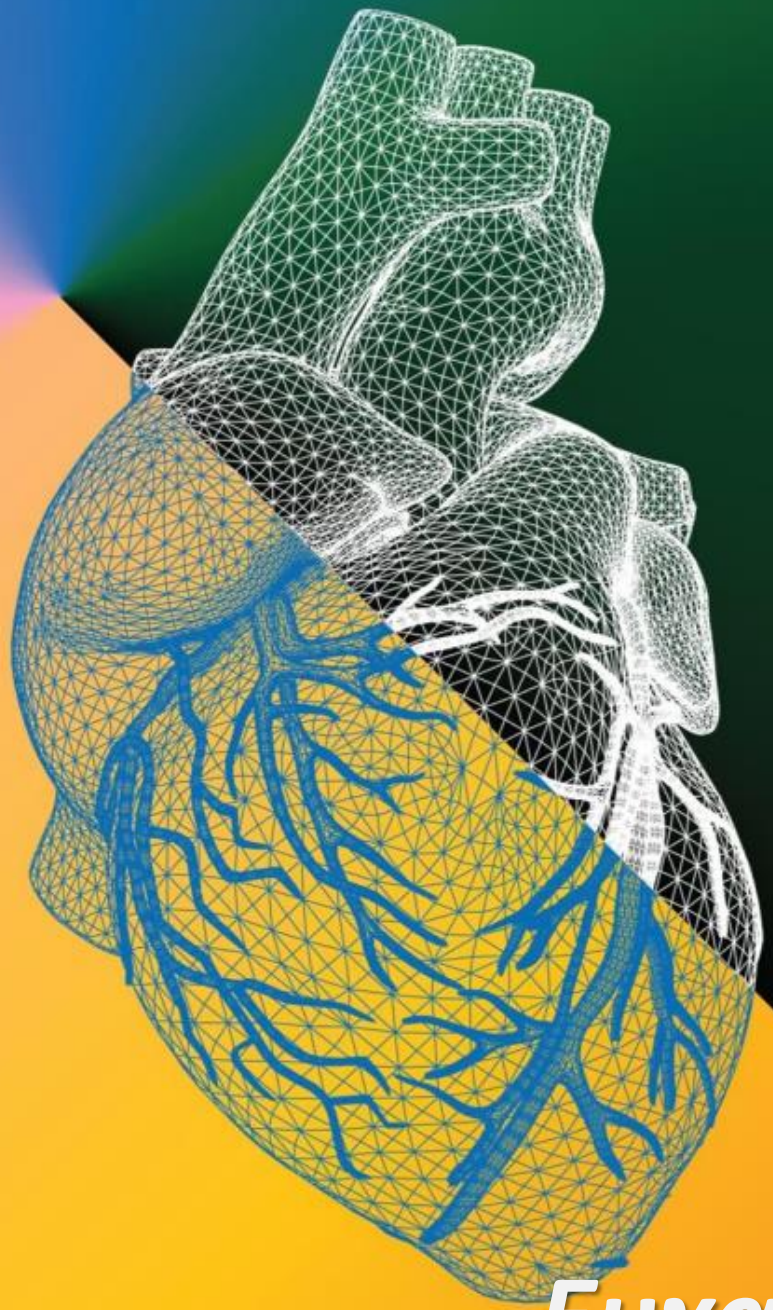
ACC.24: New data suggest early PCI limits risks of vulnerable plaques—cardiologists are skeptical

Michael Walter | April 09, 2024 | Cardiovascular Business | Interventional Cardiolo

PREVENT trial

ISCHEMIA

International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA)



Ευχαριστώ πολύ

When all fails, just reduce the ischemia!

Γιώργος Τζάνης

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EAPCI young ambassador

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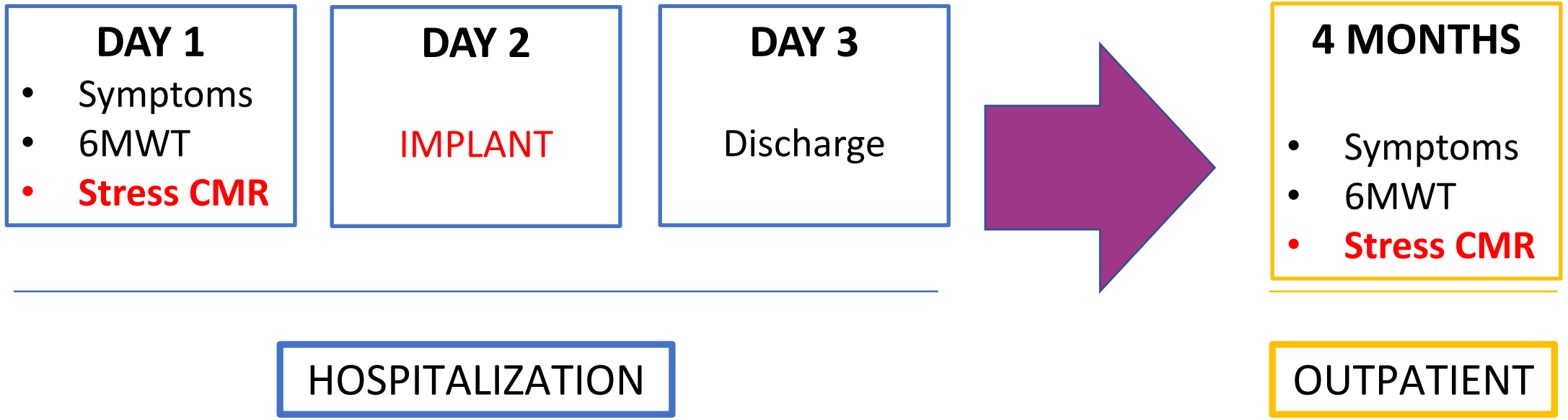
CS Reducer & **LV** Function Protocol

- **Non-randomized**, single-center experience
- **19 patients** with CCS class ≥ II, refractory angina under OMT, with no-revascularization options

STUDY DESIGN

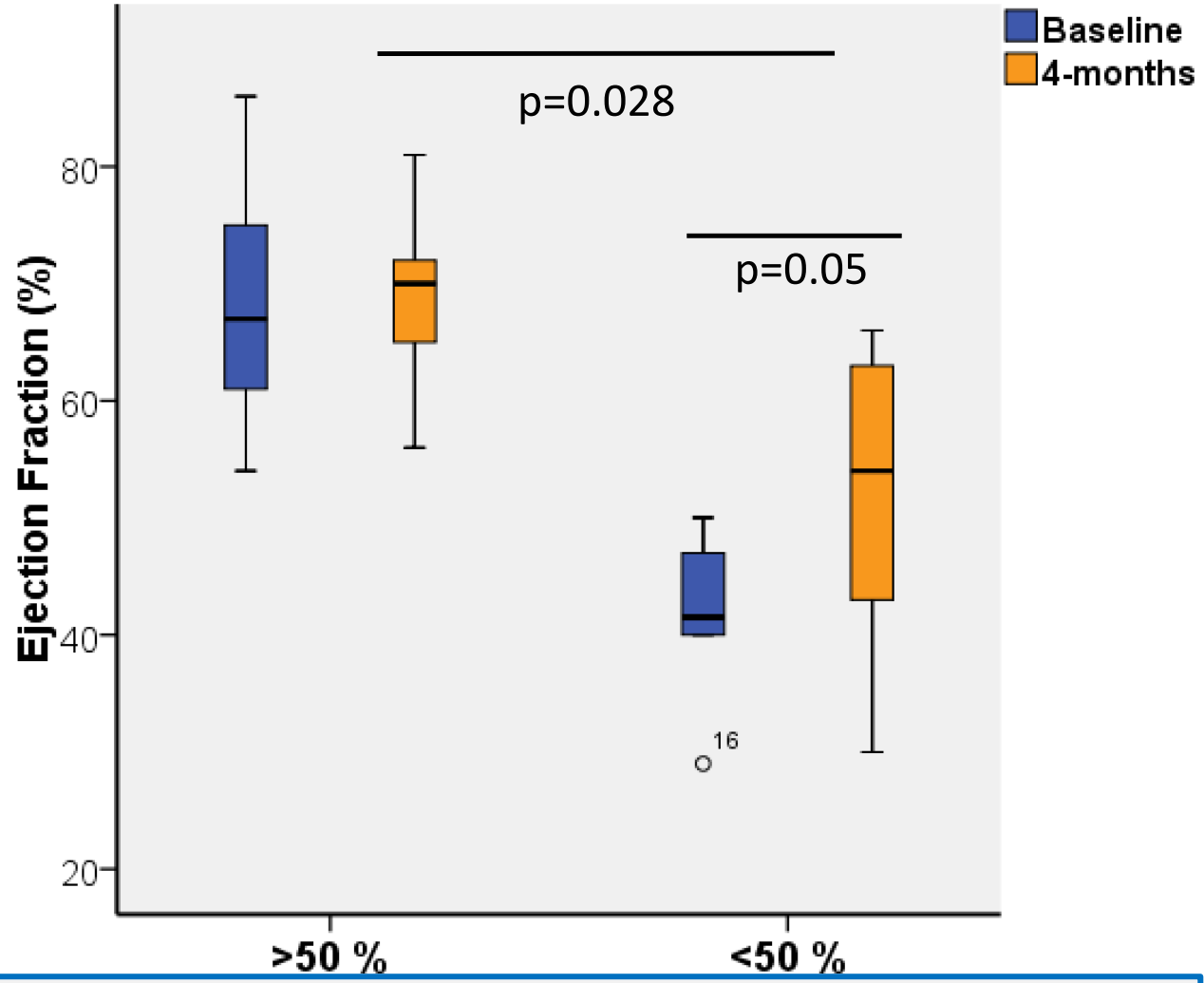


Stress CMR: myocardial perfusion reserve index (MPRI) & LV function-volumes

CS Reducer in perspective: systolic function

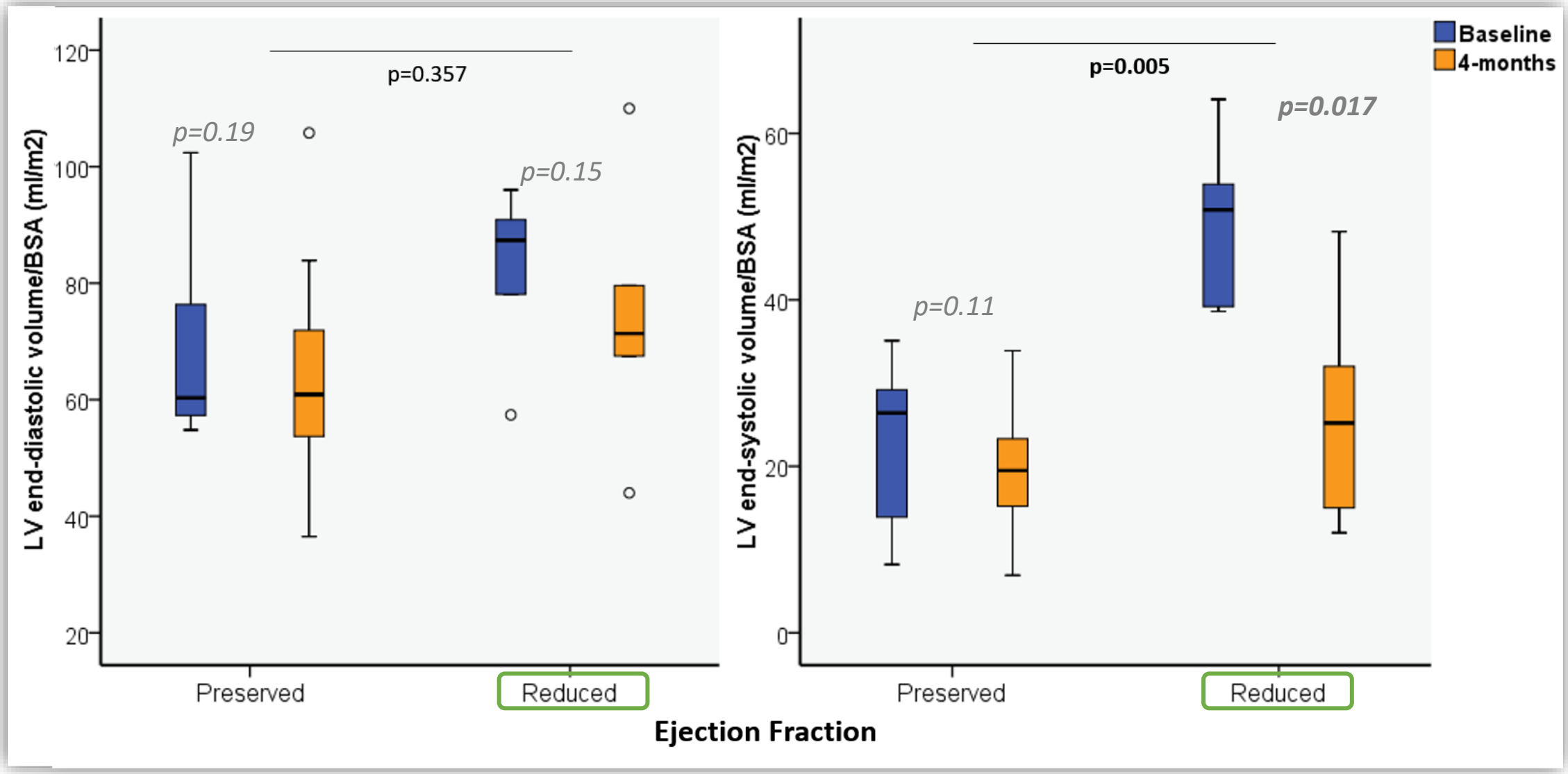
30 patients included
Systolic function assessed by cardiac MRI

	Baseline	4-Months	P value
CCS class	**3** [3-3]	1 [1-2]	**<0.001**
6-MWT, meters	**300** [240-382]	**420** [353-515]	**0.002**
EF, %	**61** [47-71]	**66** [57-72]	**0.009**
LV- EDV, ml	**132** [118-174]	**123** [100-158]	**0.033**
LV-ESV, ml	**55** [38-75]	**41** [31-70]	**0.007**
LV- EDV/BSA, ml/m^2	66 [57-90]	64 [54-74]	**0.036**
LV- ESV/BSA, ml/m^2	29 [19-39]	20 [15-31]	**0.007**
LV-EDWM/BSA, gr/m^2	56 [51-60]	53 [46-62]	0.653



Tzanis G, et al. Catheter Cardiovasc Interv. 2020; 95(6)

LV remodelling



Tzanis G, et al. Catheter Cardiovasc Interv. 2020; 95(6)

Ischemia improvement - accompanied by LV remodeling