#FullPhysiology

In Daily Practice

Lights and shadows in the therapy of ANOCA

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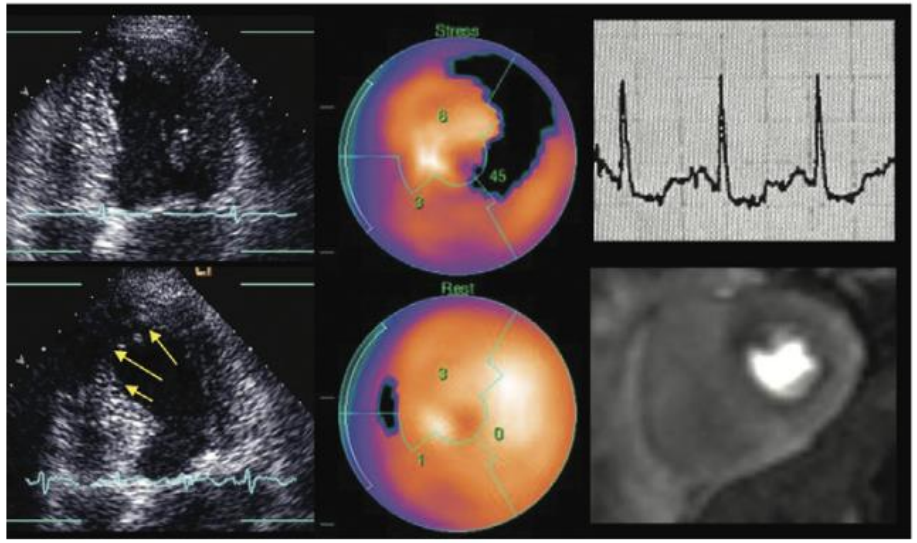
Speaker's name: Italo Porto

☑ I have the following potential conflicts of interest to report:

Prof Porto is an advisor for Abbott Vascular and received speaking honoraria from Abbott Vascular.

INOCA is (relatively) common

8,518 ISCHEMIA Enrolled Participants

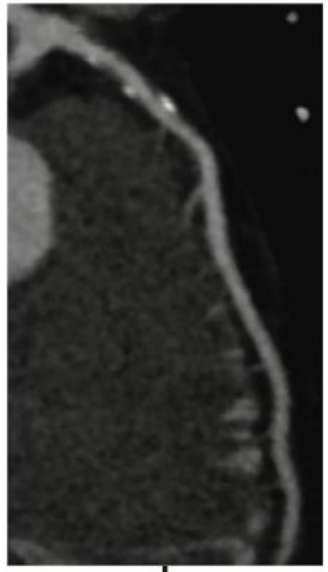


Moderate or severe ischemia

Core lab-verified

Exclusion of prior PCI, CABG, uninterpretable CCTA or no CCTA

13% INOCA



Ischemia severity not associated with extent of nonobstructive CAD on CCTA

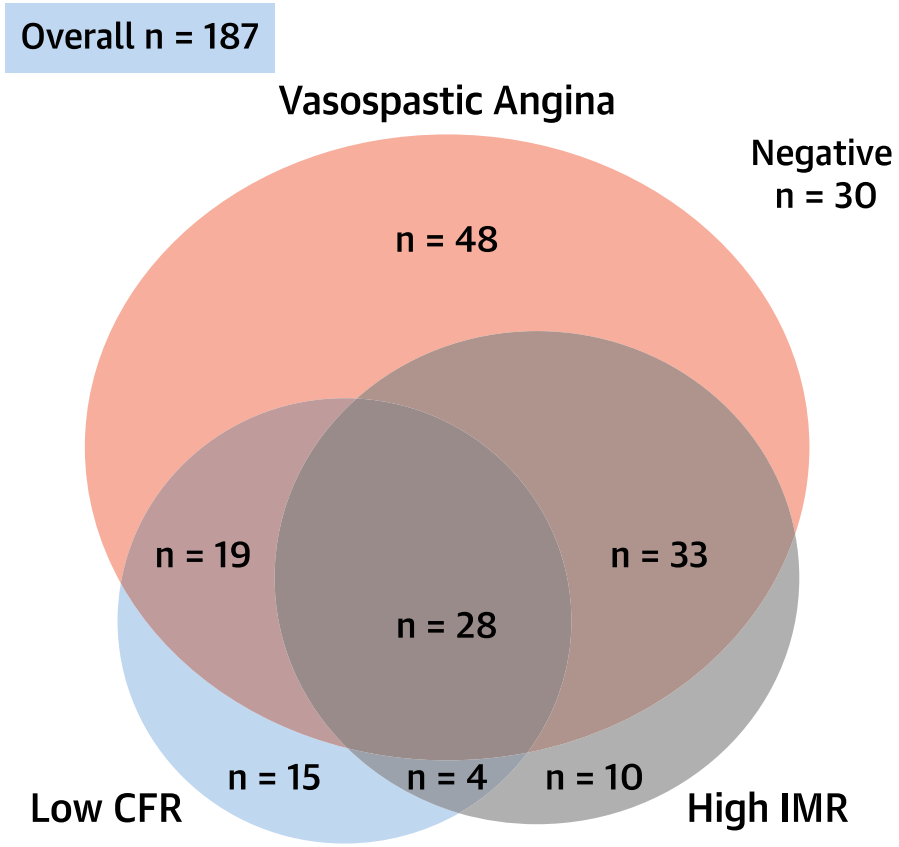
INOCA associated with:

- Female sex
- Younger age
- Relatively less severe ischemia

Women >4-fold odds of INOCA vs men on multivariate analysis

Reynolds HR, et al. J Am Coll Cardiol Img. 2023;16(1):63-74.

INOCA is a mixed bag

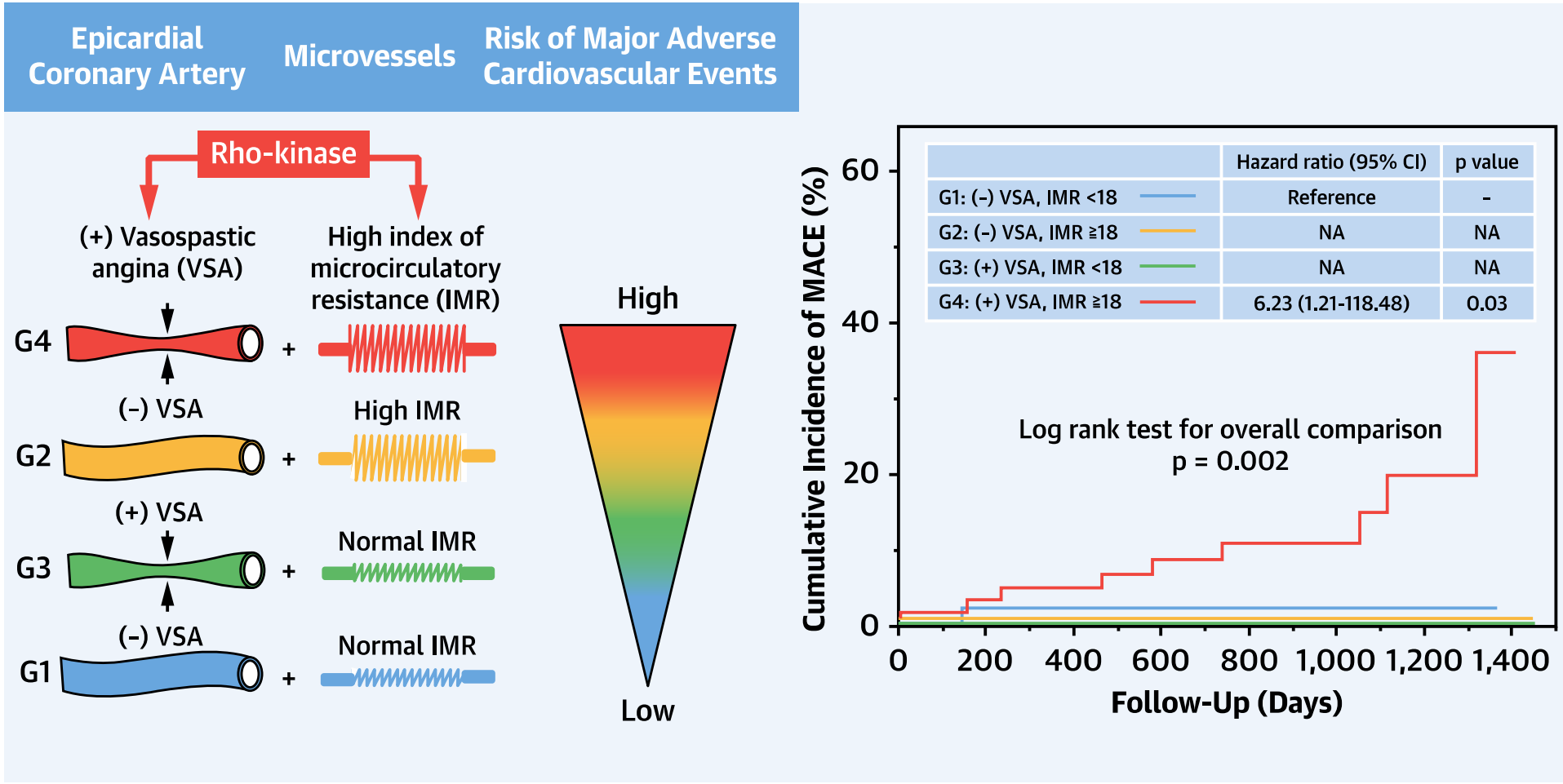


More than one-half of VSA patients had microvascular functional abnormalities

Suda A. et al. J Am Coll Cardiol 2019;74:2350–60

INOCA is a mixed bag

CENTRAL ILLUSTRATION Vasospastic Angina and High Index of Microcirculatory Resistance: Prognostic Impact of Coexistence



Suda, A. et al. J Am Coll Cardiol. 2019;74(19):2350-60.

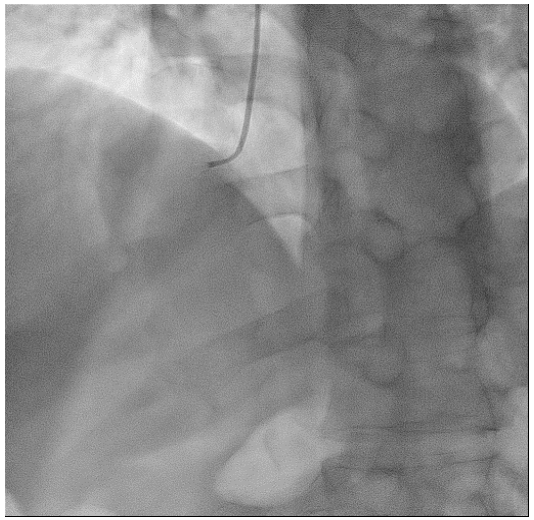
INOCA is a mixed bag

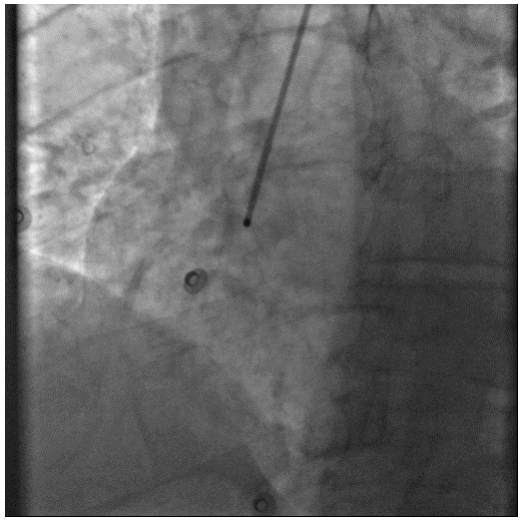
Effort angina (CCS 3)

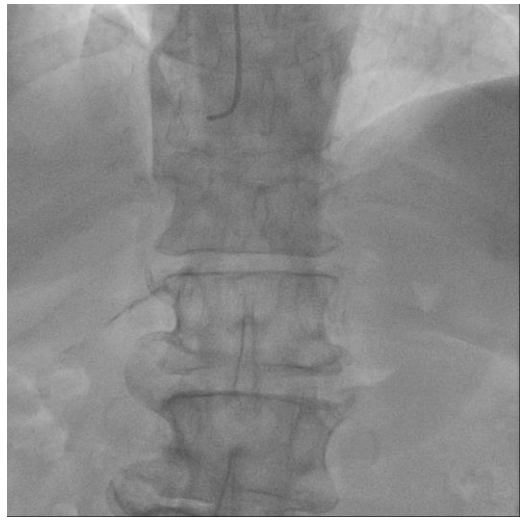
Positive Stress Test

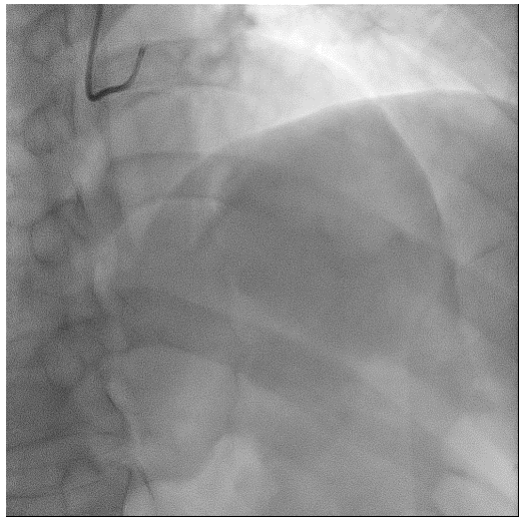
Normal LV function

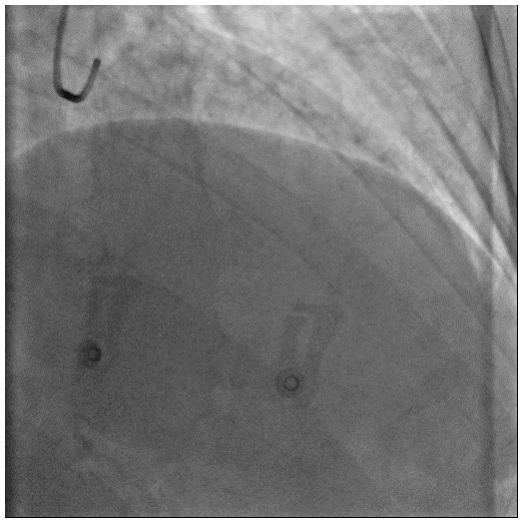
No VHD

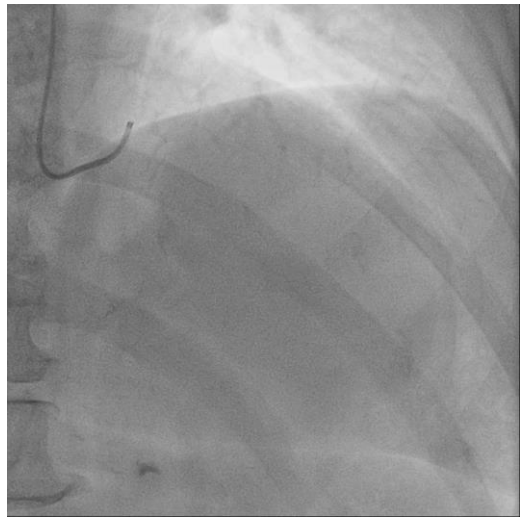










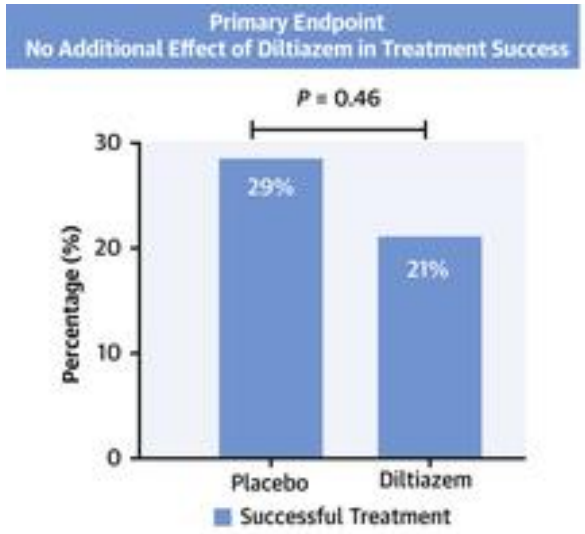


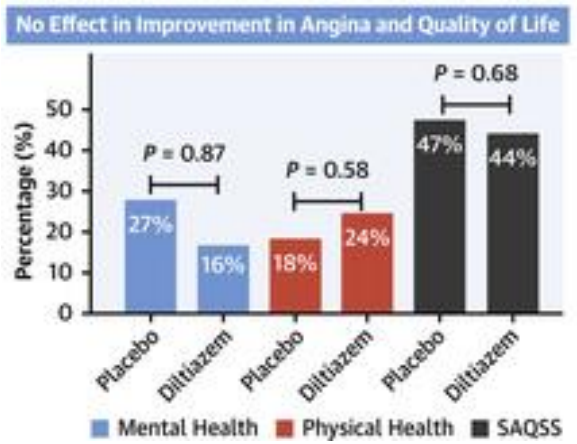
A) M 74 yrs

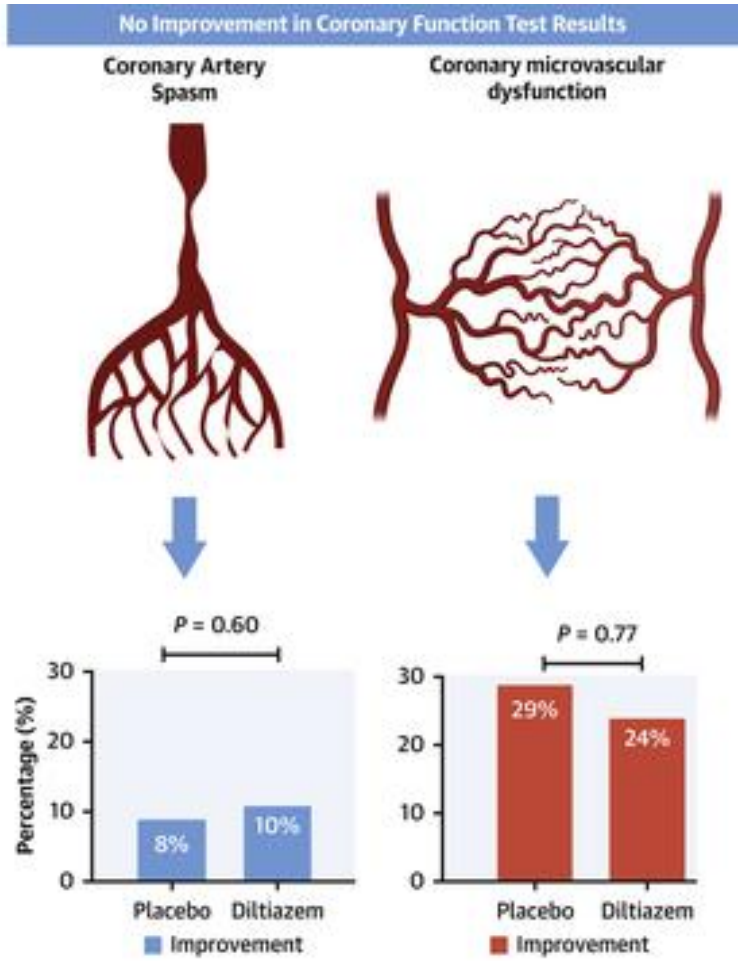
B) M 66 yrs

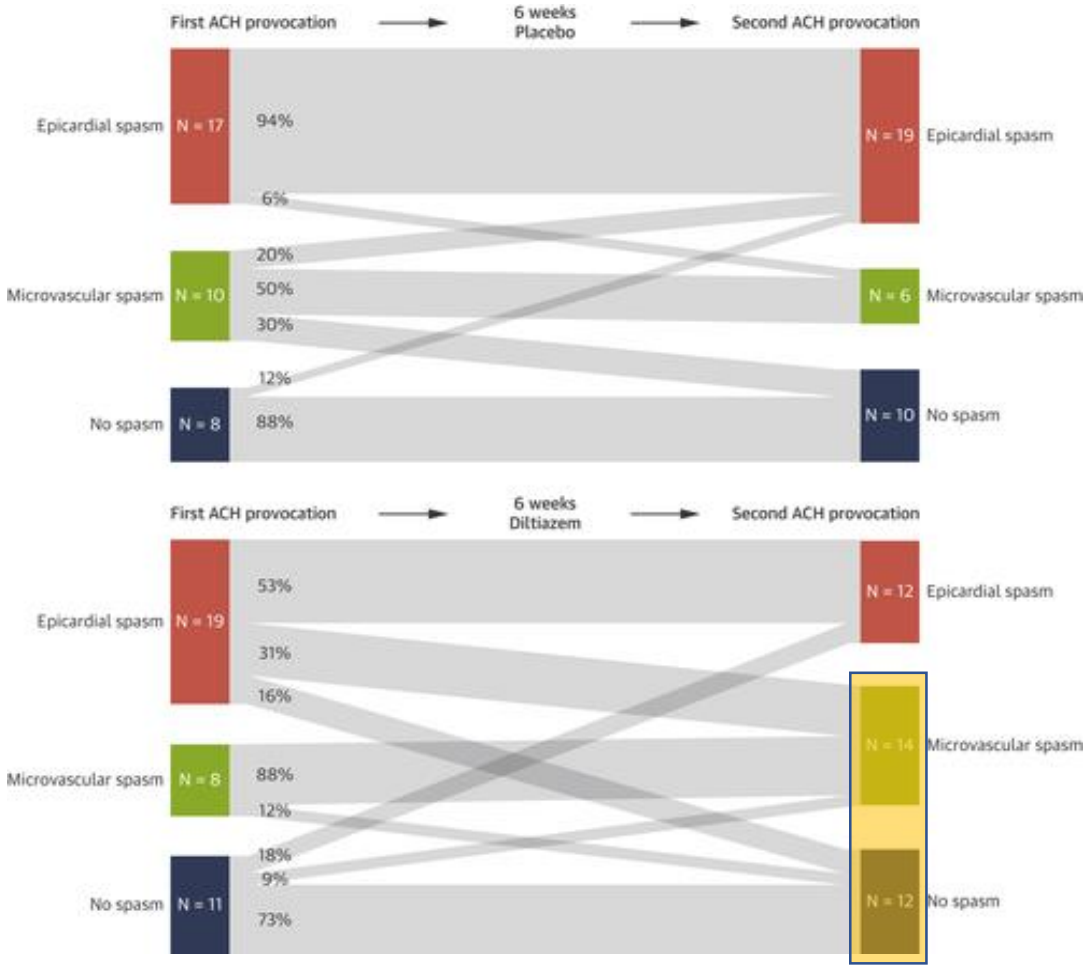
C) F 70 yrs

Empiric use of CCB: the EDIT-CMD trial









Tijn P.J. Jansen et al. *J Am Coll Cardiol Img* 2022;

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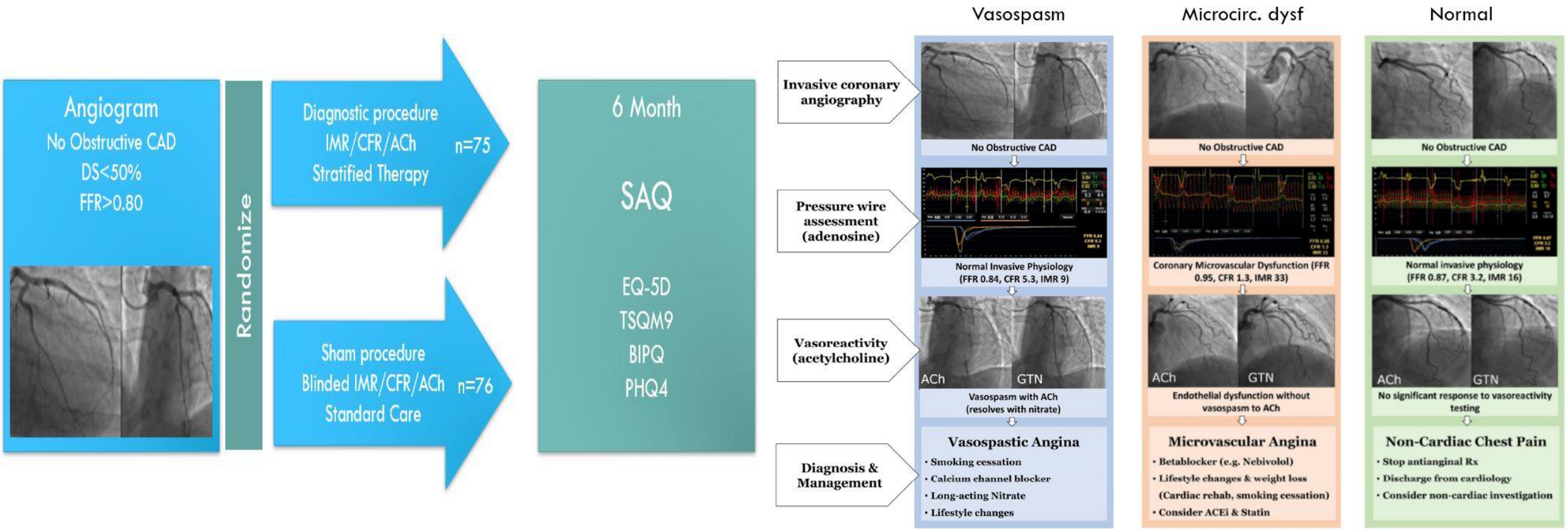
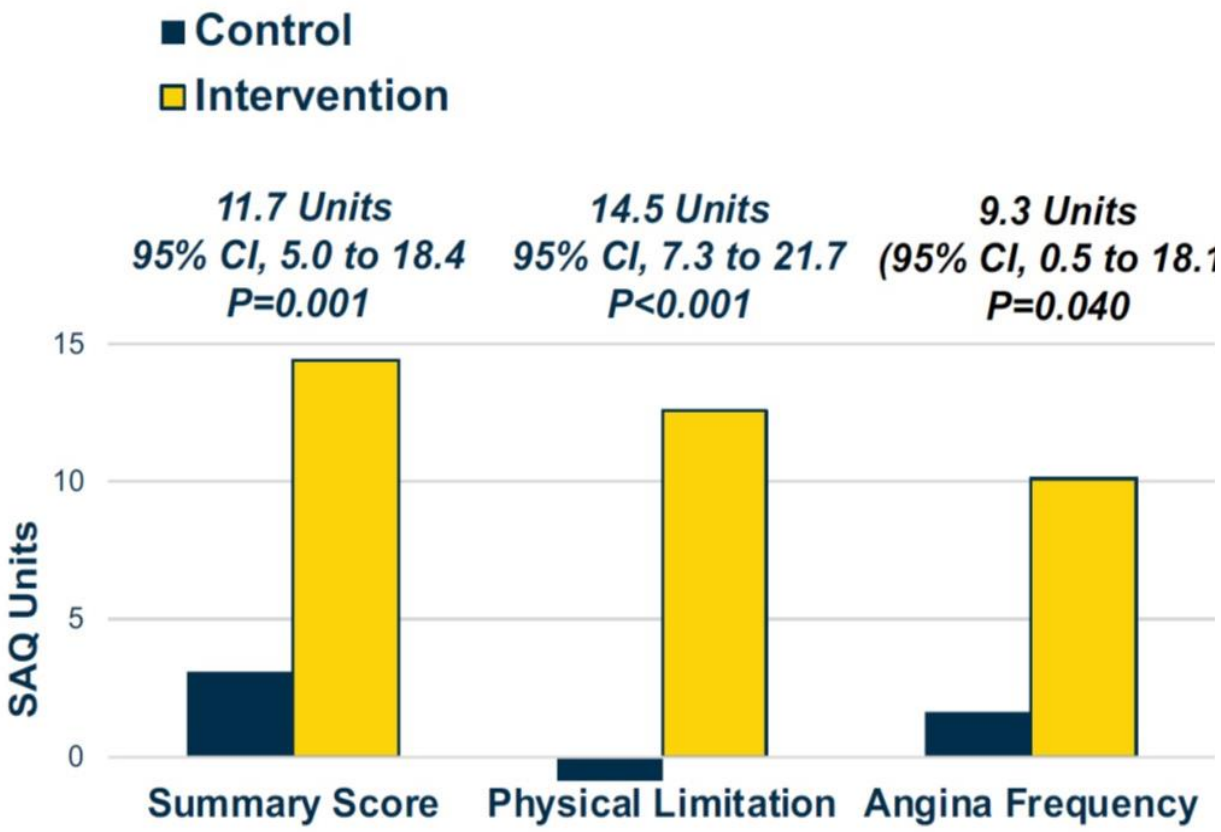
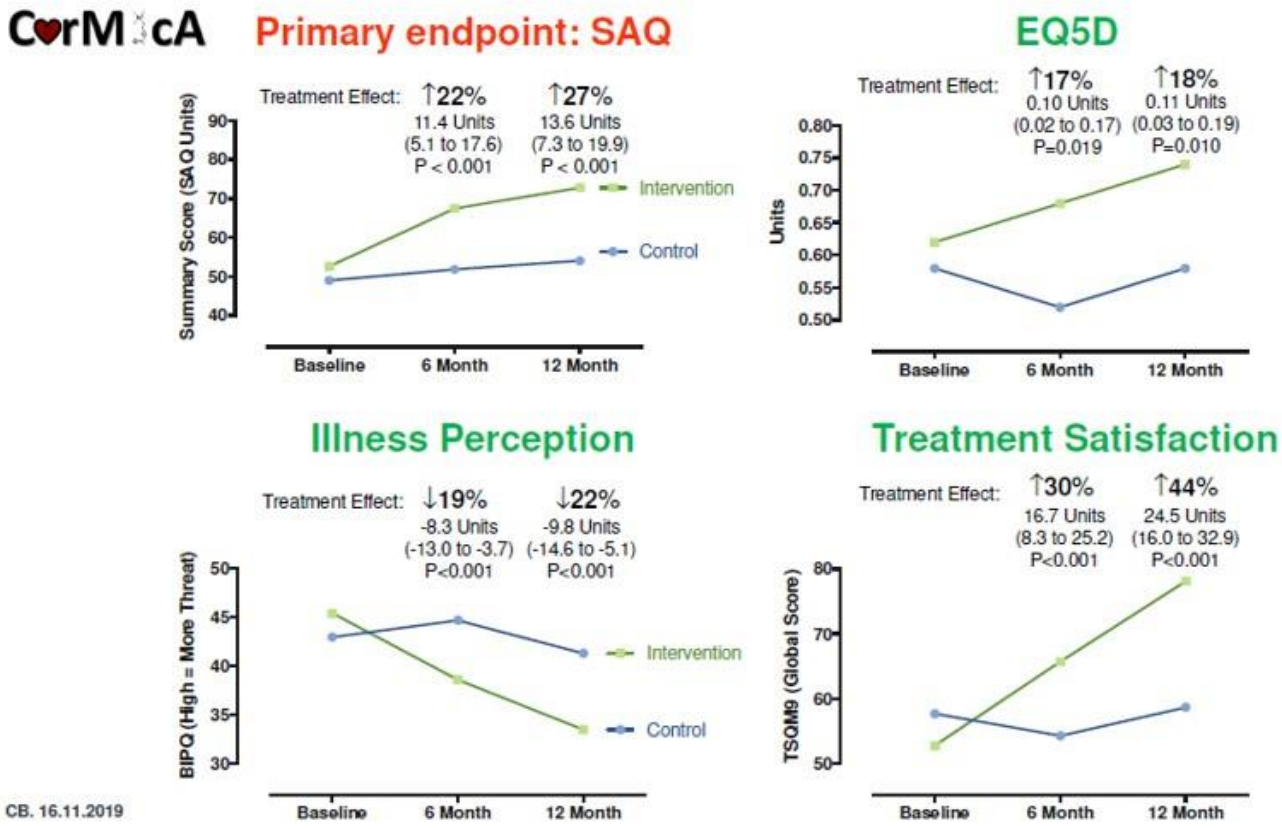
CORMICA trial: efficacy of a tailored approach



Ford JACC 2018

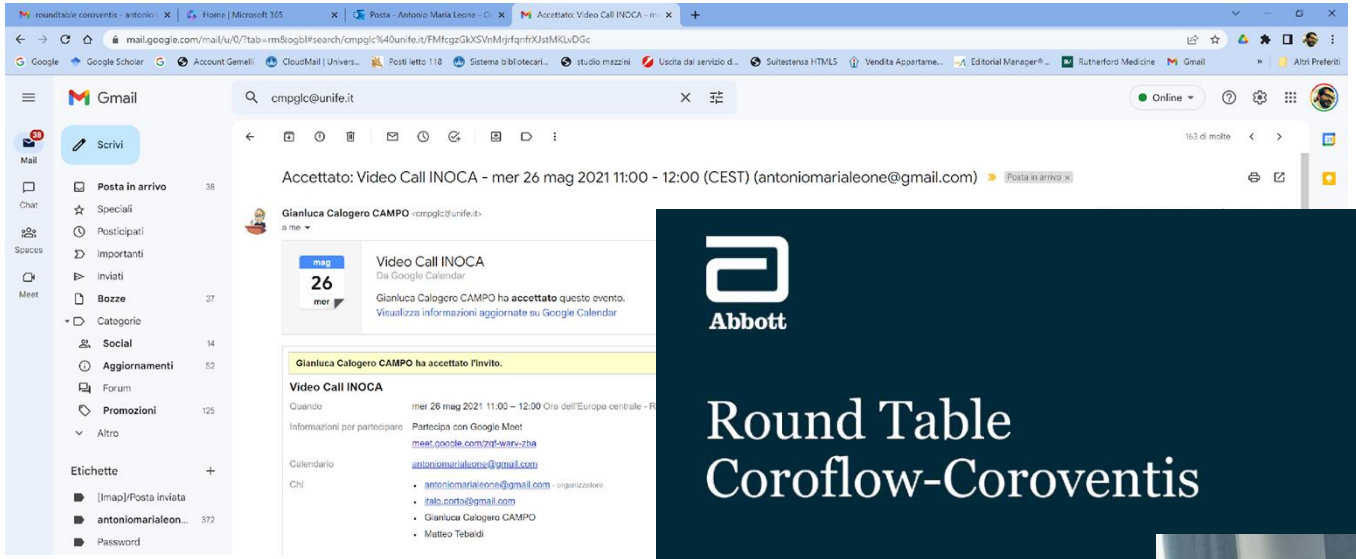
CORMICA trial: efficacy of a tailored approach





CB. 16.11.2019

Ford JACC 2018



- No Club / «niche»
- Sharing a common language
- Expressing the full potential of physiology in daily practice (case-based approach)

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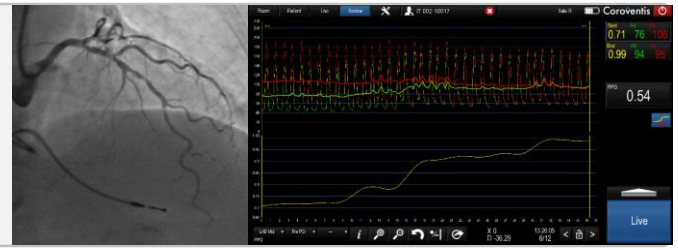
InDailyPractice

1 Epicardial disease assessment

- NHPR (≤0.89)
- cFFR (≤0.83)
- FFR (≤0.80) -> perform pullback



2 Microvascular disease assessment

- IMR (>25)
- CFR (< 2.0)
- RRR (<2.0)*

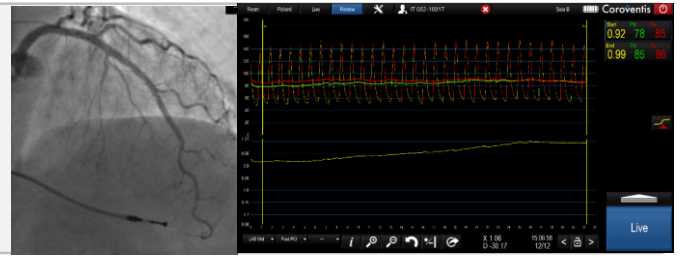
Resistive resistance ratio $= \frac{Trm*Pdr}{Thm*Pdh}$

3 Vasomotor testing

- Ach

4 Post PCI Full Physiology assessment if applicable

- NHPR/cFFR/IMR/CFR/FFR -> perform pullback



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Different types of CMD. All are bad

	Mechanism	Systemic Vasculature			Myocardium			
		Nitric Oxide Synthase Activity	Acetylcholine Dilatation	Exercise Blood Pressure	NT-proBNP	Exercise Coronary Perfusion Efficiency	Inducible Ischemia	
Reference Group (n = 40)	High vascular tone at rest → Low vascular tone at stress	Normal	Normal	Normal	34 pgml^{-1}	65%	22%	CFR>2 IMR<25 **Normal**
Functional CMD (n = 28)	Low vascular tone at rest → Low vascular tone at stress	Increased ↑↑	Normal	Normal	69 pgml^{-1}	46%	77%	CFR<2 IMR<25 **Impaired Vasodilation**
Structural CMD (n = 18)	High vascular tone at rest → High vascular tone at stress	Increased ↑	Reduced ↓	High	132 pgml^{-1}	41%	88%	CFR<2 IMR≥25 **Abnormal MV resistance**

Compensated Structural CMD

Microvascular Spasm

CFR>2 IMR≥25 **Early Abnormal MV resistance**

Angina + ST deviation w/o epicardial spasm

Modifed from Rahman H et al. JACC 2020;75:2538–2549.
COVADIS criteria

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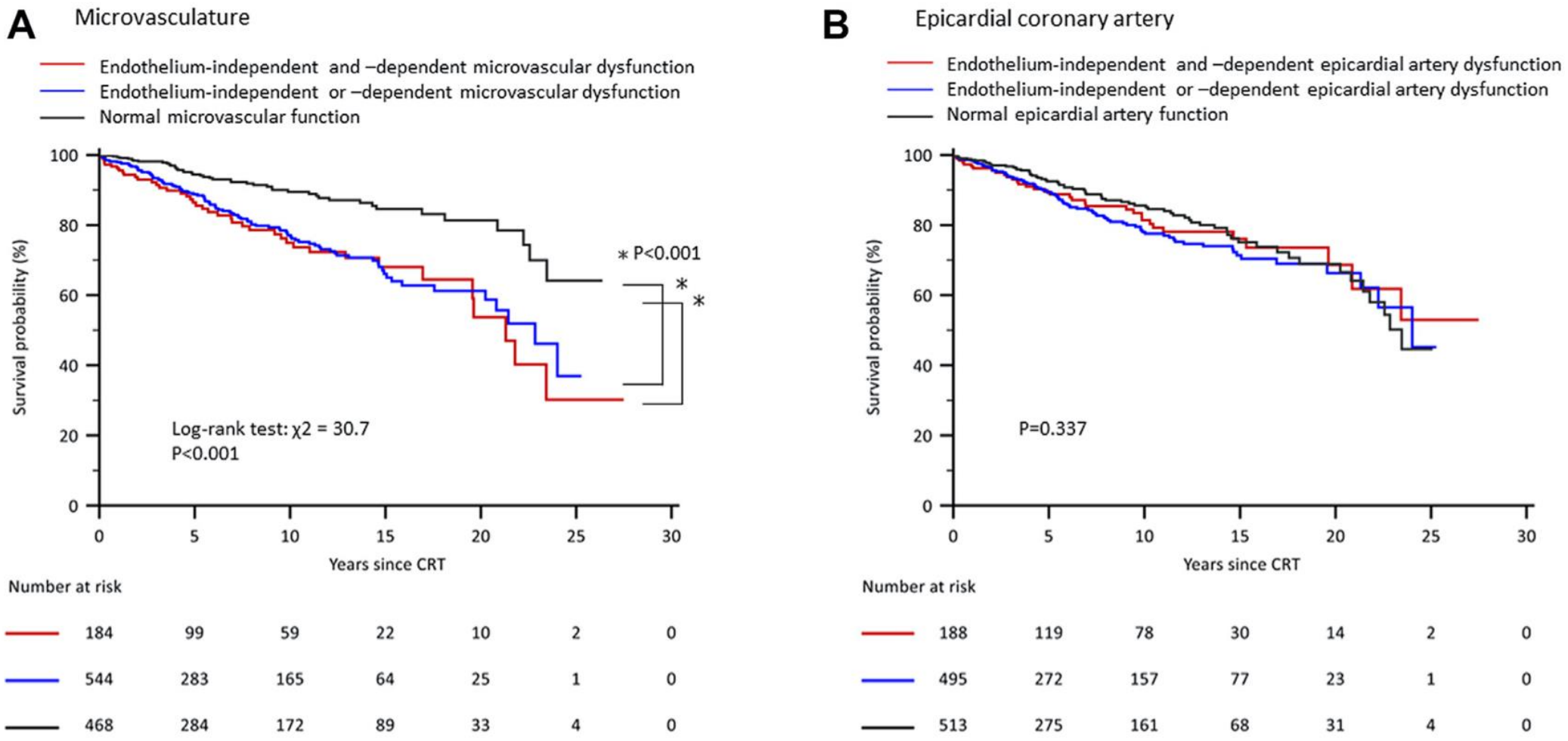
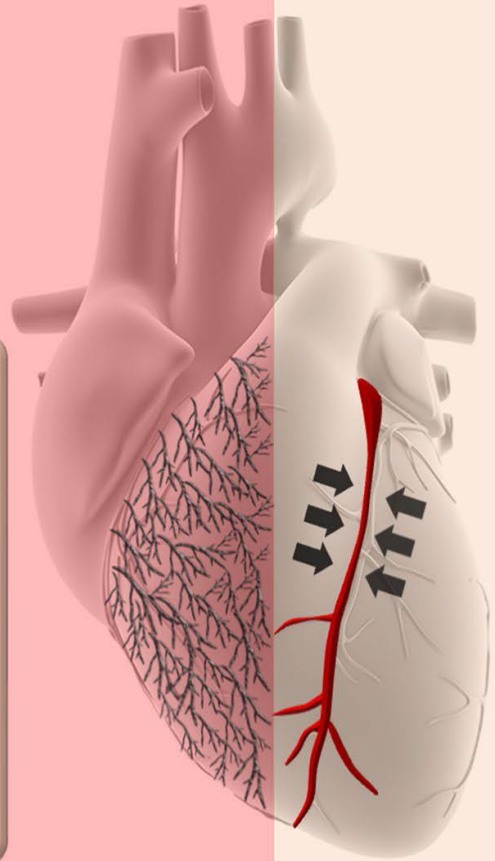
Different types of CMD. All are bad



Kanaji Y, et al. J Am Coll Cardiol Intv. 2024;17(4):474–487

Therapy for CMD

Consider statins and ACEI/ARB



MICROVASCULAR ANGINA

- Beta Blockers (Nebivolol)
- Ranolazine
- Trimetazidine
- Quinapril
- Nicorandil
- Ivabradine

- PDE inhibitors (Sildenafil)
- Rho Kinase Inhibitors (Fasudil)
- Endothelin Receptors Antagonists (Darusentan, Atrasentan, Zibotentan)
- Adenosine Active Agents (Dypiridamole)
- Xanthine Derivates (Aminophylline)
- Autologous CD34+ stem cell therapy
- Tricyclic antidepressant drugs
- sGC stimulators (Vericiguat,Riociguat)

VASOSPASTIC ANGINA

- Calcium Channel Blockers*
- Nitrates
- Nicorandil
- Cilostazol
- Molsidomin

*first line treatment in vasospastic angina but they can also be used in microvascular angina

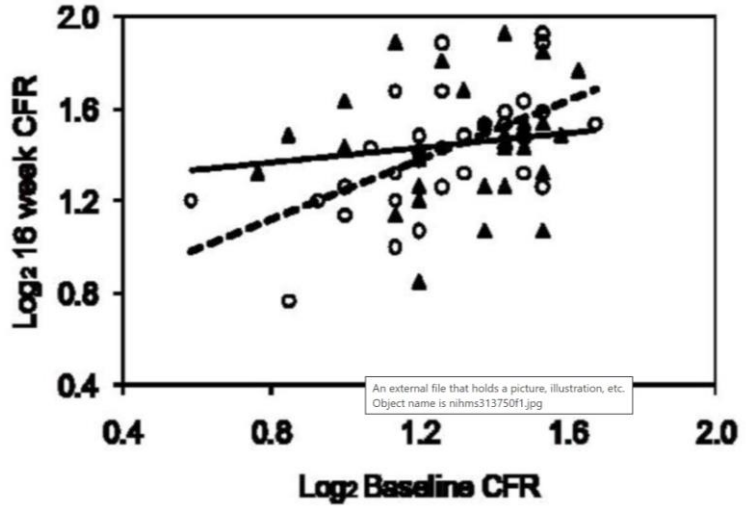
Marchini et al. Cardiovasc Drug Ther 2022; 2022 Jun 9. doi: 10.1007/s10557-022-07351-x

CMD Tx: ACE-inhibitors

In another study, treadmill exercise tests were performed in 14 patients with chest pain and non-obstructive CAD before and after i.v. aminophylline infusion. Aminophylline lengthened the time before the occurrence of ischemia by increasing the ischemia threshold and it also shows a beneficial effect on chest pain induced by exercise [17, 61].

Trimetazidine

Figure 1



ated with chronic pain [63]. In a randomized, double-blind, cross-over trial performed on 18 women with chest pain and non-obstructive CAD, imipramine reduced the incidence of chest pain compared with placebo but failed to improve quality of life [66].

Conclusion

Coronary (micro)vascular spasm and microvascular dysfunction are clinical entities characterized by high prevalence and clinical representation, burdened by an important clinical and symptomatologic impact. Numerous therapeutic strategies, both innovative and established, are available to optimize treatment and improve the quality of life of these patients (Fig. 1).

Author Contribution All authors contributed to this work.

Funding Open access funding provided by Università degli Studi di Ferrara within the CRUI-CARE Agreement.

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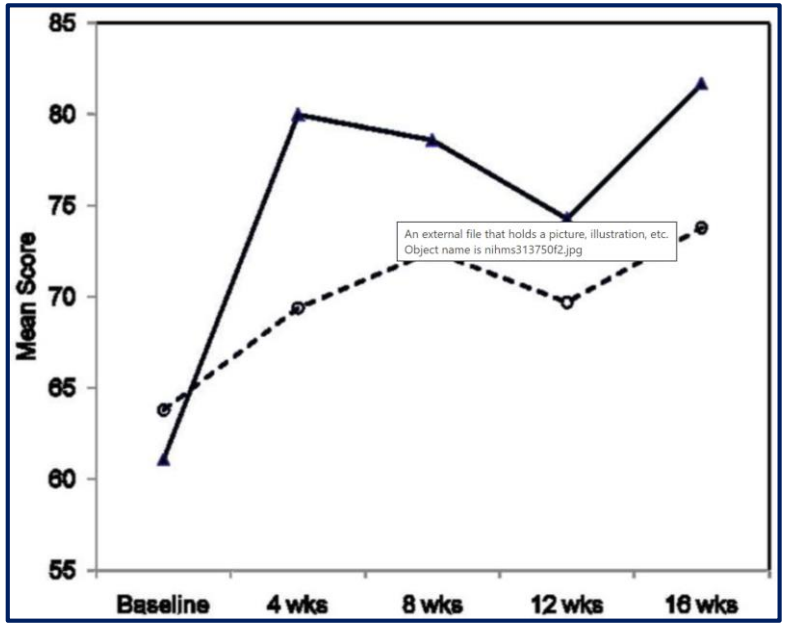

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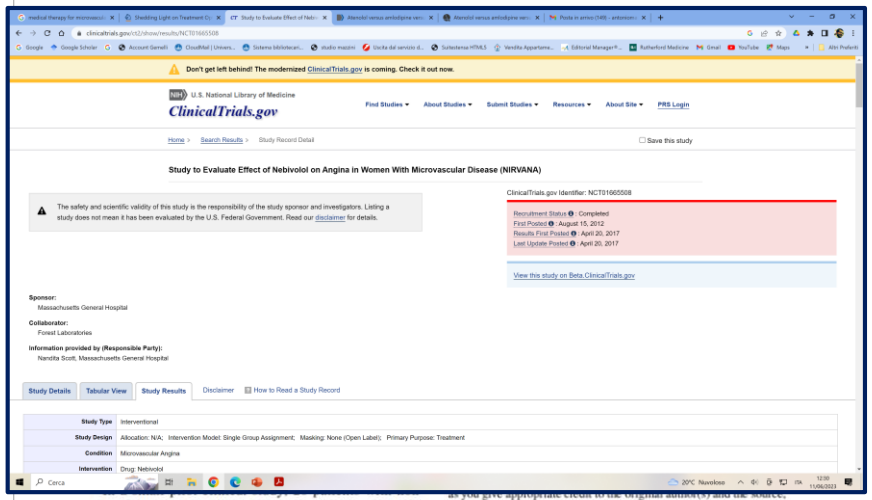
CMD Tx: Beta-Blockers



obstructive CAD, persistent angina and CFR ≤ 2.5 received a single intracoronary infusion of isolated CD34 + cells in the left anterior descending artery. After 6 months, CFR improved (from 2.08 ± 0.32 at baseline to 2.68 ± 0.79, $P < 0.005$), angina frequency decreased ($P < 0.004$), Canadian Cardiovascular Society class improved ($P < 0.001$), and quality of life improved as assessed by the Seattle Angina Questionnaire ($P \leq 0.03$) and SF-36 ($P \leq 0.04$) [64].

Tricyclic Antidepressant Drugs

Tricyclic antidepressant drugs are a class of medications used for the management and treatment of major depressive disorders. Previous studies have suggested that they may have a beneficial effect on a wide range of conditions associated with chronic pain [65]. In a randomized, double-blind, cross-over trial performed on 18 women with chest pain and non-obstructive CAD, imipramine reduced the incidence of chest pain compared with placebo but failed to improve quality of life [66].

Conclusion

Coronary (micro)vascular spasm and microvascular dysfunction are clinical entities characterized by high prevalence and clinical representation, burdened by an important clinical and symptomatologic impact. Numerous

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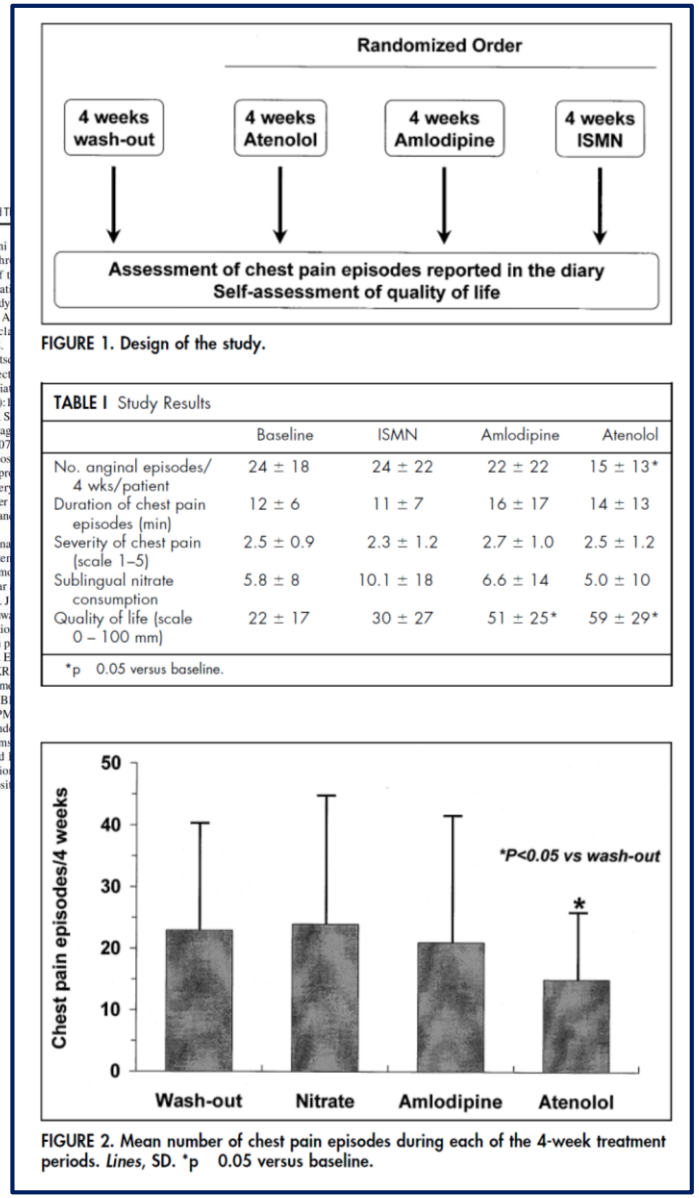

FIGURE 1. Design of the study.

TABLE I Study Results

	Baseline	ISMN	Amlodipine	Atenolol
No. anginal episodes/ 4 wks/patient	24 ± 18	24 ± 22	22 ± 22	15 ± 13*
Duration of chest pain episodes (min)	12 ± 6	11 ± 7	16 ± 17	14 ± 13
Severity of chest pain (scale 1–5)	2.5 ± 0.9	2.3 ± 1.2	2.7 ± 1.0	2.5 ± 1.2
Sublingual nitrate consumption	5.8 ± 8	10.1 ± 18	6.6 ± 14	5.0 ± 10
Quality of life (scale 0 – 100 mm)	22 ± 17	30 ± 27	51 ± 25*	59 ± 29*

*p 0.05 versus baseline.

FIGURE 2. Mean number of chest pain episodes during each of the 4-week treatment periods. *Lines*, SD. *p 0.05 versus baseline.

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CMD Tx: Nicorandil Ranolazine Ivabradine

Table 2
SAQ and EuroQoL scores at baseline and after 4 weeks of treatment in the 3 groups

	Ivabradine	Ranolazine	Placebo	p	p*
Physical limitation					<0.001
Baseline	65.4 ± 15	69.8 ± 16	68.2 ± 20	0.78	
Follow-up	76.5 ± 16	84.1 ± 12	67.0 ± 21	<0.001‡	
Angina stability					<0.001
Baseline	43.8 ± 30	40.0 ± 25	56.7 ± 26	0.23	
Follow-up	56.3 ± 33	90.0 ± 18†	55.0 ± 25	<0.001‡	
Angina frequency					<0.001
Baseline	64.4 ± 14	61.3 ± 12	72.7 ± 17	0.10	
Follow-up	73.1 ± 18	81.3 ± 17†	71.3 ± 18	0.001‡	
Treatment satisfaction					<0.001
Baseline	75.8 ± 15	68.8 ± 16	75.8 ± 15	0.36	
Follow-up	84.4 ± 14	90.8 ± 9†	74.2 ± 14	<0.001‡	
Disease perception					<0.001
Baseline	49.5 ± 23	45.0 ± 17	60.0 ± 22	0.15	
Follow-up	62.5 ± 26	79.4 ± 14†	57.2 ± 23	<0.001‡	
EuroQoL VAS					<0.001
Baseline	66.6 ± 14	61.3 ± 17	65.7 ± 17	0.62	
Follow-up	72.5 ± 17	79.3 ± 13†	64.3 ± 19	<0.001‡	

Data are reported as means (SD).
* p for differences in changes from baseline to follow-up in the 3 groups.
† p <0.05 for differences in changes versus ivabradine.
‡ p values for direct comparisons of follow-up variables, adjusted for basal values.

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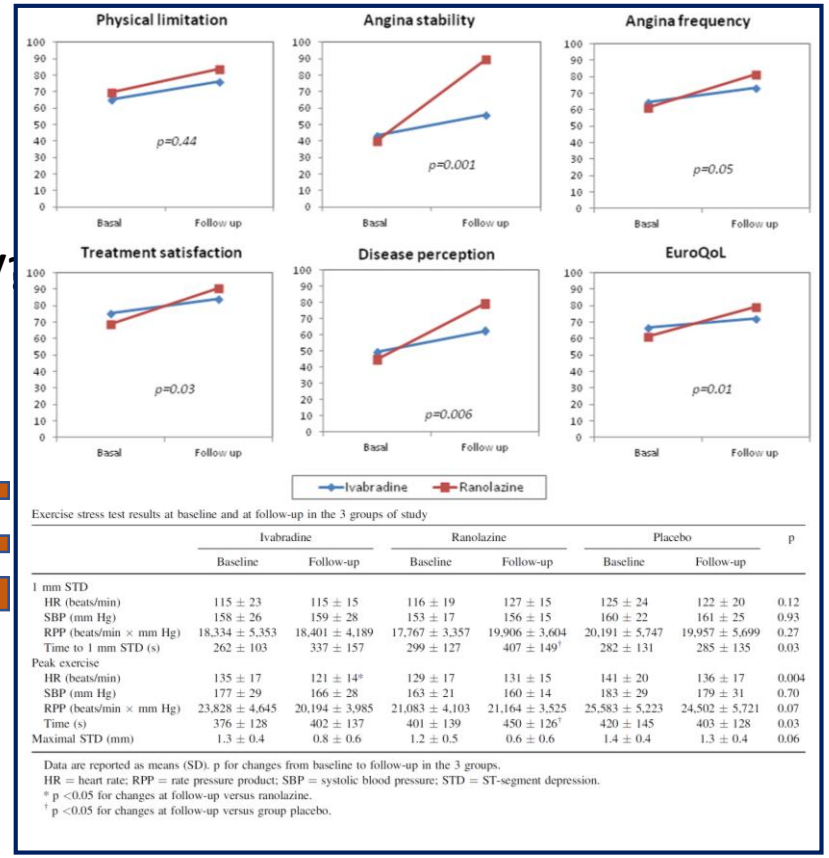

Exercise stress test results at baseline and at follow-up in the 3 groups of study

	Ivabradine		Ranolazine		Placebo		p
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	
1 mm STD							
HR (beats/min)	115 ± 23	115 ± 15	116 ± 19	127 ± 15	125 ± 24	122 ± 20	0.12
SBP (mm Hg)	158 ± 26	159 ± 28	153 ± 17	156 ± 15	160 ± 22	161 ± 25	0.93
RPP (beats/min × mm Hg)	18,334 ± 5,353	18,401 ± 4,189	17,767 ± 3,357	19,906 ± 3,604	20,191 ± 5,747	19,957 ± 5,699	0.27
Time to 1 mm STD (s)	262 ± 103	337 ± 157	299 ± 127	407 ± 149†	282 ± 131	285 ± 135	0.03
Peak exercise							
HR (beats/min)	135 ± 17	121 ± 14*	129 ± 17	131 ± 15	141 ± 20	136 ± 17	0.004
SBP (mm Hg)	177 ± 29	166 ± 28	163 ± 21	160 ± 14	183 ± 29	179 ± 31	0.70
RPP (beats/min × mm Hg)	23,828 ± 4,645	20,194 ± 3,985	21,083 ± 4,103	21,164 ± 3,525	25,583 ± 5,223	24,502 ± 5,721	0.07
Time (s)	376 ± 128	402 ± 137	401 ± 139	450 ± 126†	420 ± 145	403 ± 128	0.03
Maximal STD (mm)	1.3 ± 0.4	0.8 ± 0.6	1.2 ± 0.5	0.6 ± 0.6	1.4 ± 0.4	1.3 ± 0.4	0.06

Data are reported as means (SD). p for changes from baseline to follow-up in the 3 groups.
HR = heart rate; RPP = rate pressure product; SBP = systolic blood pressure; STD = ST-segment depression.
* p <0.05 for changes at follow-up versus ranolazine.
† p <0.05 for changes at follow-up versus group placebo.

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CMD Tx: Xanthine Derivates

In another study, treadmill exercise tests were performed in 14 patients with chest pain and non-obstructive CAD before and after i.v. aminophylline infusion. Aminophylline lengthened the time before the occurrence of ischemia by increasing the ischemia threshold and it also shows a beneficial effect on chest pain induced by exercise [17, 61].

Trimetazidine

Trimetazidine is an antianginal agent which is able to modulate cardiac metabolism without altering the hemodynamic functions. Furthermore, it has a positive effect on the inflammatory profile and endothelial function [62]. In a randomized trial of patients with MVA, trimetazidine on top of medical therapy for 3 months improved symptoms, quality of life and exercise tolerance by the improvement of myocardial perfusion and endothelial function [17, 63].

Autologous CD34 + Stem Cell Therapy

Stem cell therapy using autologous CD34 + may be a promising therapy for patients with microvascular dysfunction. In fact, CD34 + cells stimulate capillary growth and regeneration of damaged microcirculation in pre-clinical models.

In a small pilot clinical study, 20 patients with non-obstructive CAD, persistent angina and CFR ≤ 2.5 received a single intracoronary infusion of isolated CD34 + cells in the left anterior descending artery. After 6 months, CFR improved (from 2.08 ± 0.32 at baseline to 2.68 ± 0.79, $P < 0.005$), angina frequency decreased ($P < 0.004$), Canadian Cardiovascular Society class improved ($P < 0.001$), and quality of life improved as assessed by the Seattle Angina Questionnaire ($P \leq 0.03$) and SF-36 ($P \leq 0.04$) [64].

Tricyclic Antidepressant Drugs

Tricyclic antidepressant drugs are a class of medications used for the management and treatment of major depressive disorders. Previous studies have suggested that they may have a beneficial effect on a wide range of conditions associated with chronic pain [65]. In a randomized, double-blind, cross-over trial performed on 18 women with chest pain and non-obstructive CAD, imipramine reduced the incidence of chest pain compared with placebo but failed to improve quality of life [66].

Conclusion

Coronary (micro)vascular spasm and microvascular dysfunction are clinical entities characterized by high prevalence and clinical representation, burdened by an important clinical and symptomatologic impact. Numerous therapeutic strategies, both innovative and established, are available to optimize treatment and improve the quality of life of these patients (Fig. 1).

Author Contribution All authors contribut

Funding Open access funding provided b
Ferrara within the CRUI-CARE Agreemen

Data Availability Not applicable.

Code Availability Not applicable.

Declarations

Ethics Approval Not applicable.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

Competing Interests The authors declare

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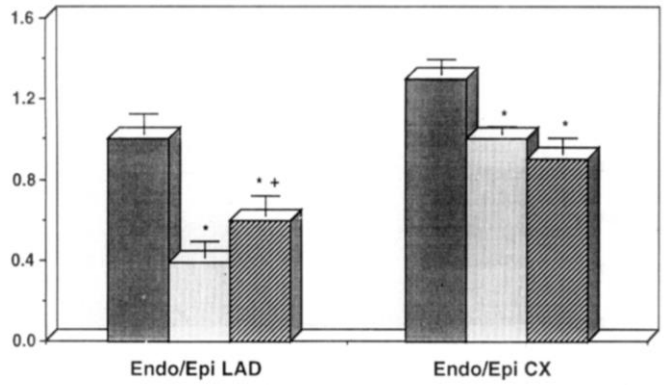

Fig. 4. Values (mean ± SEM) of endo/epi flow ratio in the left anterior descending coronary artery (Endo/Epi LAD) and in circumflex artery *(Endo/Epi Cx)* territories during baseline *(dark stippled histograms)*, during control pacing *(pale stippled histograms)*, and during pacing after aminophylline *(hatched histograms)*. *Asterisk*, $p < 0.01$ vs baseline; *Plus*, $p < 0.01$ vs control pacing.

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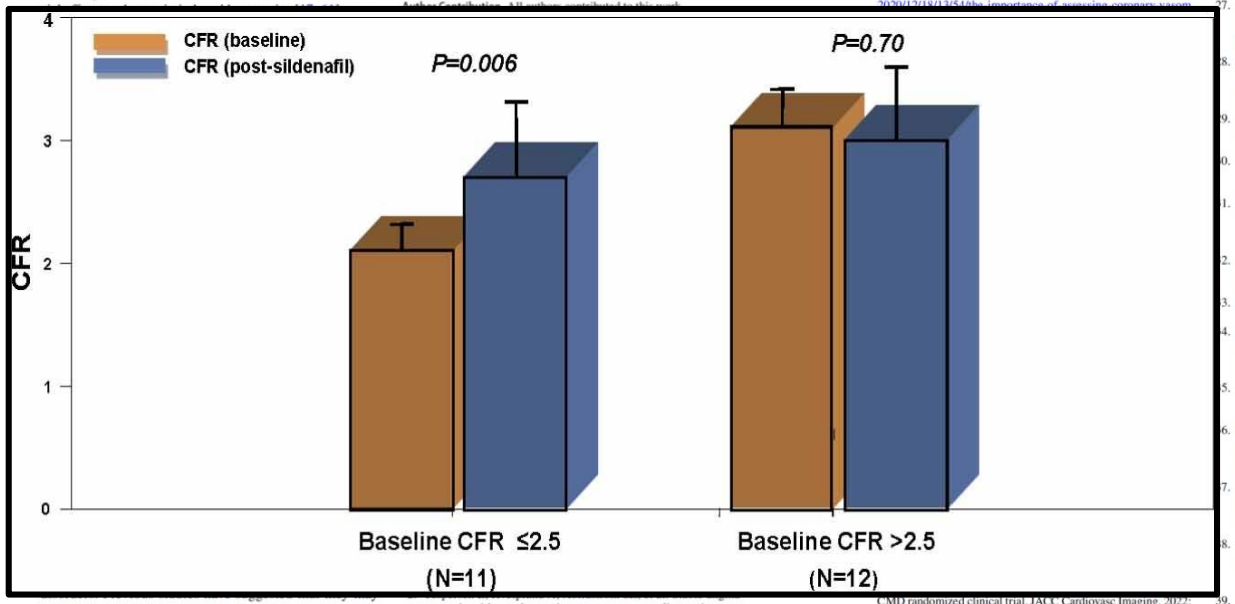
CMD Tx: Nitric Oxide and cGMP Pathway

In another study, treadmill exercise tests were performed in 14 patients with chest pain and non-obstructive CAD before and after i.v. aminophylline infusion. Aminophylline lengthened the time before the occurrence of ischemia by increasing the ischemia threshold and it also shows a benefi-

therapeutic strategies, both innovative and established, are available to optimize treatment and improve the quality of life of these patients (Fig. 1).



have a beneficial effect on a wide range of conditions associated with chronic pain [65]. In a randomized, double-blind, cross-over trial performed on 18 women with chest pain and non-obstructive CAD, imipramine reduced the incidence of chest pain compared with placebo but failed to improve quality of life [66].

Conclusion

Coronary (micro)vascular spasm and microvascular dysfunction are clinical entities characterized by high prevalence and clinical representation, burdened by an important clinical and symptomatologic impact. Numerous

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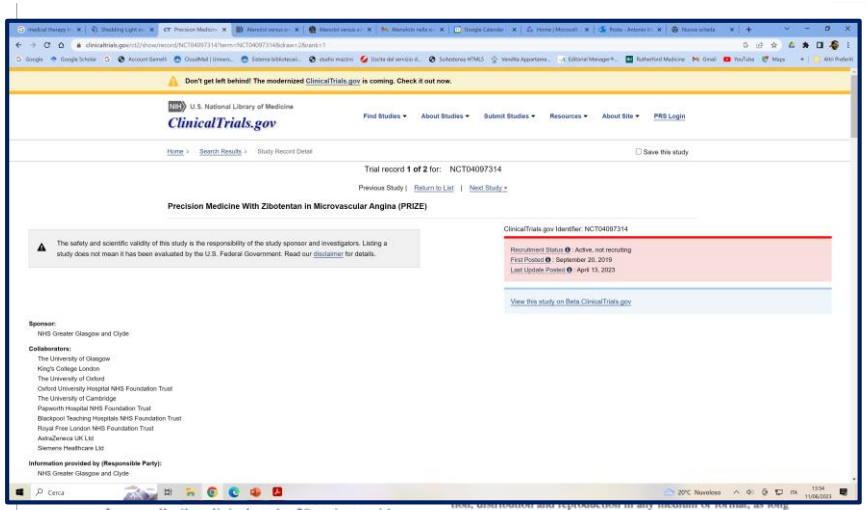
CMD Tx: Endothelin Receptor Antagonists



In a small pilot clinical study, 20 patients with non-obstructive CAD, persistent angina and CFR ≤ 2.5 received a single intracoronary infusion of isolated CD34+cells in the left anterior descending artery. After 6 months, CFR improved (from 2.08 ± 0.32 at baseline to 2.68 ± 0.79, $P < 0.005$), angina frequency decreased ($P < 0.004$), Canadian Cardiovascular Society class improved ($P < 0.001$), and quality of life improved as assessed by the Seattle Angina Questionnaire ($P \leq 0.03$) and SF-36 ($P \leq 0.04$) [64].

Tricyclic Antidepressant Drugs

Tricyclic antidepressant drugs are a class of medications used for the management and treatment of major depressive disorders. Previous studies have suggested that they may have a beneficial effect on a wide range of conditions associated with chronic pain [65]. In a randomized, double-blind, cross-over trial performed on 18 women with chest pain and non-obstructive CAD, imipramine reduced the incidence of chest pain compared with placebo but failed to improve quality of life [66].

Conclusion

Coronary (micro)vascular spasm and microvascular dysfunction are clinical entities characterized by high prevalence and clinical representation, burdened by an important clinical and symptomatologic impact. Numerous

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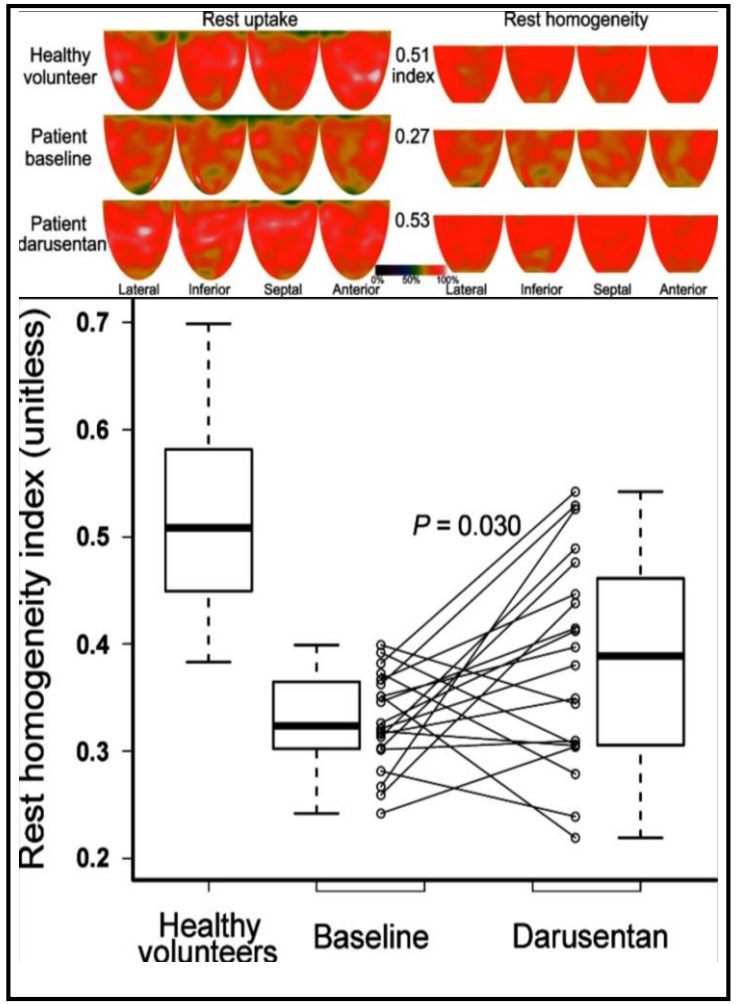

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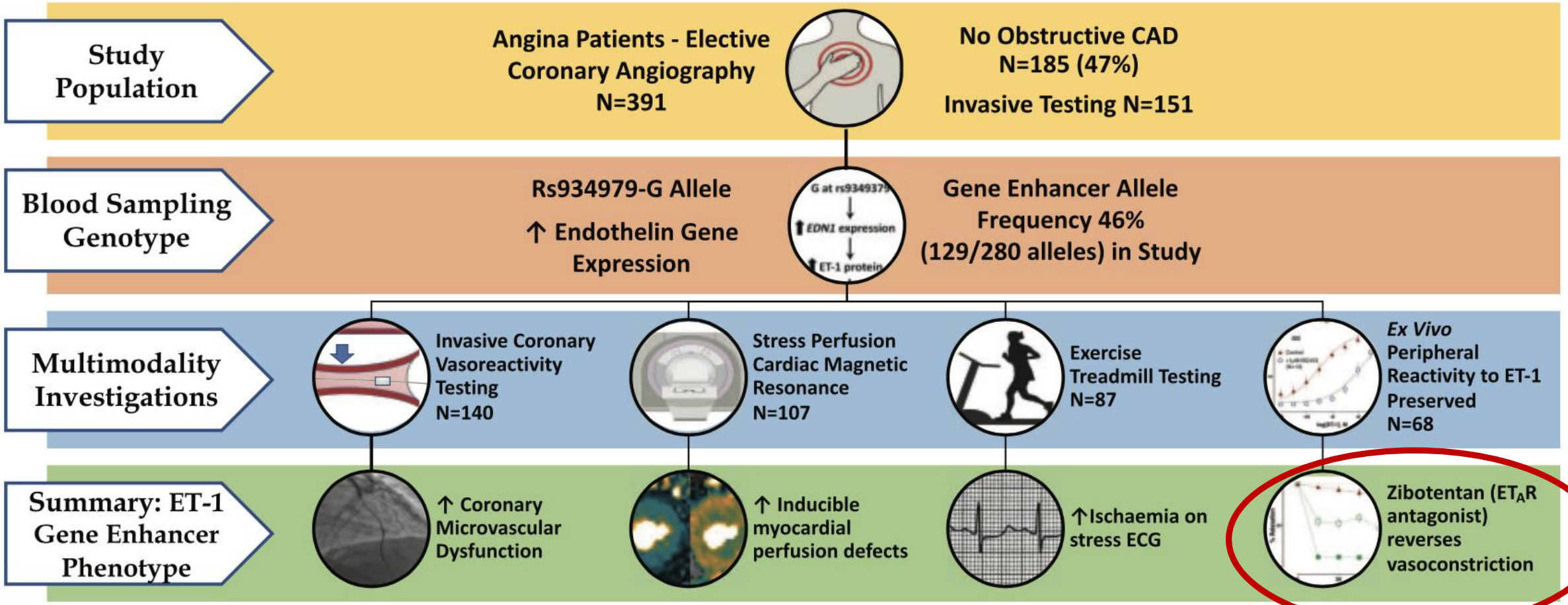
#FullPhysiology InDailyPractice

Genetic dysregulation of endothelin-1 is implicated in coronary microvascular dysfunction

Thomas J. Ford [1,2,3], David Corcoran [1,4], Sandosh Padmanabhan [1],



European Heart Journal (2020) 41, 3239–3251

CMD Tx: Ivabradine

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Trimetazidine

Trimetazidine is an antianginal agent which is able to modulate cardiac metabolism without altering the hemodynamic functions. Furthermore, it has a positive effect on the inflammatory profile and endothelial function [62]. In a randomized trial of patients with MVA, trimetazidine on top of medical therapy for 3 months improved symptoms, quality of life and exercise tolerance by the improvement of myocardial perfusion and endothelial function [17, 63].

Autologous CD34 + Stem Cell Therapy

Stem cell therapy using autologous CD34 + may be a promising therapy for patients with microvascular dysfunction. In fact, CD34 + cells stimulate capillary growth and regeneration of damaged microcirculation in pre-clinical models.

In a small pilot clinical study, 20 patients with non-obstructive CAD, persistent angina and CFR ≤ 2.5 received a single intracoronary infusion of isolated CD34 + cells in the left anterior descending artery. After 6 months, CFR improved (from 2.08 ± 0.32 at baseline to 2.68 ± 0.79, $P < 0.005$), angina frequency decreased ($P < 0.004$), Canadian Cardiovascular Society class improved ($P < 0.001$), and quality of life improved as assessed by the Seattle Angina Questionnaire ($P \leq 0.03$) and SF-36 ($P \leq 0.04$) [64].

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Author Contribution All authors contributed to this work.

Funding Open access funding provided by Università degli Studi di Ferrara within the CRUI-CARE Agreement.

Data Availability Not applicable.

Code Availability Not applicable.

Declarations

Ethics Approval Not applicable.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

Competing Interests The authors declare no competing interests.

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Marchini et al. Cardiovasc Drug Ther 2022; 2022 Jun 9. doi: 10.1007/s10557-022-07351-x

#FullPhysiology InDailyPractice

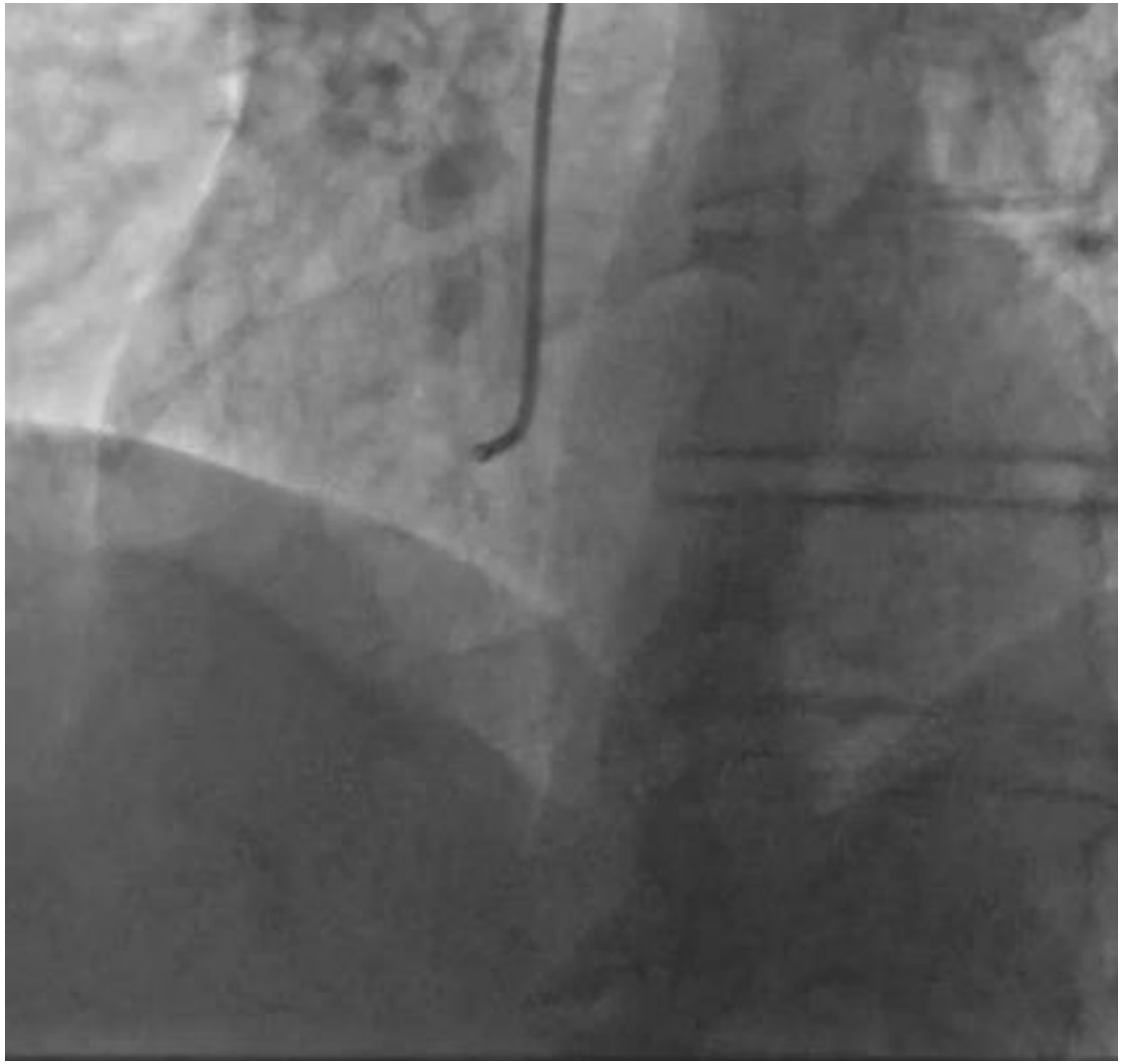
MiVA case 1 – clinical presentation

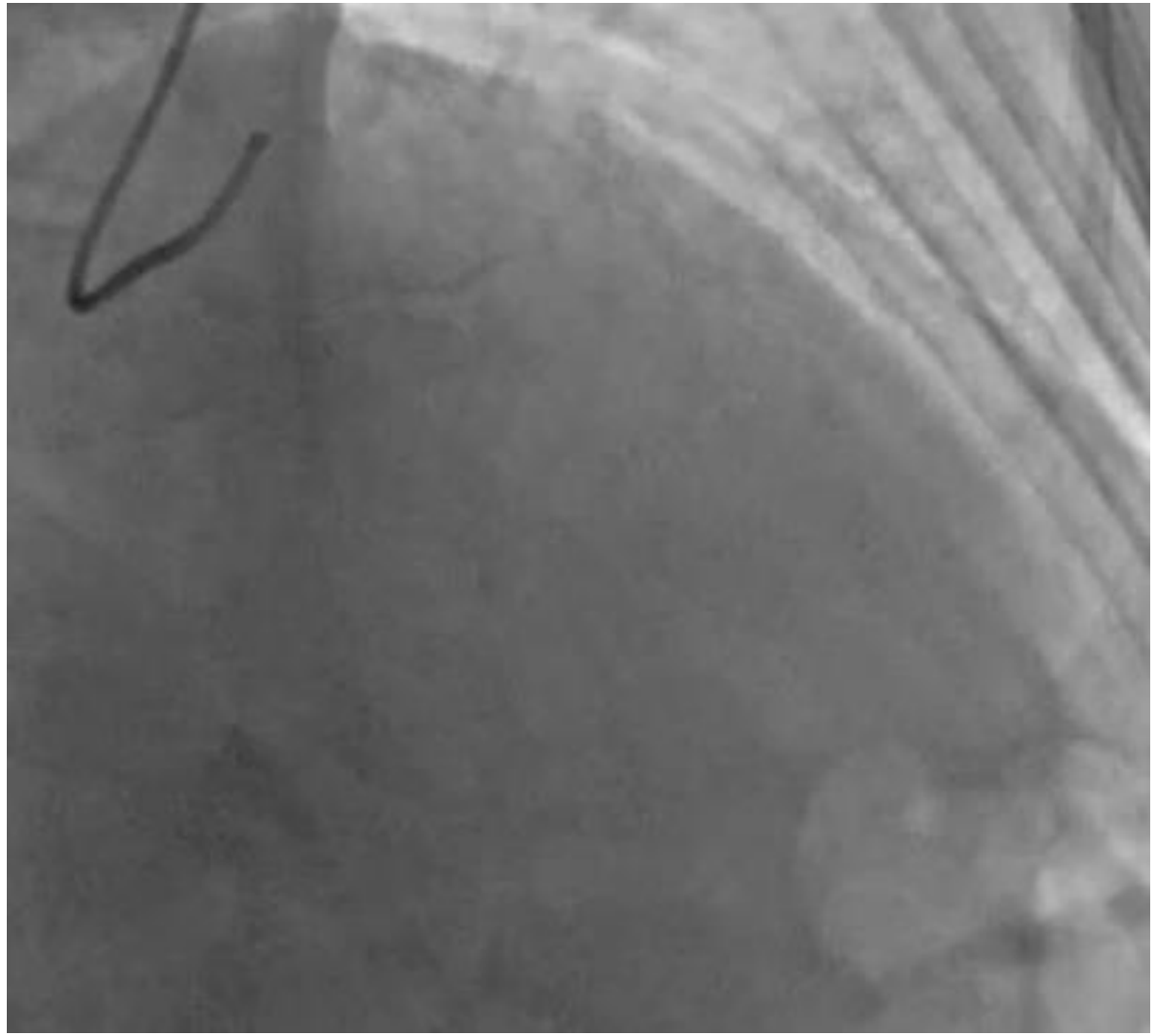
- 65 year-old male gentleman
- HTN, active smoker, dyslipidemia

- Exertional chest pain for the past 3 years (CCS II)
- March 2023 – SPET shows inferior ischemia
- July 2023 – CTCA shows unobstructed coronary arteries
- February 2024 – outpatient evaluation due to persistent chest pain

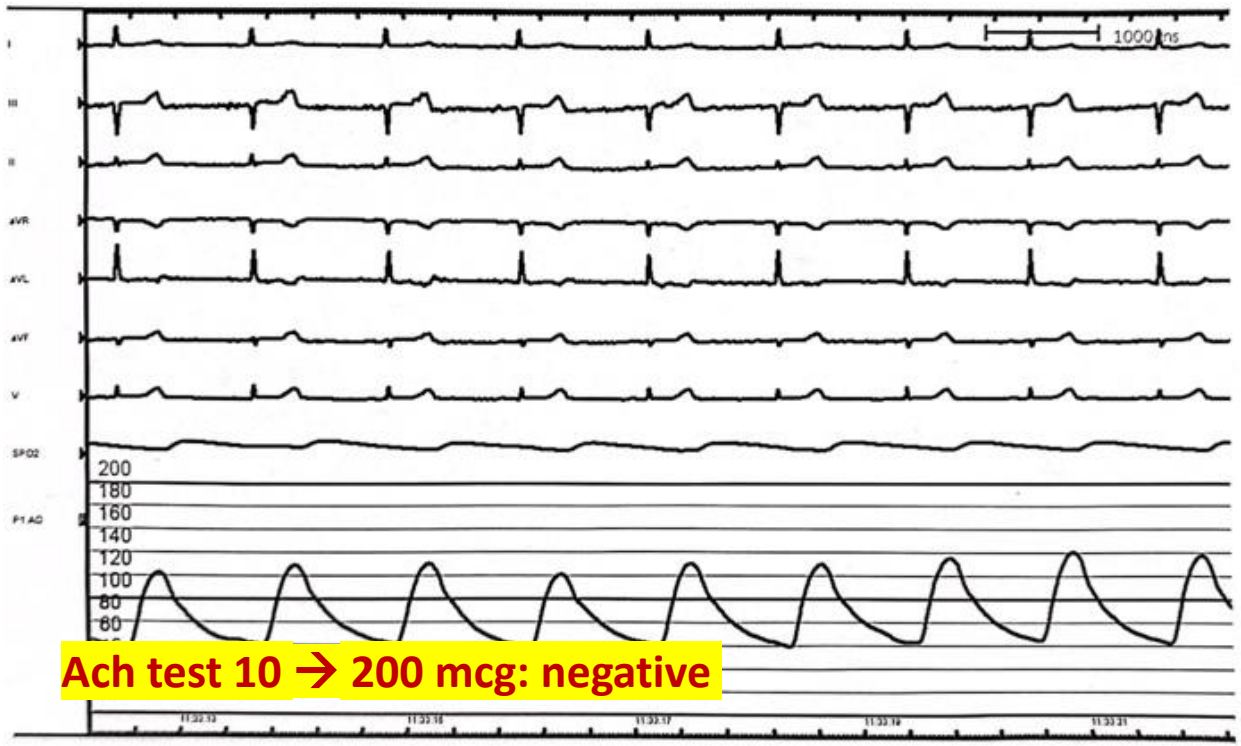
Tx: aspirin, bisoprolol 2.5 mg OD, rosuvastatin/ezetimibe 10/10 mg, PPI, ivabradine 5 mg BID, ranolazine 375 mg BID

MiVA case 1 – coronary angiogram

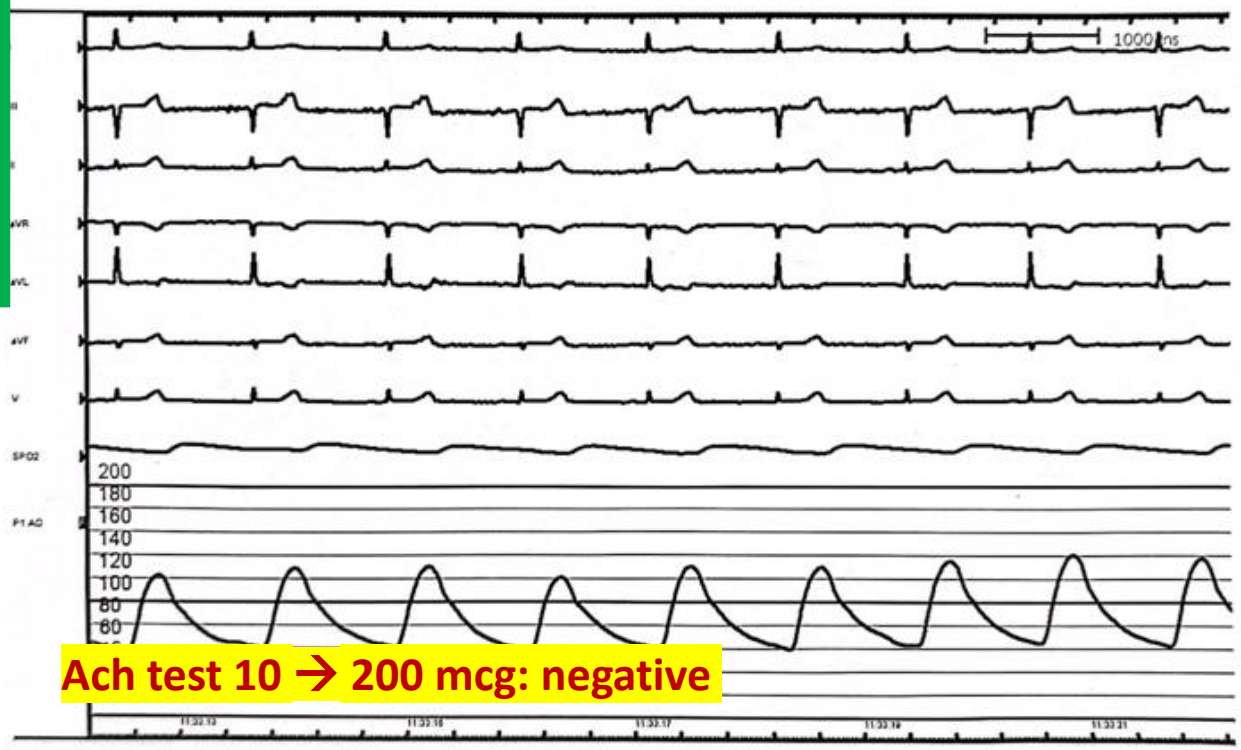




MiVA case 1 - #FullPhysiology, final diagnosis and management



MiVA case 1 - #FullPhysiology, final diagnosis and management



- Non-cardiac chest pain
- Stop aspirin, PPI, bisoprolol, ranolazine and ivabradine

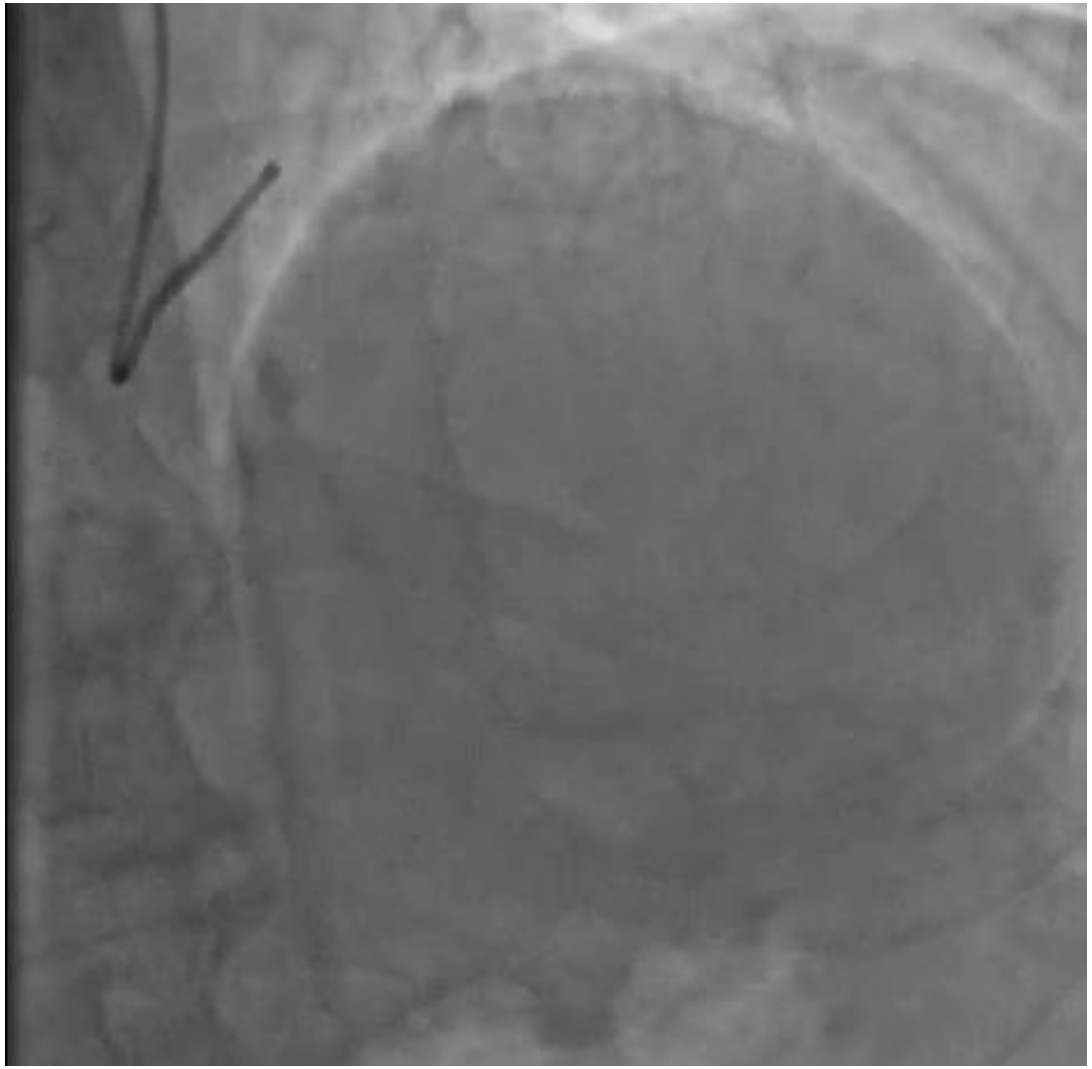
MiVA case 2 – clinical presentation

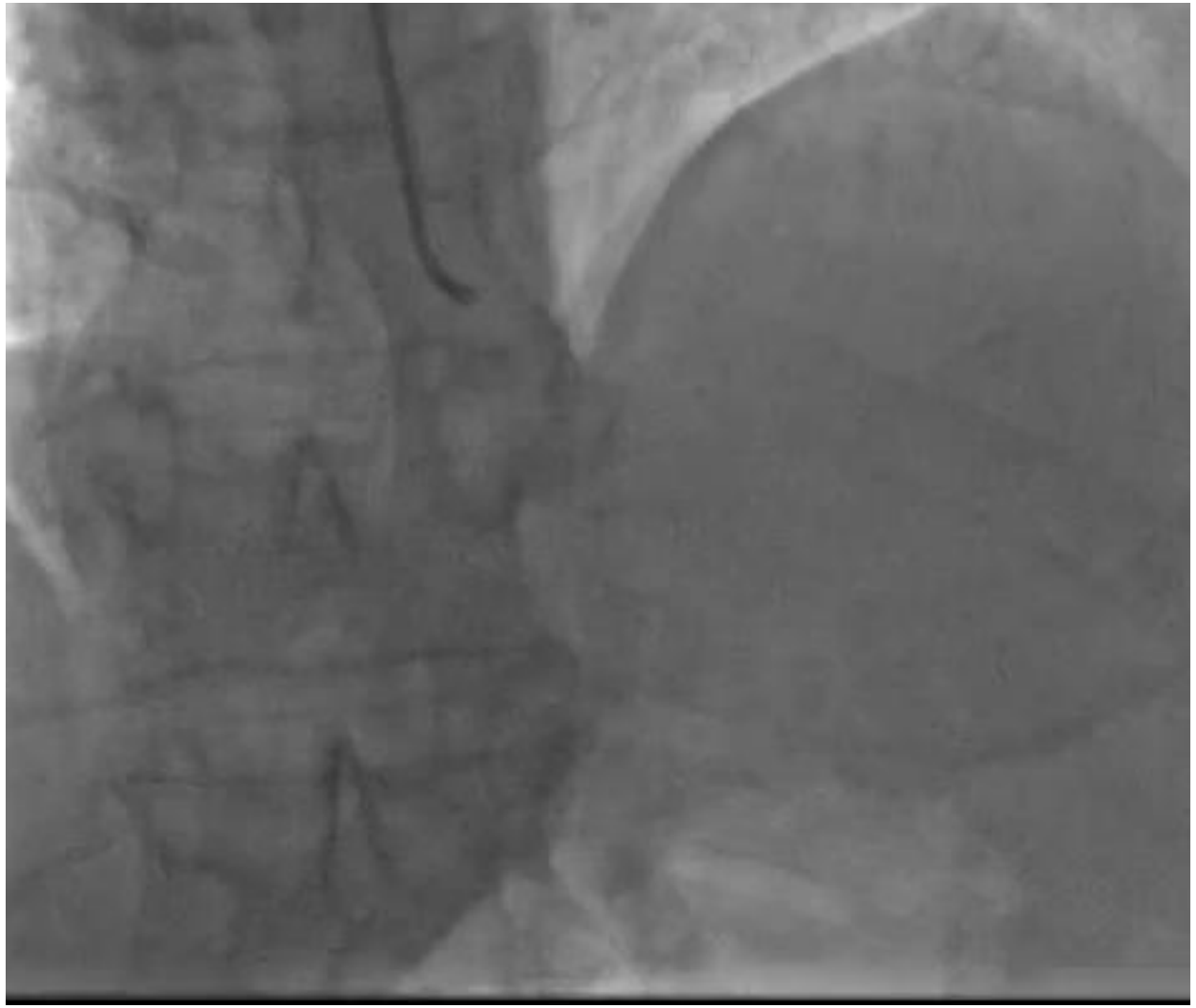
- 75 year-old male gentleman
- HTN, former smoker, family history CV disease, dyslipidemia

- 2014 – inferior STEMI, DES to RCA
- 2023 – new onset of exertional chest pain
- January 2024 – Treadmill test positive for symptoms (chest pain, 150 W) with borderline ECG

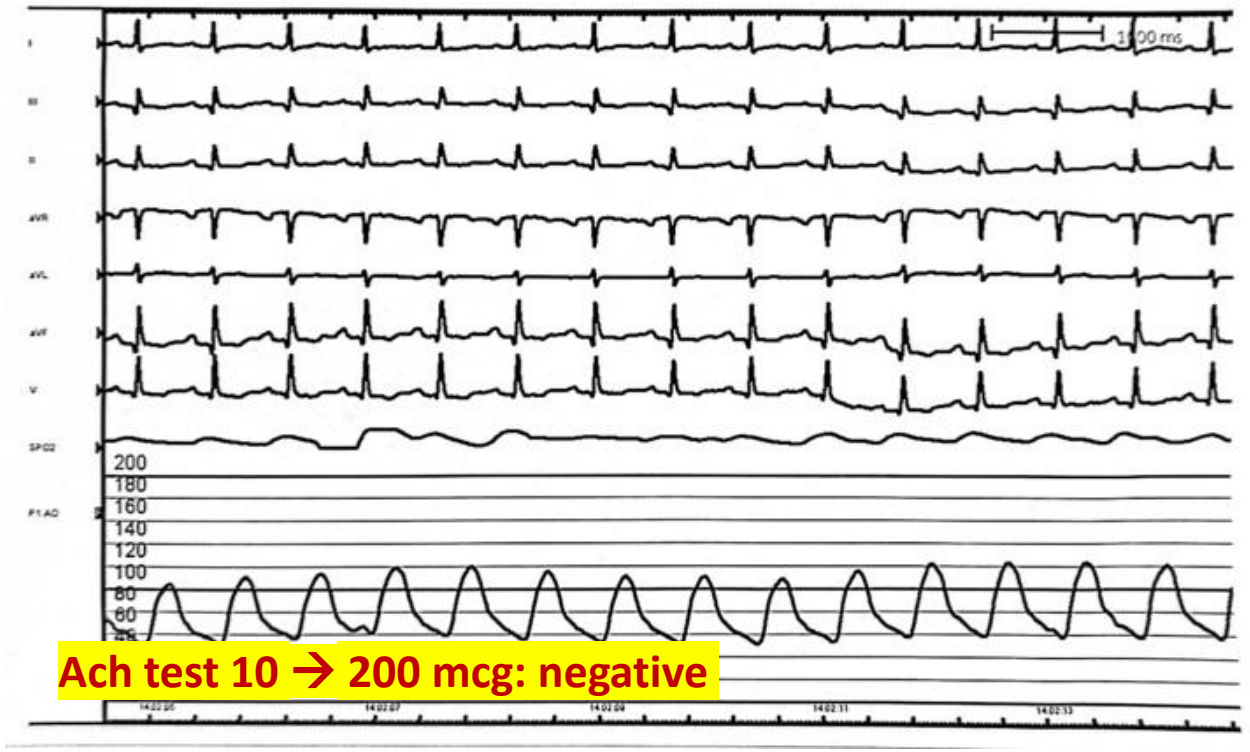
Tx: aspirin, bisoprolol 1.25 mg, rosuvastatin/ezetimibe 10/10 mg, PPI, ramipril 2.5 mg

MiVA case 1 – coronary angiogram

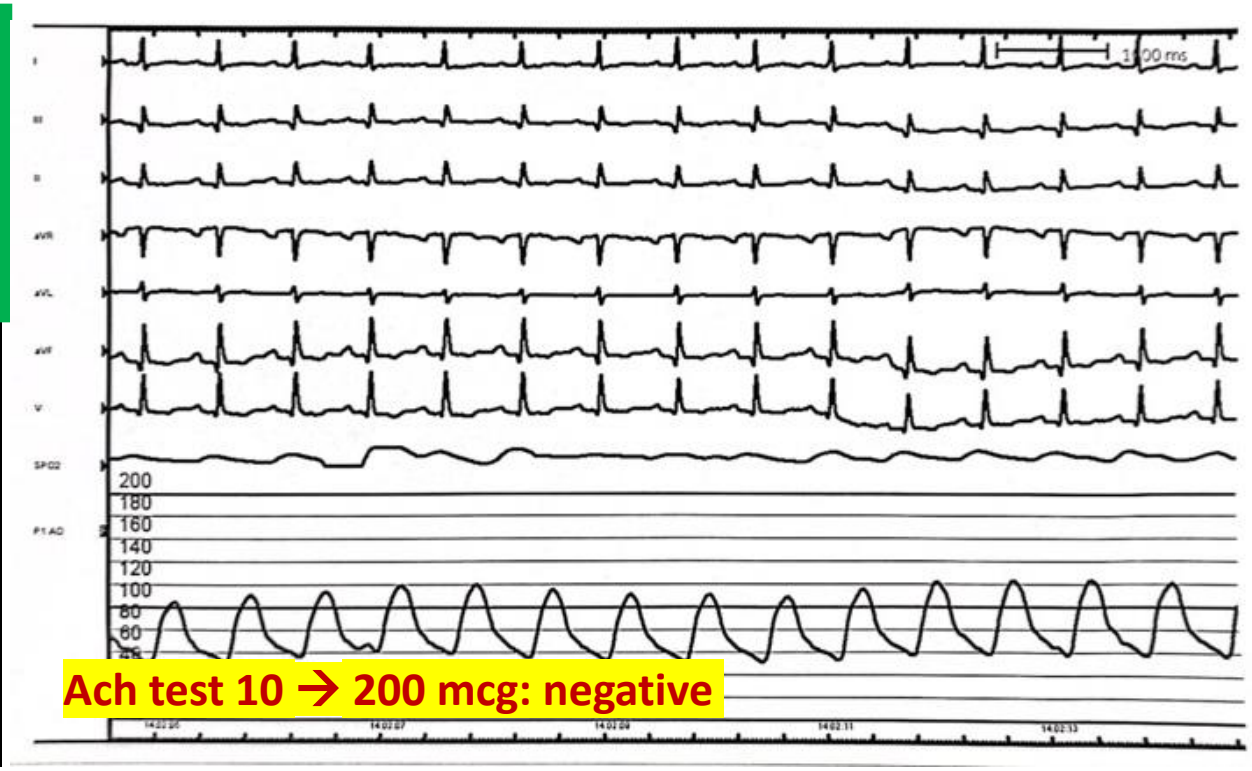




MiVA case 1 - #FullPhysiology, final diagnosis and management



MiVA case 1 - #FullPhysiology, final diagnosis and management



- Functional CMD
- Bisoprol up-titration up to 2.5 mg BD and start ranolazine 375 mg BD

CorCTCA trial

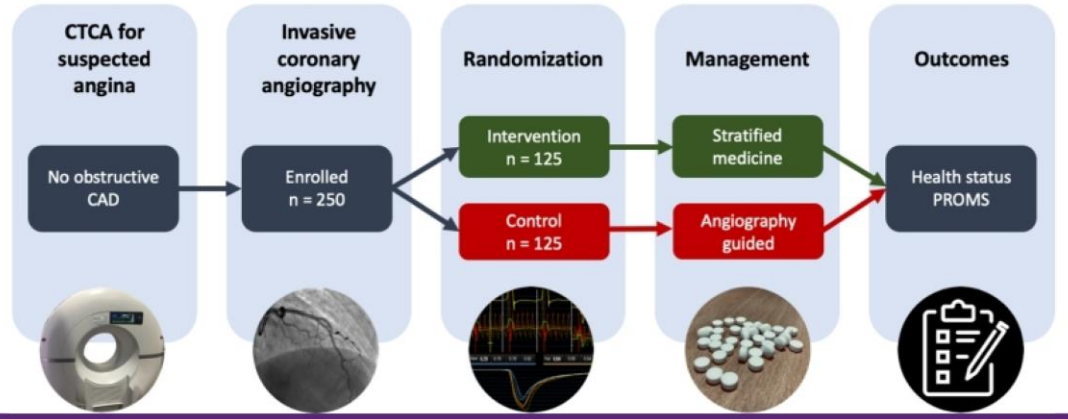
Study Design

The BHF COR-CTCA Trial

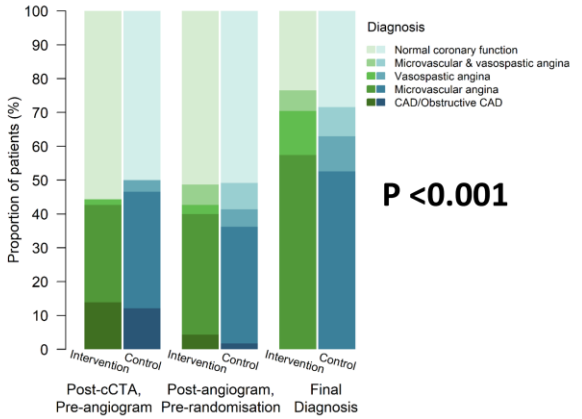
Multicentre, randomized-controlled, blinded clinical trial

Clinicaltrials.gov - NCT03477890

British Heart Foundation



Primary outcome – final diagnosis, intervention vs. control.



P <0.001

↑ MVA and/or VSA

Odds ratio (95% CI): 4.05 (2.32 to 7.24) (p<0.001) ↑ diagnosis MVA / VSA; ↑ to 76.5% (frequency)

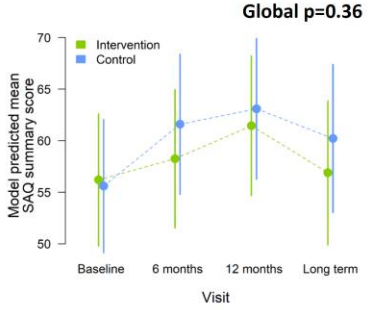
↓ Non-cardiac chest pain (normal coronary function)

Pre- randomization - 51.3% vs 50.9%

↓x2 post - 23.5% vs 50.9%, (p<0.001).

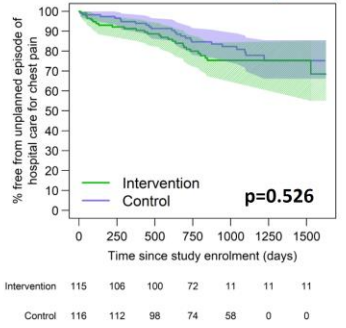
Secondary outcomes

Angina burden, SAQ



Mild angina at baseline, not different in follow-up

Unplanned episodes of care for chest pain



High burden, not different

Improvements –

↑ Treatment satisfaction (TSQM-9)
9.24 (1.97 to 16.52); p=0.013

↑ Normal Systolic BP < 130 mmHg
43.3% vs. 32.3%;
1.97 (1.00 to 3.90); p=0.051

↓ Systolic BP
5.59 (-10.99 to -0.19); p=0.044

↓ Healthcare tests

CV	0 vs 6%; p=0.014
Non-CV	3.5 vs 17.2%; p<0.001

Italian registries

INOCA Ischemia with Non-Obstructive Coronary Artery disease

INOCA-IT Registry

- IRCCS San Raffaele Hospital, Milano
- Policlinico Universitario A. Gemelli IRCCS/ Ospedale Fatebenefratelli Gemelli Isola, Roma
- Azienda Ospedaliera Universitaria Federico II, Napoli

Cardiologia Federico II

Università degli Studi di Napoli FEDERICO II
AZIENDA OSPEDALIERA UNIVERSITARIA

Dipartimento ad Attività Integrate di Emergenze Cardiovascolari, Medicina Clinica e dell'Invecchiamento

UOC Cardiologia Emodinamica e UTIC
Direttore: Prof. **Giovanni Esposito**

PROTOCOLLO DI STUDIO CLINICO

Caratterizzazione di diversi fenotipi di disfunzione microvascolare e il loro impatto sulla severità dell'angina nei pazienti con angina cronica in assenza di malattia coronarica ostruttiva.

Versione 1.1 del 12/05/2023

Titolo breve: Studio MiVa: uno studio di registro multicentrico in pazienti con angina microvascolare

Sponsor
Dipartimento di Scienze Biomediche Avanzate dell'università Federico II di Napoli
P.I. Prof. Giovanni Esposito-Prof. Ciro Indolfi
Co-P.I. Prof. Luigi Di Serafino; Prof. Alberto Polimeni
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COMPLETED

Precision Medicine With Zibotentan in Microvascular Angina (PRIZE)

ClinicalTrials.gov ID NCT04097314

Sponsor NHS Greater Glasgow and Clyde

Information provided by NHS Greater Glasgow and Clyde (Responsible Party)

Last Update Posted 2023-08-04

Official Title	ICMJE	A Randomised, Double-blind, Placebo-controlled, Cross-over Trial of Zibotentan in Microvascular Angina
Brief Summary		Microvascular angina (MVA) is caused by abnormalities of the small vessels in the heart. Endothelin is a small chemical that circulates and accumulates in the blood vessel walls, causing them to narrow or go into spasm and thicken in the longer term especially as levels of endothelin increase. As a result, patients experience pain, psychological burden and an inability to carry out daily activities. Originally developed by AstraZeneca for cancer treatment, prior research has confirmed that Zibotentan relaxes the small blood vessels of patients with MVA which lends support to the idea that Zibotentan may bring some benefits to patients with MVA. This trial therefore proposes to look into re-purposing zibotentan as a new treatment for patients with MVA. The primary objective is to assess the effect of add-on treatment with Zibotentan to treadmill exercise times in adult patients with MVA and impaired exercise intolerance. Zibotentan could provide a new treatment pathway for patients, as well as be made available to the NHS at substantially lower cost than the currently used medications.

Conclusions

1. Microvascular angina can derive from some different endotypes of CMD

2. #FullPhysiology can allow a **correct diagnosis** with potentially relevant therapeutic and prognostic implications

3. This approach is currently being evaluated in the Italian clinical reality

4. Probably, in the next future, new drugs will be available and more effective in microvascular angina

#Grazi

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