ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ
ΚΑΡΔΙΟΜΕΤΑΒΟΛΙΚΗ ΙΑΤΡΙΚΗ

Μικροκυκλοφορία στην Αρτηριακή Υπέρταση

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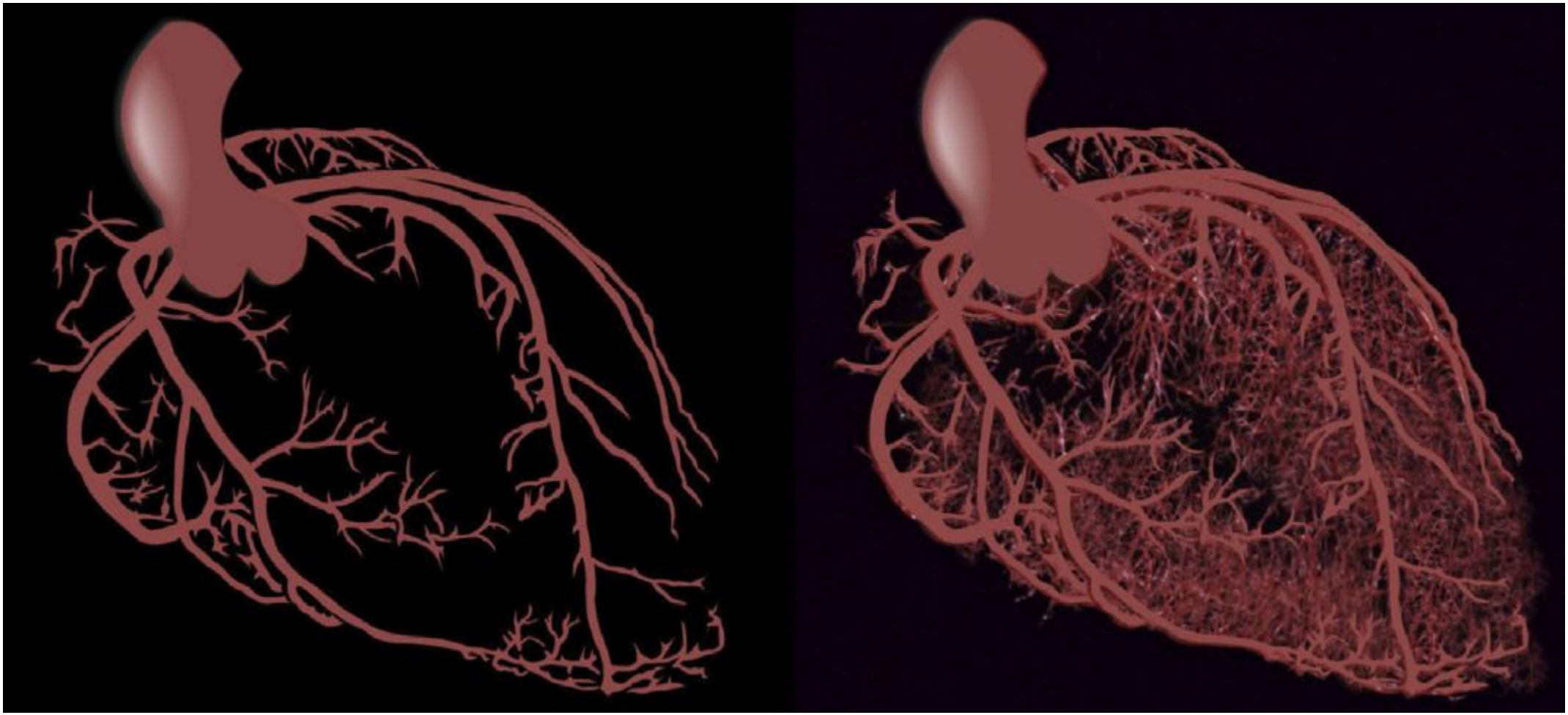
ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΑΘΗΝΩΝ
ΙΠΠΟΚΡΑΤΕΙΟ

Δήλωση Σύγκρουσης Συμφερόντων

Καμία

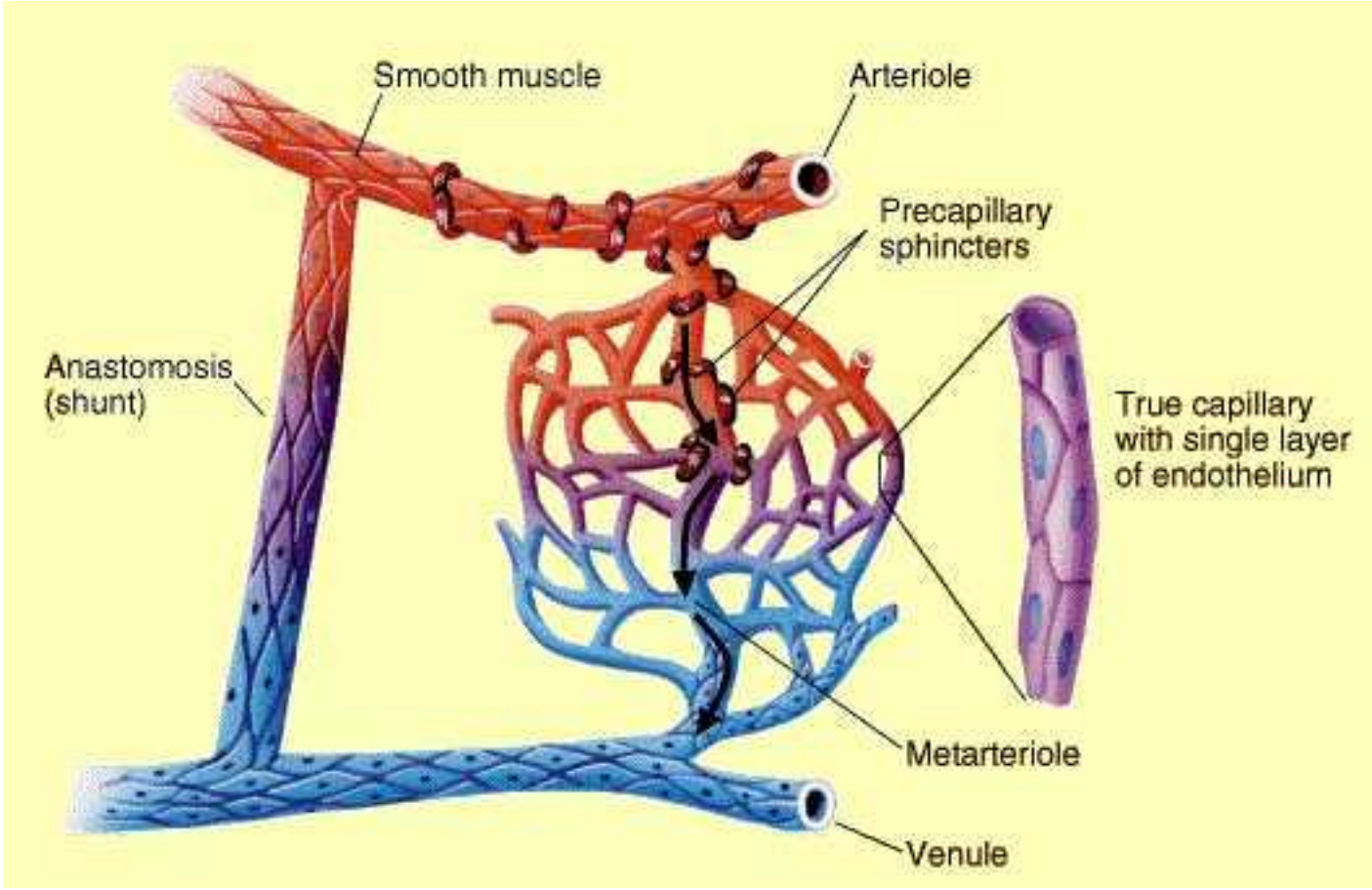
Macro and Microcirculation



Taqueti VR, Di Carli MF. J Am Coll Cardiol. 2018;72:2625-2641.

Microcirculation: structure and function

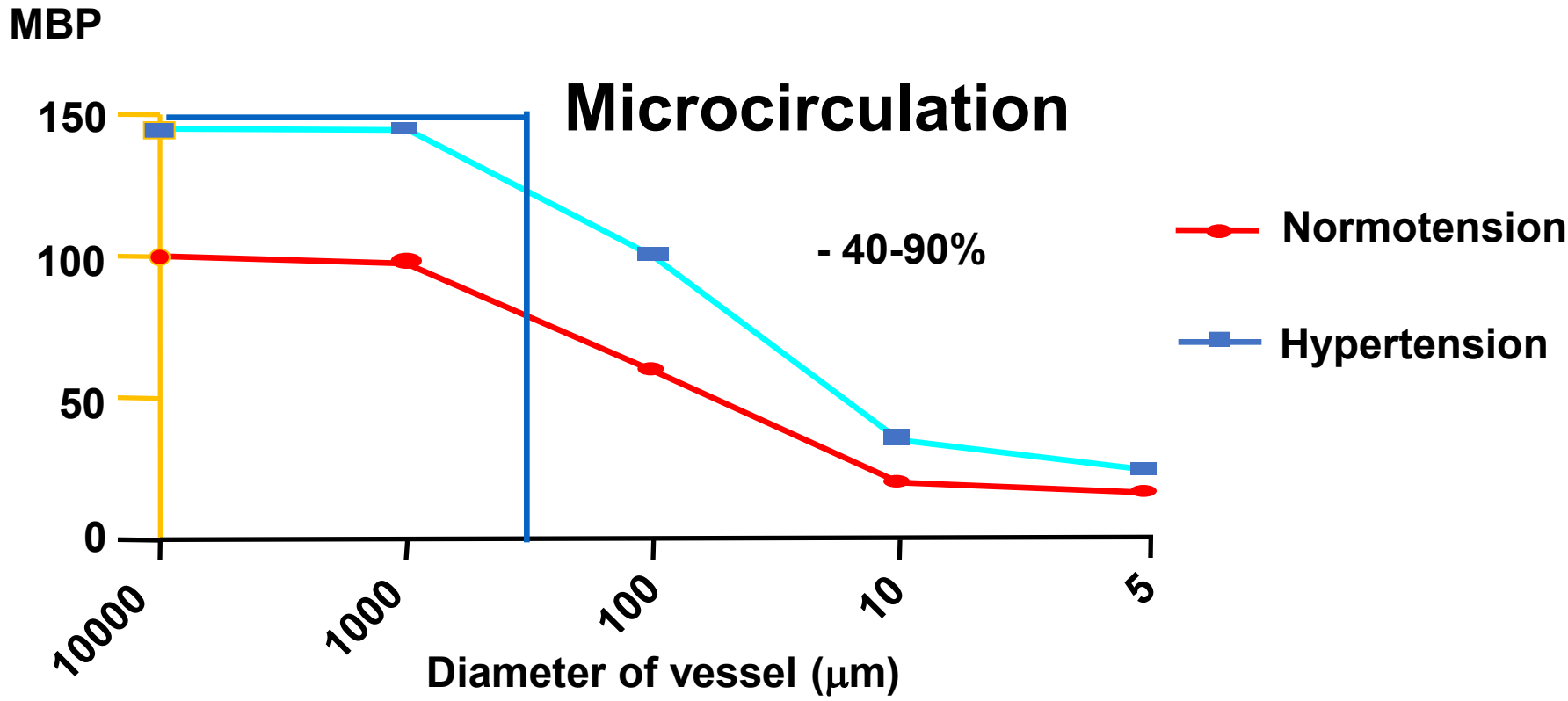
- **Structure**



- **Function**

Transport and exchange of nutrients and metabolic products between blood and tissue

Microcirculation: major site of peripheral resistance

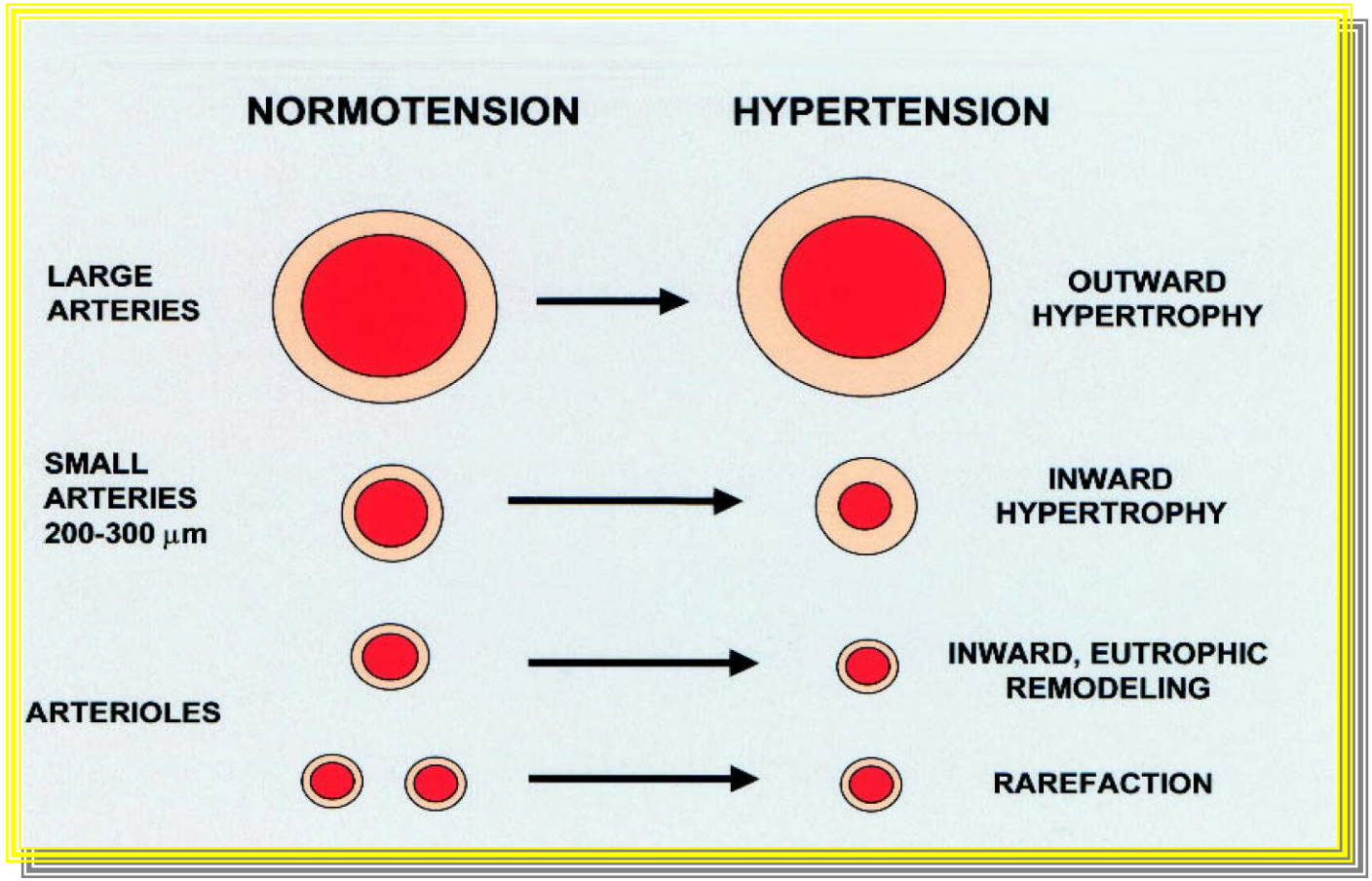


40% to 90% of the BP is located in the microcirculation

Struijker Boudier HAJ. J Hypertens.1992

Arterial remodeling in hypertension:

Representation of adaptive remodeling of arteries during the development of hypertension

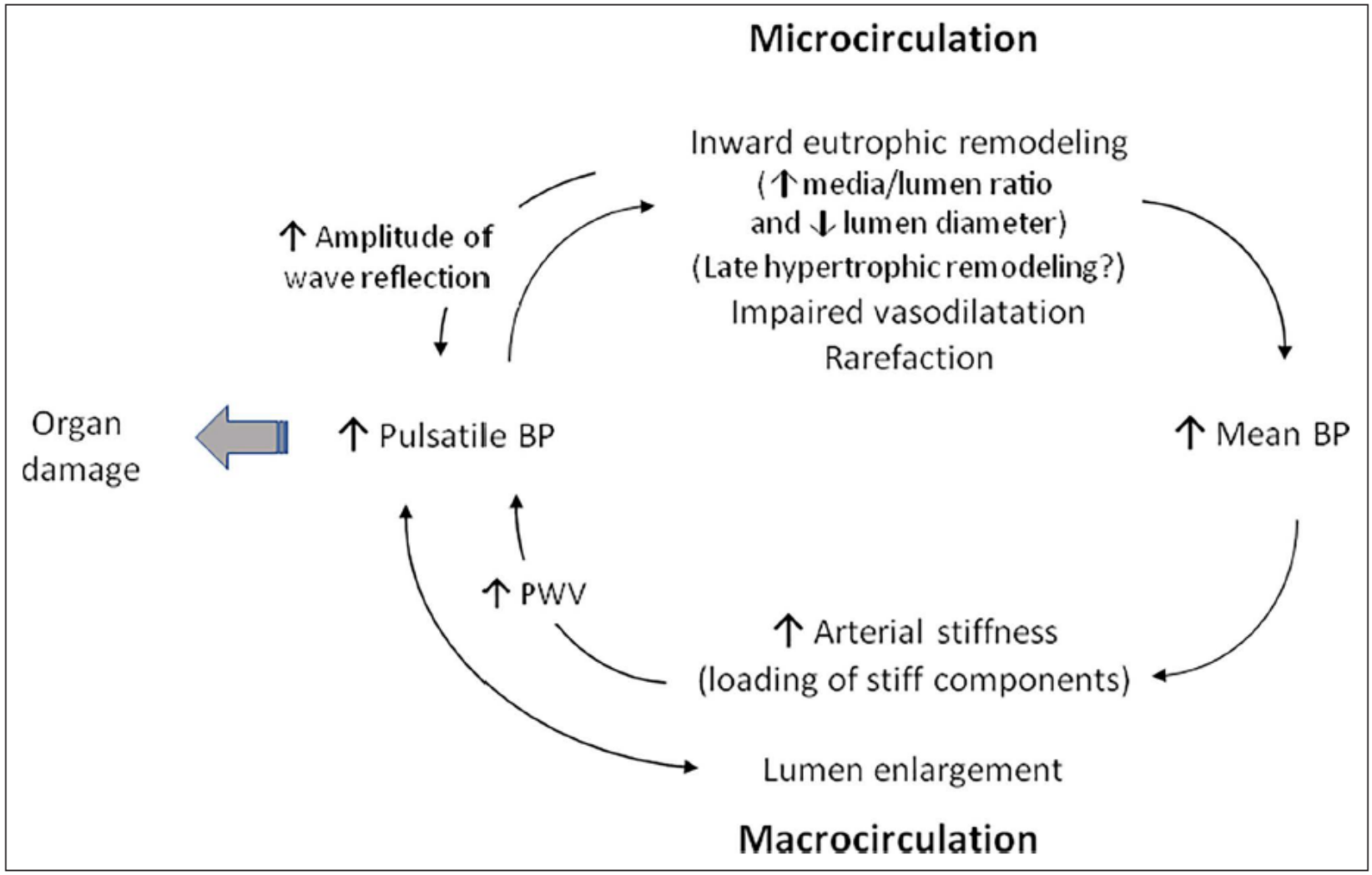


Microcirculation 2002; 9: 295-304

Integrated approach to Microcirculation alterations in hypertension

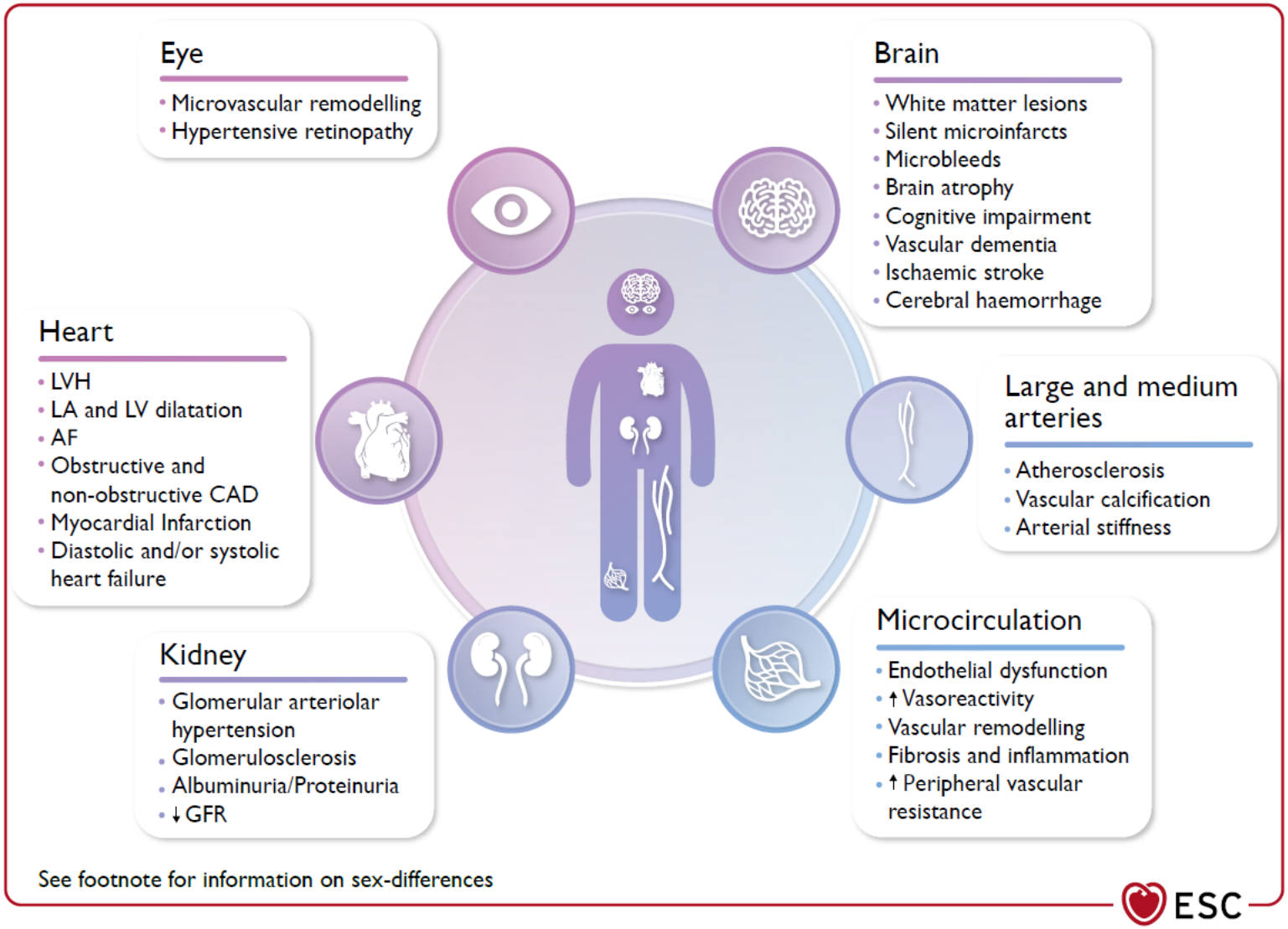
Chade A. Comp Physiol 2013

Microcirculation in hypertension



Laurent S, et al. Hypertension. 2022;79:479-490.

Microcirculation in hypertension

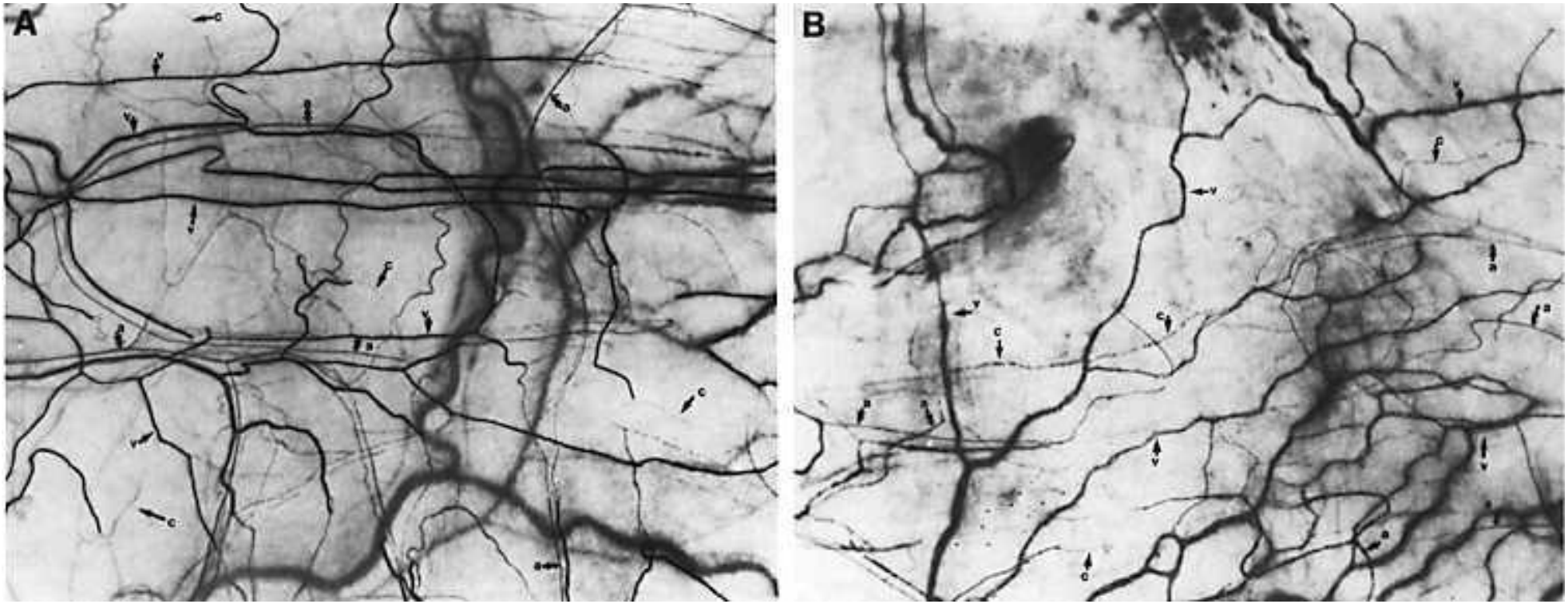


McEvoy JW, et al. Eur Heart J. 2024;45:3912-4018.

Capillary rarefaction in HT humans

Normal

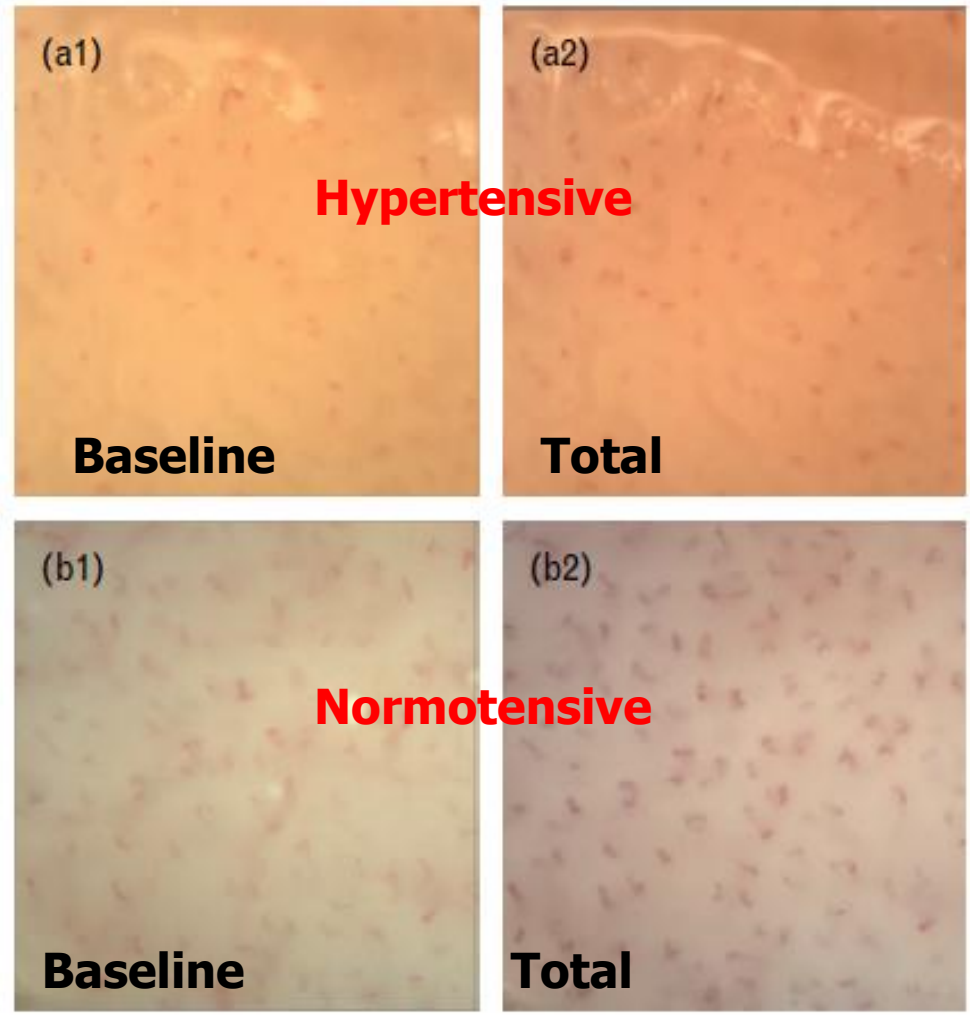
Hypertension



Sullivan J. Hypertension. 1993;5:844-851.

Rarefaction: facts in hypertension

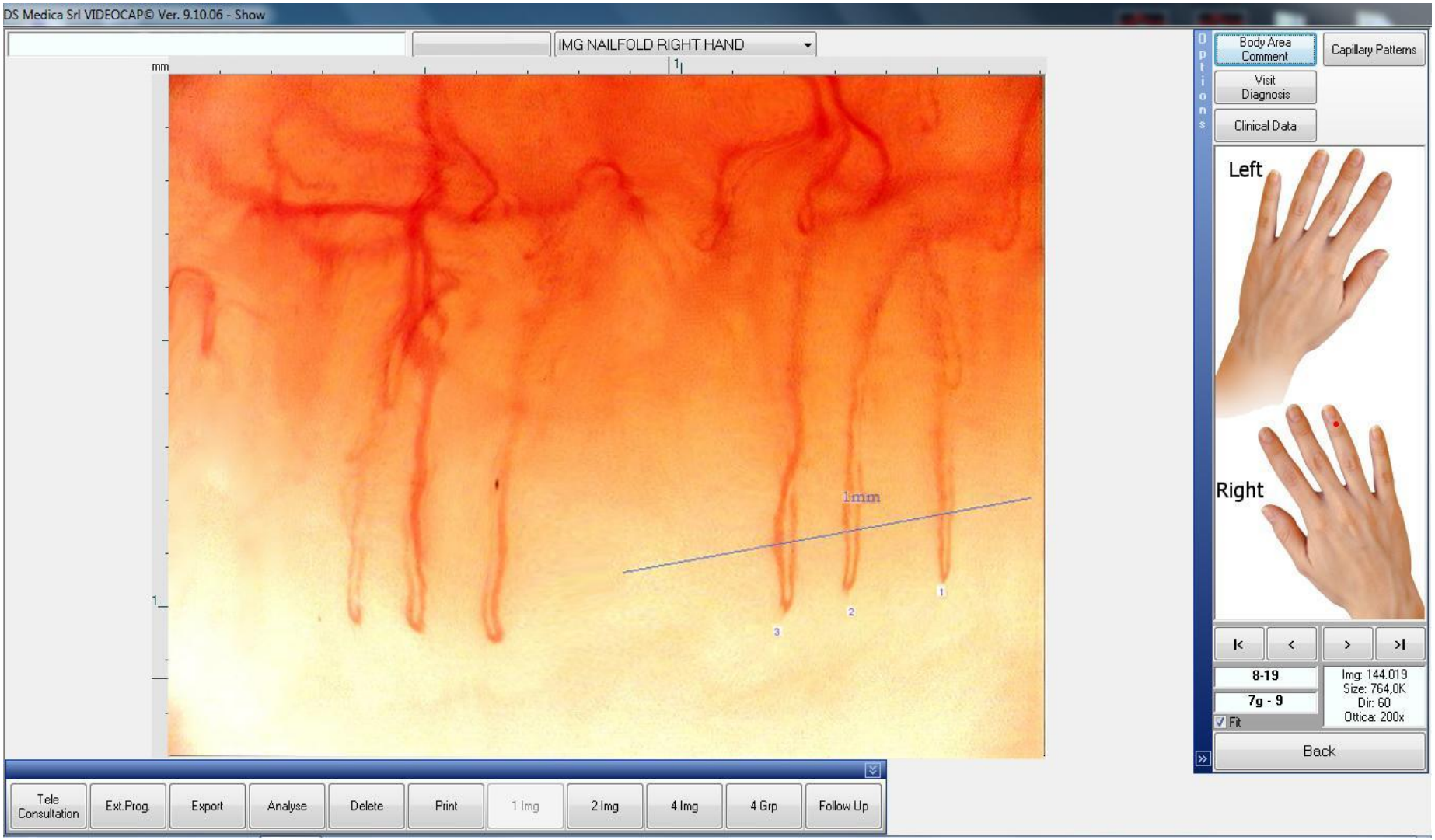
- ✓42% rarefraction increases tissue flow resistance
- ✓20% reduction in hypertensives (nailfold)
- ✓Relation to M/L
- ✓Prognostic role?



Normal pattern (A)

Normal pattern (B)

Capillary rarefaction



Media to Lumen ratio

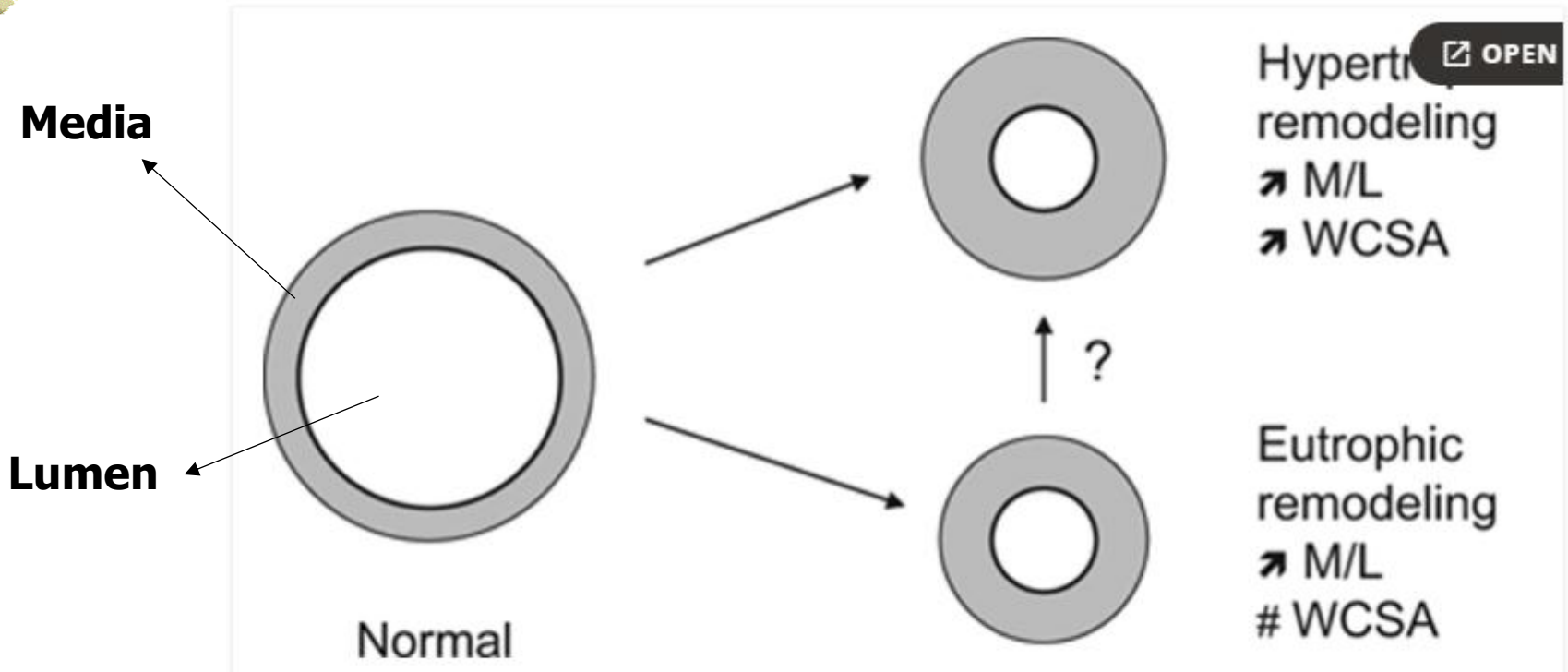
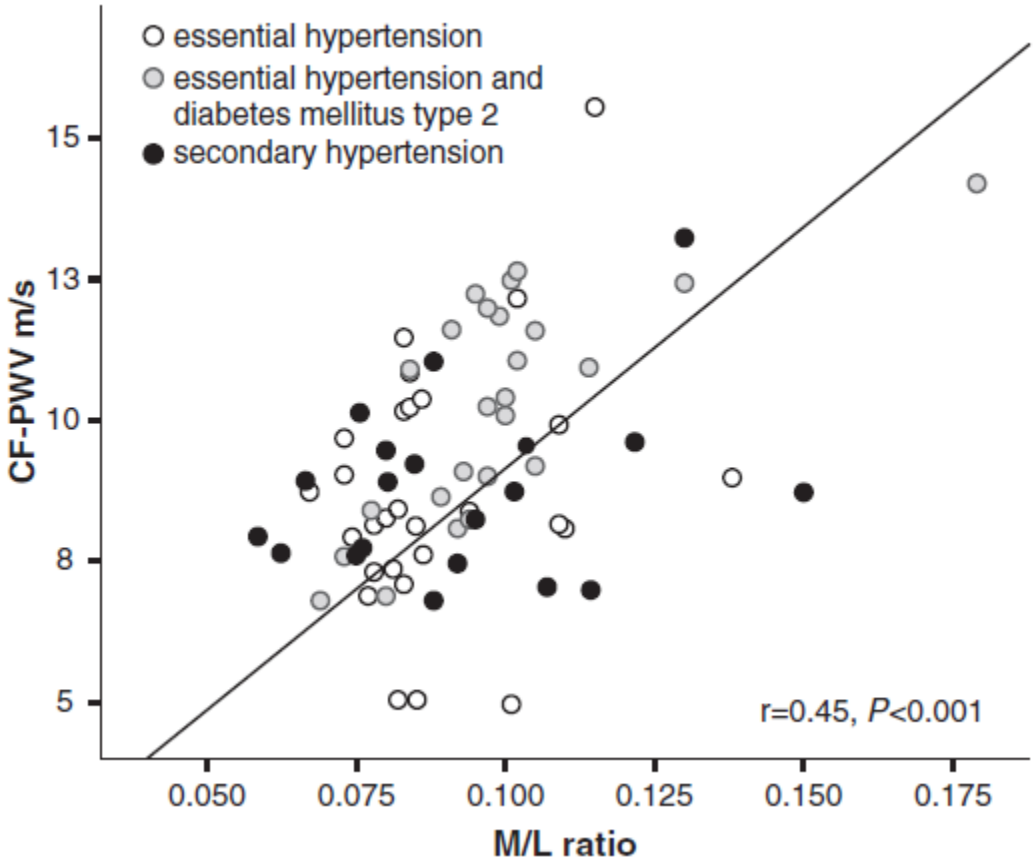


Figure 1. Schematic drawing depicting eutrophic remodeling and hypertrophic remodeling of resistance arteries in hypertension. Eutrophic remodeling corresponds to a greater media thickness, a reduced lumen and external diameter with increased media-to-lumen ratio (M/L), without any significant change of the total amount of wall tissue, as indicated by an unchanged media cross-sectional area (MCSA). There is a rearrangement of the same amount of wall material around a smaller vessel lumen without net cell growth (inspired by figure in Ref. [14]).

Laurent S, Boutouyrie P. Circ Res. 2015;116:1007-21.

Small-artery structure and arterial stiffness



Age, MAP and M/L predictors of c-f PWV

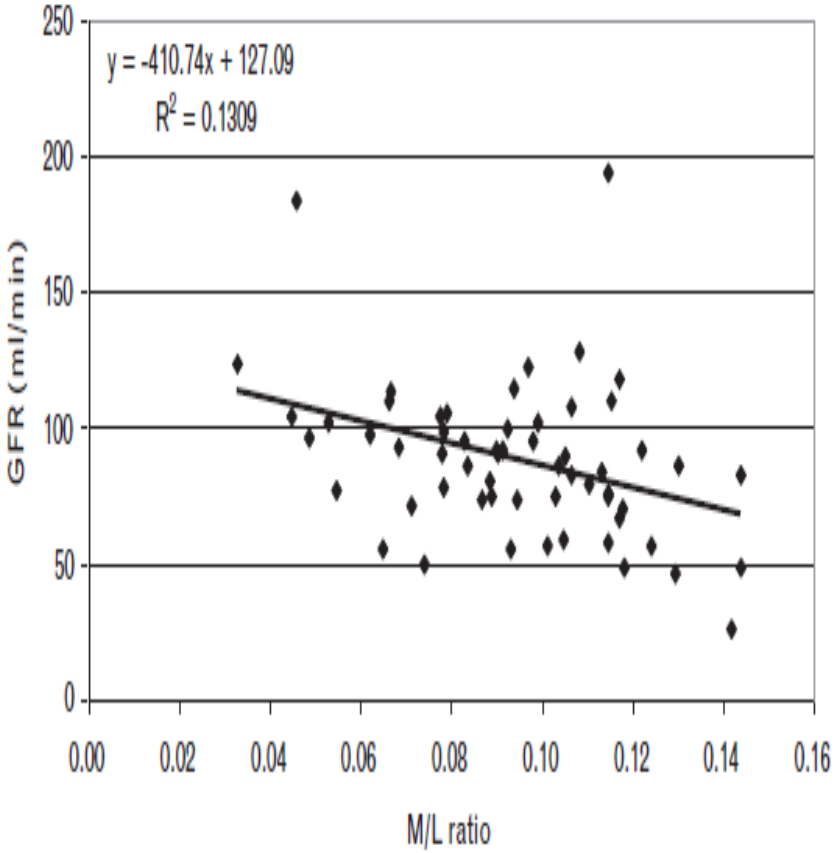
c-f PWV and M/L predictors of central SBP

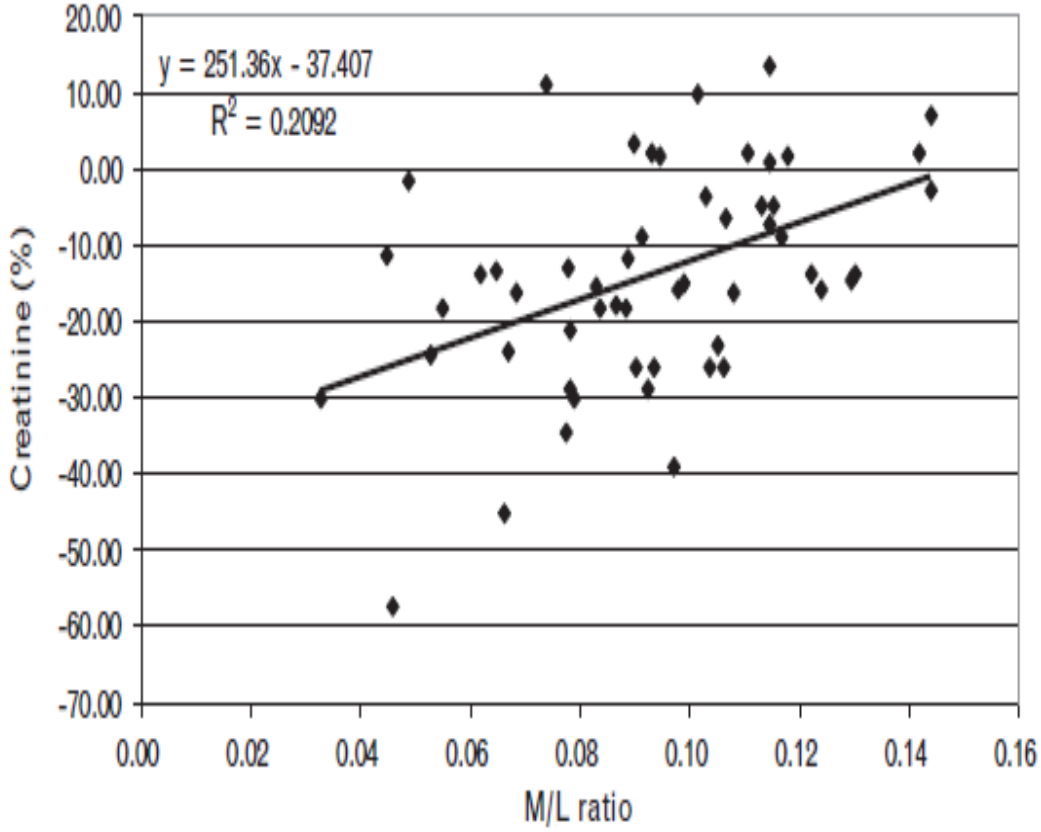
HR, Height, SBP and M/L predictors of Aix

Vascular damage at macro-and micro level correlate. M/L increase contributes to central BP augmentation by heightening wave reflections

Muiessan M, et al. Hypertension 2013

Small-artery structure and renal function

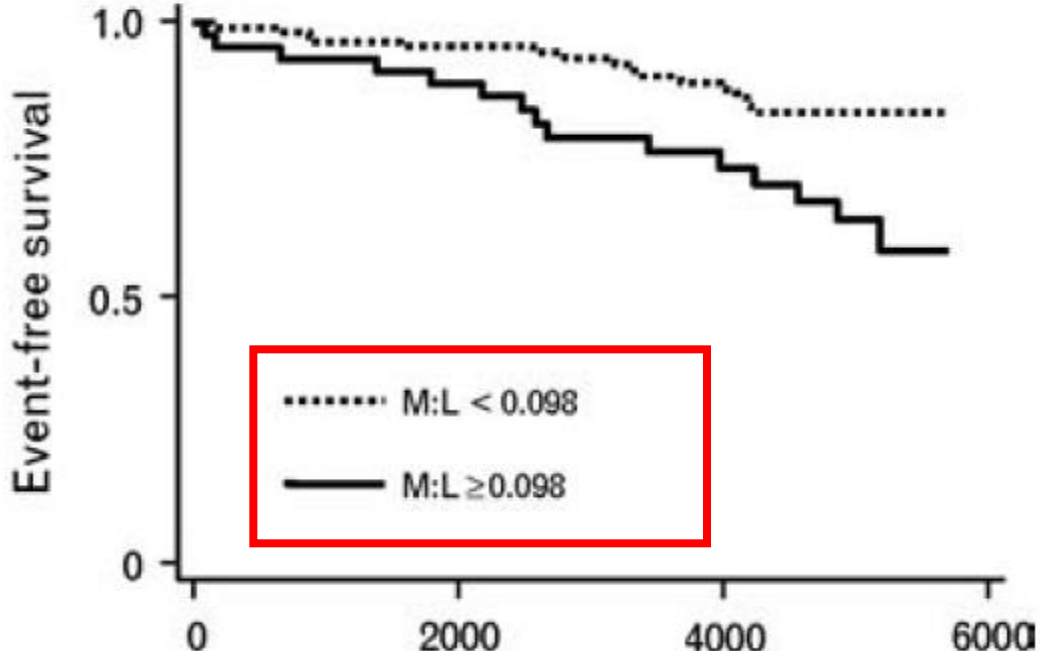




M/L, SBP and DM at baseline prognosticators of renal function change overtime (9 years) in 60 subjects

Boari G, et al. J Hypertens 2010

Prognostic role of small-artery structure in hypertension: Moderate risk pts



✓**M/L of subcutaneous small arteries potent predictor of CV events in moderate-risk population**

✓**Even after adjustment for Heart Score-similar power of prognosis**

	Hazard ratio	95% confidence int.	*P* value
M : L ≥ 0.083	2.19	1.04–4.64	0.040
Heart Score > 4%	2.22	1.08–4.57	0.029
M : L ≥ 0.098	2.20	1.06–4.56	0.030
Heart Score > 4%	2.12	1.03–4.38	0.042

Mathiassen O, et al. J Hypertens 2007

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Current Vascular Pharmacology, 2015, *13*, 000-000

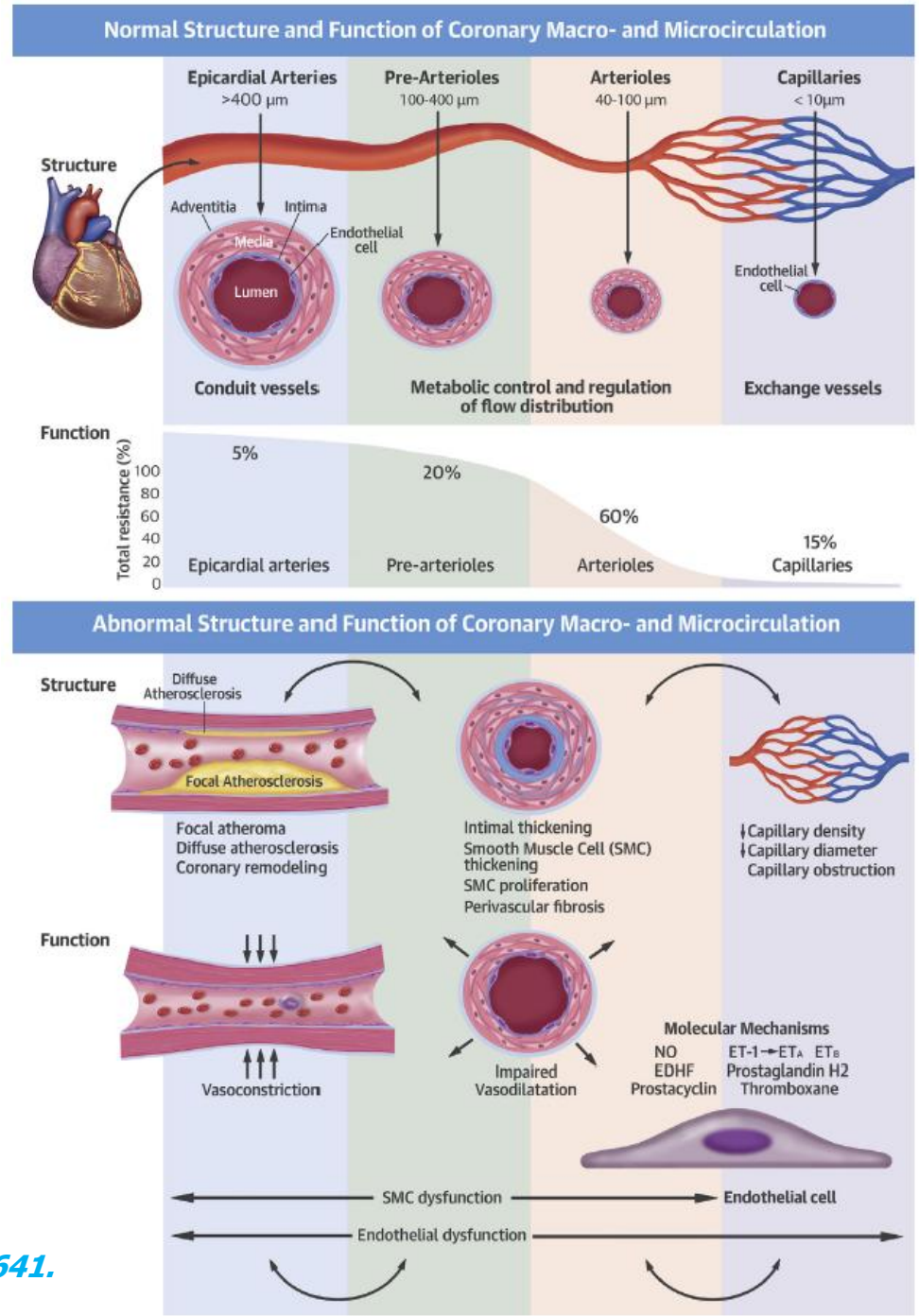
Microcirculation in Hypertension: An Update on Clinical Significance and Therapy

Costas Tsioufis[a,*], Kyriakos Dimitriadis[a], Niki Katsiki[b] and Dimitris Tousoulis[a]

[a]*First Cardiology Clinic, University of Athens, Hippocration Hospital, Athens, Greece;* [b]*Second Propedeutic Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Hippocration Hospital, Thessaloniki, Greece*

Reference	Patients (n)	Average duration of follow-up	Method of microcirculation assessment	Outcome
Rizzoni D, *et al.* [20]	128	5.4 years	Biopsy of subcutaneous fat (M/L estimation of small resistance arteries)	M/L≥0.098 related to CV events (RR=2.31, 95% CI, 1.15 to 4.64; p = 0.015 by the Mantel-Cox test, p = 0.036 by the Breslow test)
De Ciuceis C, *et al.* [23]	303	6.9 years	Biopsy of subcutaneous fat (M/L estimation of small resistance arteries)	Significant higher incidence of CV events in those with M/L≥0.098
Mathiassen O, *et al.* [24]	139	10 years	Biopsy of subcutaneous fat (M/L estimation of small resistance arteries)	M/L ≥0.098 related to CV events (HR = 2.49, 95% CI 1.21-5.11; p < 0.05)
Rizzoni D, *et al.* [25]	90	5.5 years	Endothelial function by estimation of vessel responses to acetylcholine and sodium nitroprusside	No relation of acetylcholine-induced vasodilatation of subcutaneous small arteries with CV events

Coronary *macro-* and *micro-* circulation

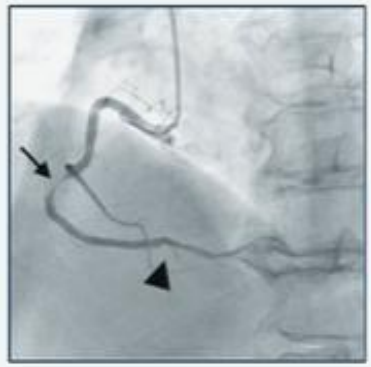


Taqueti VR, Di Carli MF. J Am Coll Cardiol. 2018;72:2625-2641.

NHS Chest Pain Clinics

~1 million p.a, £1 billion costs

Diagnostic test e.g. CTCA

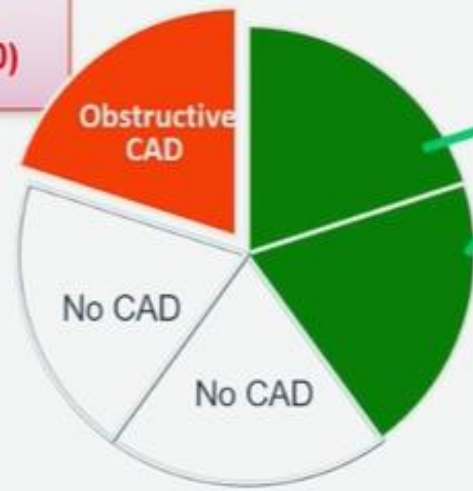


Blocked coronary arteries

No obstructive coronary lesions

Stents Bypass surgery

1 in 5 (200,000)



2 in 5 (400,000) may have Small Vessel Disease

- NHS - no specific tests
- Diagnosis & treatment sub-optimal
- 50% reattend hospital
- x2↑ risk CV death / MI

Colin Berry, 06.2020

EuroIntervention ISSUES ARTICLES TOPICS NEWS SERVICES ABOUT SUBMIT

CORONARY INTERVENTIONS - MINI FOCUS ON ISCHAEMIA WITH NON-OBSTRUCTED CORONARY ARTERIES

An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary Arteries in Collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group

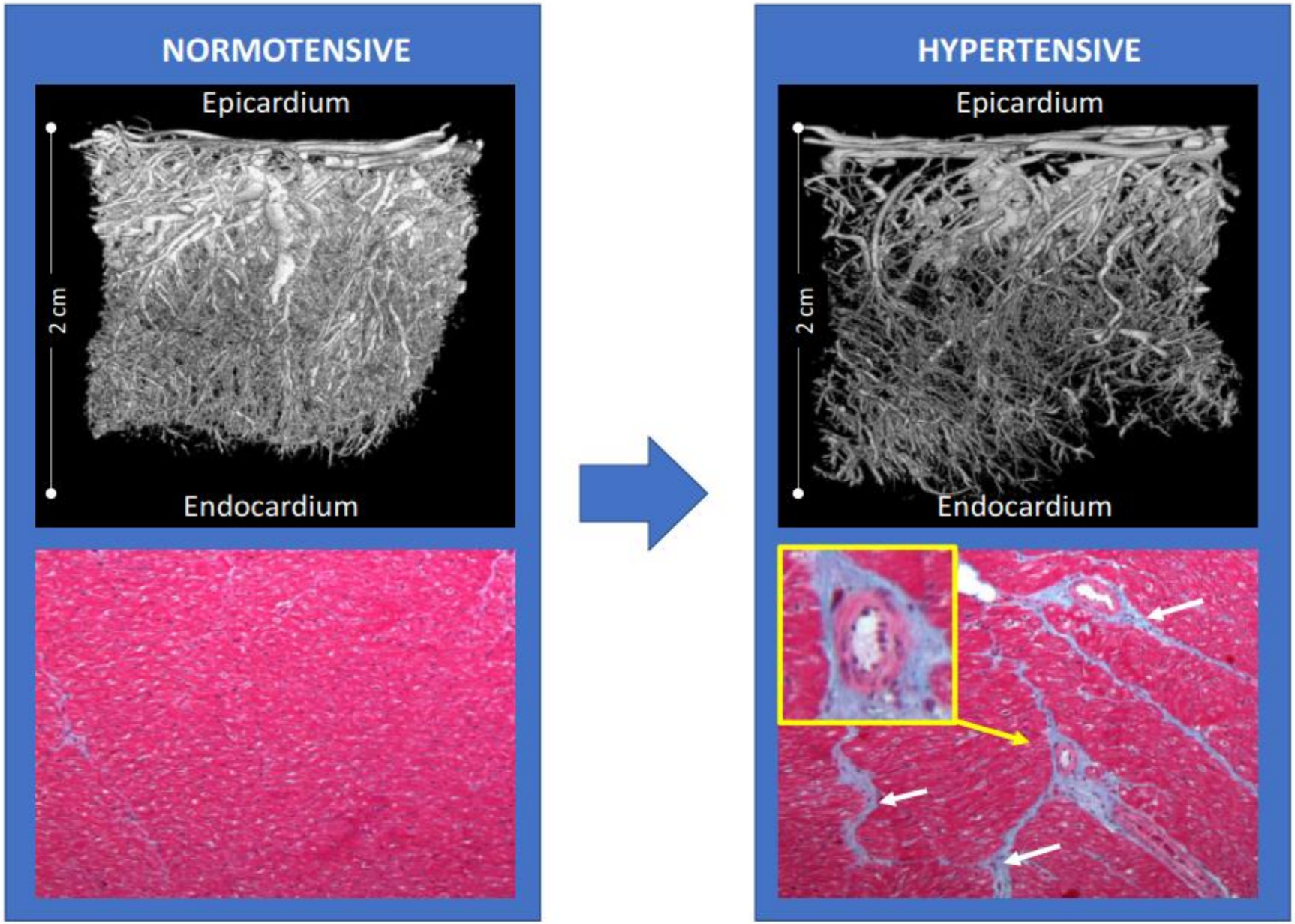
EuroIntervention 2021;16:1049-1069. DOI: 10.4244/EIJY20M07_01

Vijay Kunadian[1]; Alaide Chieffo[2]; Paolo G. Camici[3]; Colin Berry[4]; Javier Escaned[5]; Angela H.E.M. Maas[6]; Eva Prescott[7]; Nicole Karam[8]; Yolande Appelman[9]; Chiara Fraccaro[10]; Gill Louise Buchanan[11]; Stéphane Manzo-Silberman[12]; Rasha Al-Lamee[13]; Evelyn Regar[14]; Alexandra Lansky[15,16]; J. Dawn Abbott[17]; Lina Badimon[18]; Dirk J. Duncker[19]; Roxana Mehran[20]; Davide Capodanno[21]; Andreas Baumbach[22,23]

ESC European Society of Cardiology
European Heart Journal (2020) 41, 3504–3520
doi:10.1093/eurheartj/ehaa503
SPECIAL ARTICLE
Ischaemic heart disease

An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary Arteries in Collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group

Vijay Kunadian (UK, Document Chair)[1*†], Alaide Chieffo (Italy, Document Co-Chair)[2†], Paolo G. Camici(Italy)[3], Colin Berry (UK)[4], Javier Escaned (Spain)[5], Angela H. E. M. Maas (Netherlands)[6], Eva Prescott(Denmark)[7], Nicole Karam (France)[8], Yolande Appelman (Netherlands)[9], Chiara Fraccaro (Italy)[10], Gill Louise Buchanan(UK)[11], Stephane Manzo-Silberman(France)[12], Rasha Al-Lamee (UK)[13], Evelyn Regar (Germany)[14], Alexandra Lansky (USA, UK)[15,16], J. Dawn Abbott (USA)[17], Lina Badimon (Spain)[18], Dirk J. Duncker (Netherlands)[19], Roxana Mehran (USA)[20], Davide Capodanno(Italy)[21], and Andreas Baumbach [22,23](UK, USA)



Escaned J, et al. Eur Heart J 2020

SYSTEMATIC REVIEW AND META-ANALYSIS

Association of Isolated Coronary Microvascular Dysfunction With Mortality and Major Adverse Cardiac Events: A Systematic Review and Meta-Analysis of Aggregate Data

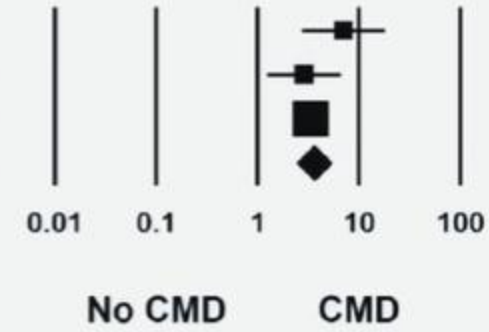
Mark A. Gdowski, MD; Venkatesh L. Murthy, MD, PhD; Michelle Doering, MLS; Andrea G. Monroy-Gonzalez, MD; Riemer Slart, MD, PhD; David L. Brown, MD

J Am Heart Assoc. 2020;9:e014954. DOI: 10.1161/JAHA.119.014954

CMD

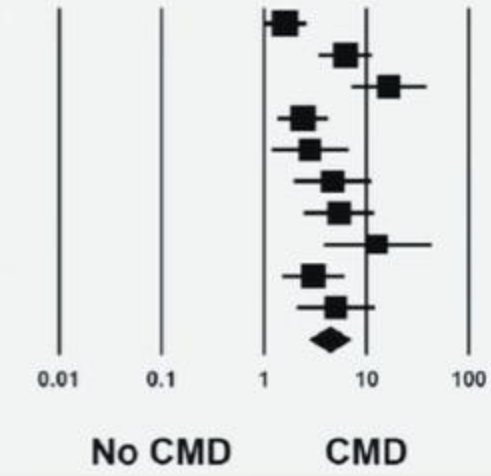
Mortality X4 ↑

Study name	Hazard ratio	Lower limit	Upper limit	Z-Value	p-Value
Marks [22]	7.010	2.743	17.917	4.067	0.000
Herzog [23]	2.860	1.241	6.593	2.466	0.014
Cortigiani [24]	3.310	2.291	4.782	6.376	0.000
Total	3.619	2.446	5.354	6.437	0.000



MACE X5 ↑

Study name		Hazard ratio	Lower limit	Upper limit	Z-Value	p-Value
Herzog [23]		1.60	1.00	2.56	1.95	0.05
Cortigiani Men [29]		6.23	3.42	11.34	5.99	0.00
Cortigiani Women [29]		16.48	7.17	37.86	6.60	0.00
Ziadi [30]		2.40	1.37	4.21	3.06	0.00
Lowenstein [25]	(CFR 1.75-1.99)	2.80	1.19	6.57	2.37	0.02
Lowenstein [25]	(CFR 1.5-1.74)	4.70	1.99	11.12	3.52	0.00
Lowenstein [25]	(CFR <1.49)	5.40	2.50	11.68	4.28	0.00
Dikic [31]		12.90	3.86	43.10	4.15	0.00
Gan [26]		3.02	1.51	6.04	3.13	0.00
Lee [27]		4.99	2.10	11.88	3.63	0.00
Total		4.42	2.79	7.01	6.33	0.00



Gdowski, Brown. JAHA 2020

Colin Berry, 06.2020

ESC European Society of Cardiology

European Heart Journal (2021) **00**, 1–15
https://doi.org/10.1093/eurheartj/ehab775

META-ANALYSIS
Ischaemic heart disease

Coronary flow reserve and cardiovascular outcomes: a systematic review and meta-analysis

Mihir A. Kelshiker [1†], Henry Seligman [1†], James P. Howard [1], Haseeb Rahman [1], Michael Foley [1], Alexandra N. Nowbar[1], Christopher A. Rajkumar[1], Matthew J. Shun-Shin [1], Yousif Ahmad [2], Sayan Sen[1], Rasha Al-Lamee[1], and Ricardo Petraco[1]*; on behalf of the Coronary Flow Outcomes reviewing committee[‡]

[1]National Heart and Lung Institute, Imperial College London, Hammersmith Campus, 72 Du Cane Road, London W12 0HS, UK; and [2]Yale School of Medicine, Yale University, 333 Cedar St, New Haven, Connecticut 06510, USA

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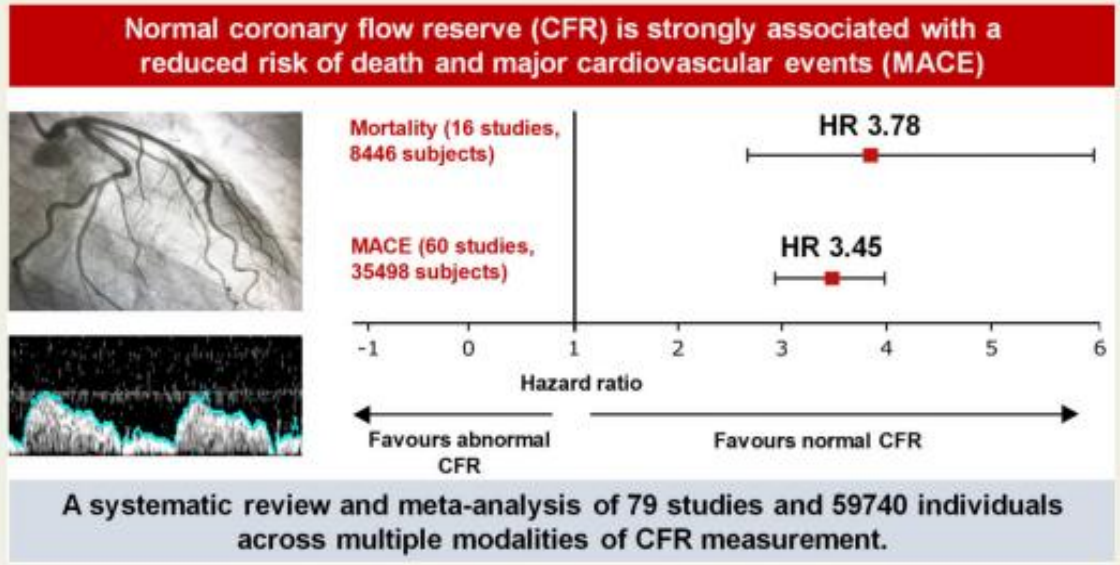
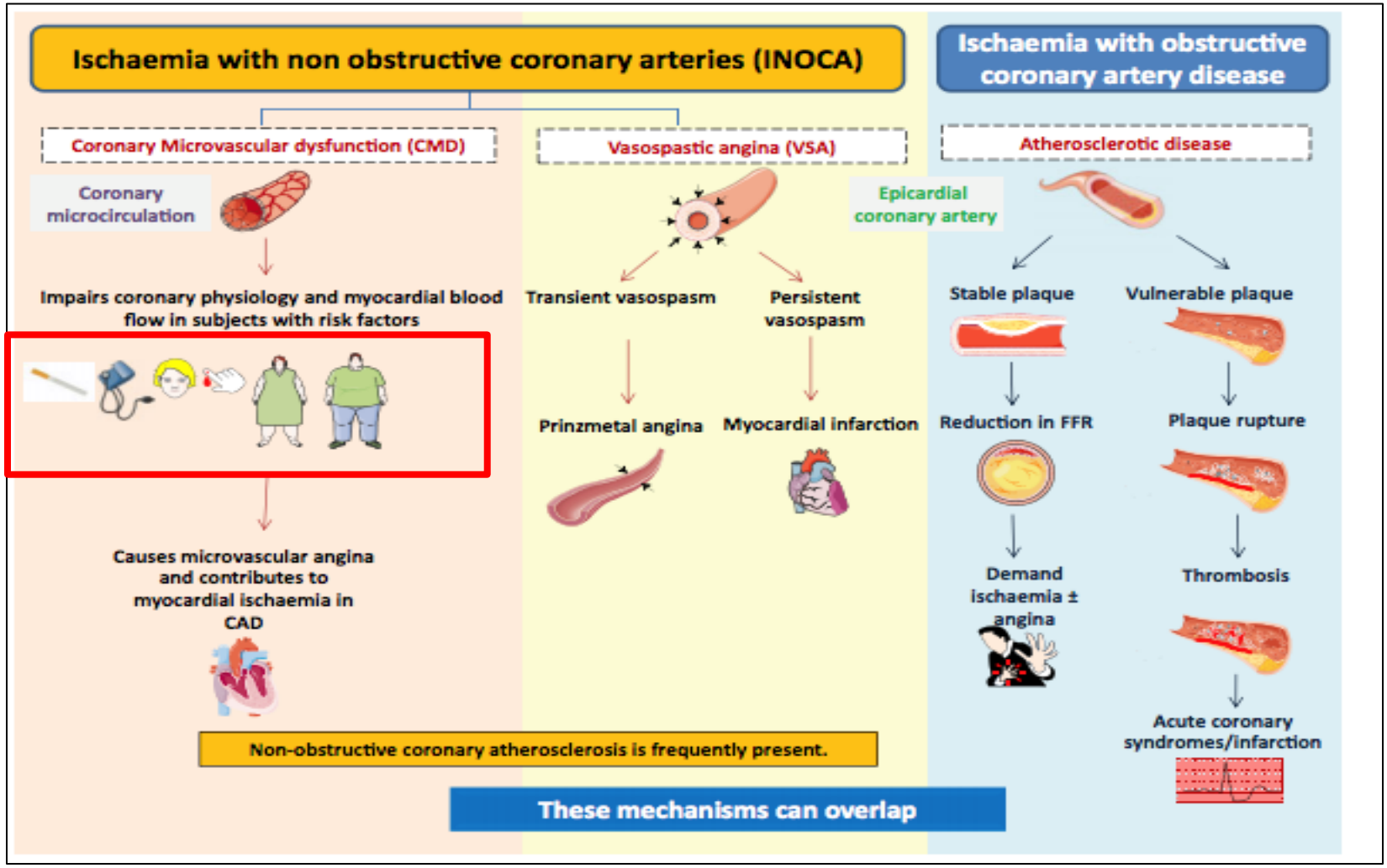
Graphical Abstract



MECHANISMS OF INOCA



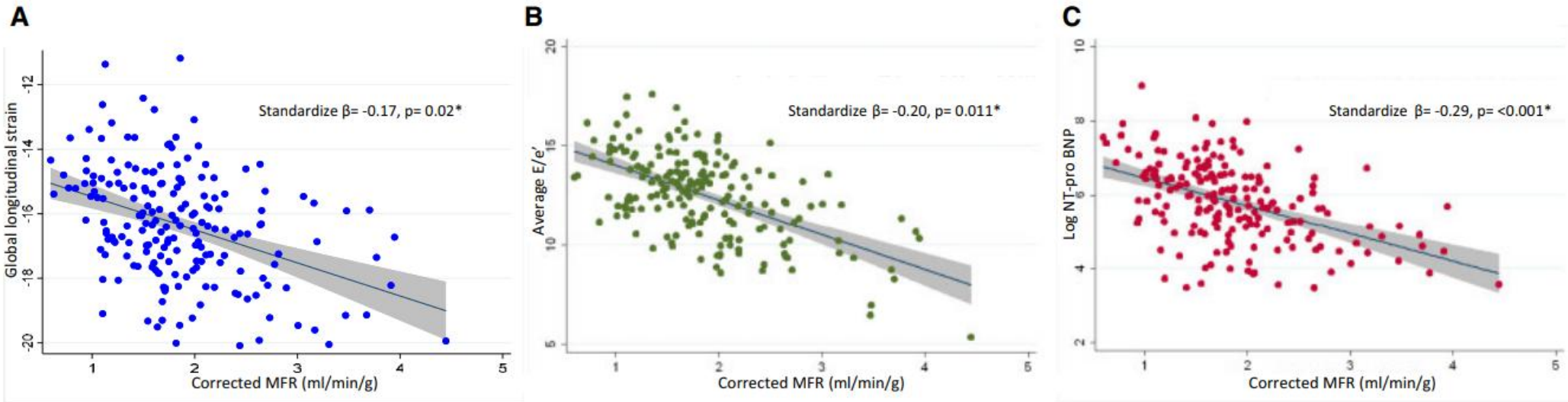
EHJ(2020), EAPCI Expert Consensus Document on INOCA

ESC European Society of Cardiology
European Heart Journal (2020) **41**, 2366–2375
doi:10.1093/eurheartj/ehaa191

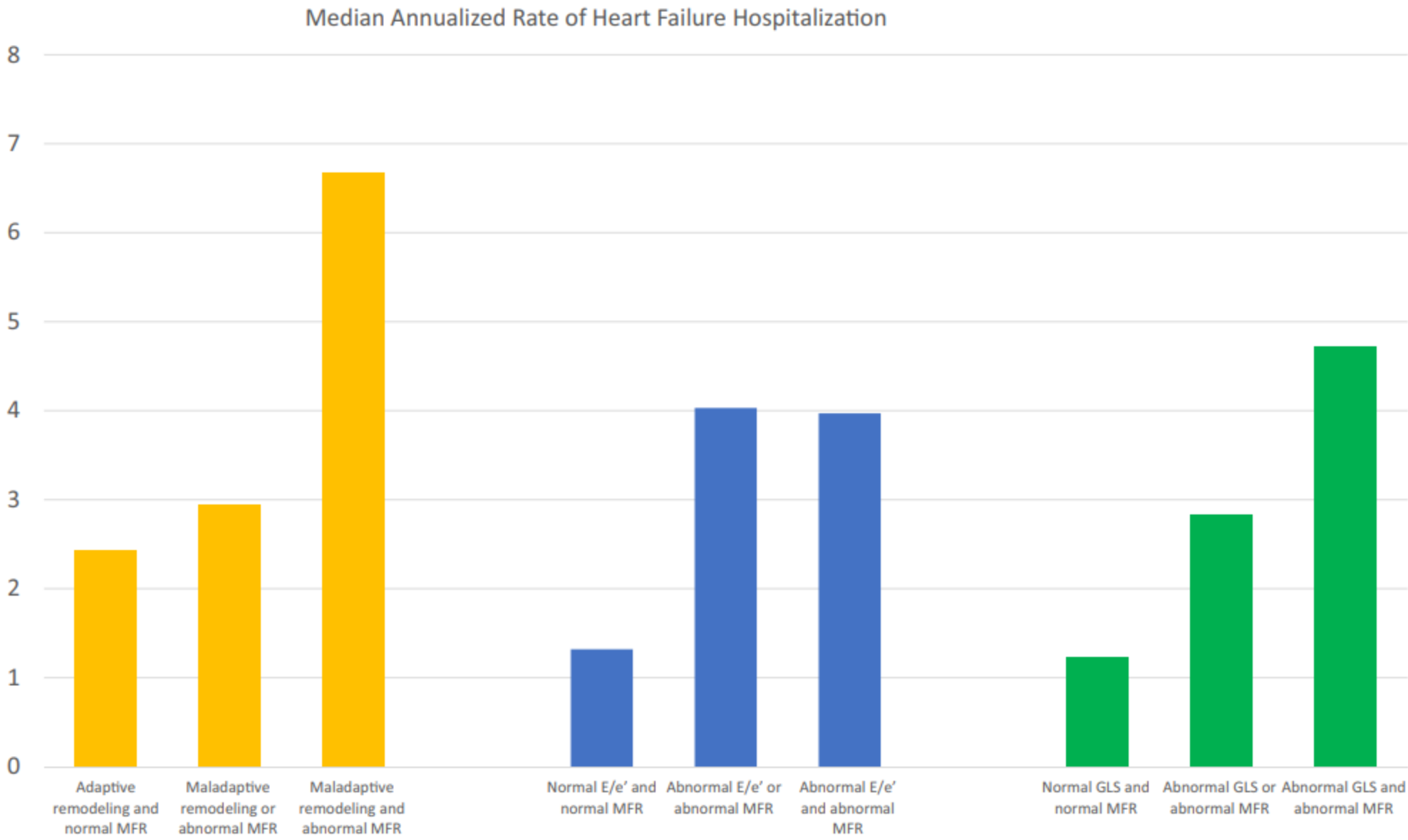
FASTTRACK CLINICAL RESEARCH
ACC.20

Hypertensive coronary microvascular dysfunction: a subclinical marker of end organ damage and heart failure

Wunan Zhou[1,2†], Jenifer M. Brown [3†], Navkaranbir S. Bajaj [4], Alvin Chandra[5], Sanjay Divakaran [3], Brittany Weber[2], Courtney F. Bibbo[2], Jon Hainer [2], Viviany R. Taqueti[2,3], Sharmila Dorbala [2,3], Ron Blankstein[2,3], Dale Adler [3], Patrick O'Gara [3], and Marcelo F. Di Carli[2,3]*



Zhou W et al . Eur Heart J 2020

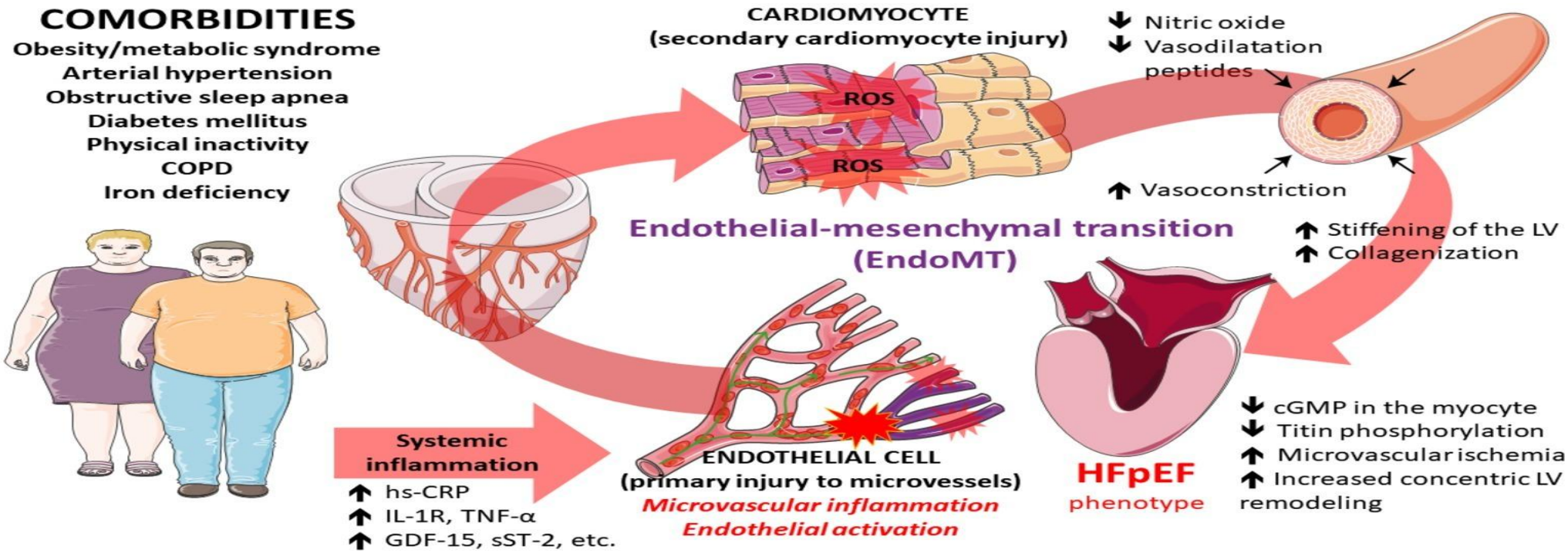


Zhou W et al . Eur Heart J 2020

frontiers in Physiology

Microvascular Dysfunction in Heart Failure With Preserved Ejection Fraction

Domenico D'Amario[1], Stefano Migliaro[1], Josip A. Borovac[2], Attilio Restivo[1], Rocco Vergallo[1], Mattia Galli[1], Antonio Maria Leone[1], Rocco A. Montone[1], Giampaolo Niccoli[1], Nadia Aspromonte[1] and Filippo Crea[1]*

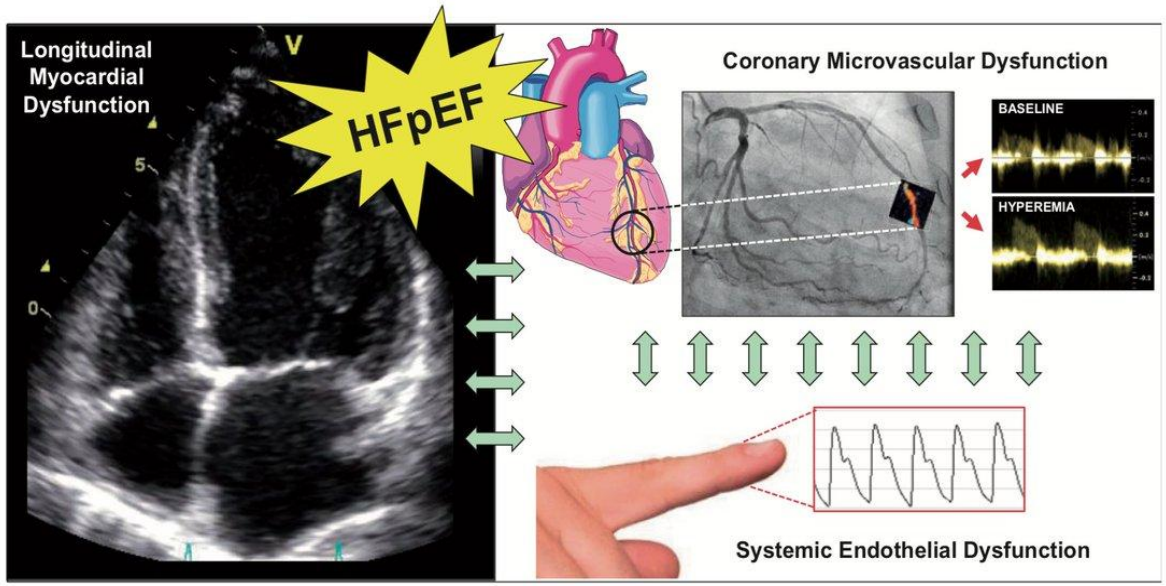


D 'Amario et al Front Physiol. 2019

MVD in HFpEF

Prevalence and correlates of coronary microvascular dysfunction in heart failure with preserved ejection fraction: PROMIS-HFpEF

Sanjiv J. Shah[1†], Carolyn S.P. Lam[2,3†], Sara Svedlund[4], Antti Saraste[5], Camilla Hage[6], Ru-San Tan[2], Lauren Beussink-Nelson[1], Maria Lagerström Fermer[7], Malin A. Broberg[7], Li-Ming Gan[7,8,9*], and Lars H. Lund[6*]



Take home figure Heart failure with preserved ejection fraction—systemic endothelial dysfunction, coronary microvascular dysfunction, and longitudinal myocardial dysfunction. Heart failure with preserved ejection fraction is associated with a high prevalence of longitudinal fibre (subendocardial) myocardial dysfunction, coronary microvascular dysfunction, and systemic endothelial dysfunction.

Published on behalf of the European Society of Cardiology

EHJ 2018

- **Largest prospective multicenter study of CMD in HFpEF**
- **High prevelance (75%) of CMD in HFpEF in the absence of unrevascularized macrovascular CAD**
- **CMD is associated with HF severity (↑ NT-pro-BNP), systemic endothelial dysfunction (↓ endoPAT RHI, ↑ UACR) cardiac dysfunction (↓LV,LA,RV strain)**
- **Microvascular dysfunction may be a promising composite risk marker and therapeutic target in HFpEF**

ESC European Society of Cardiology

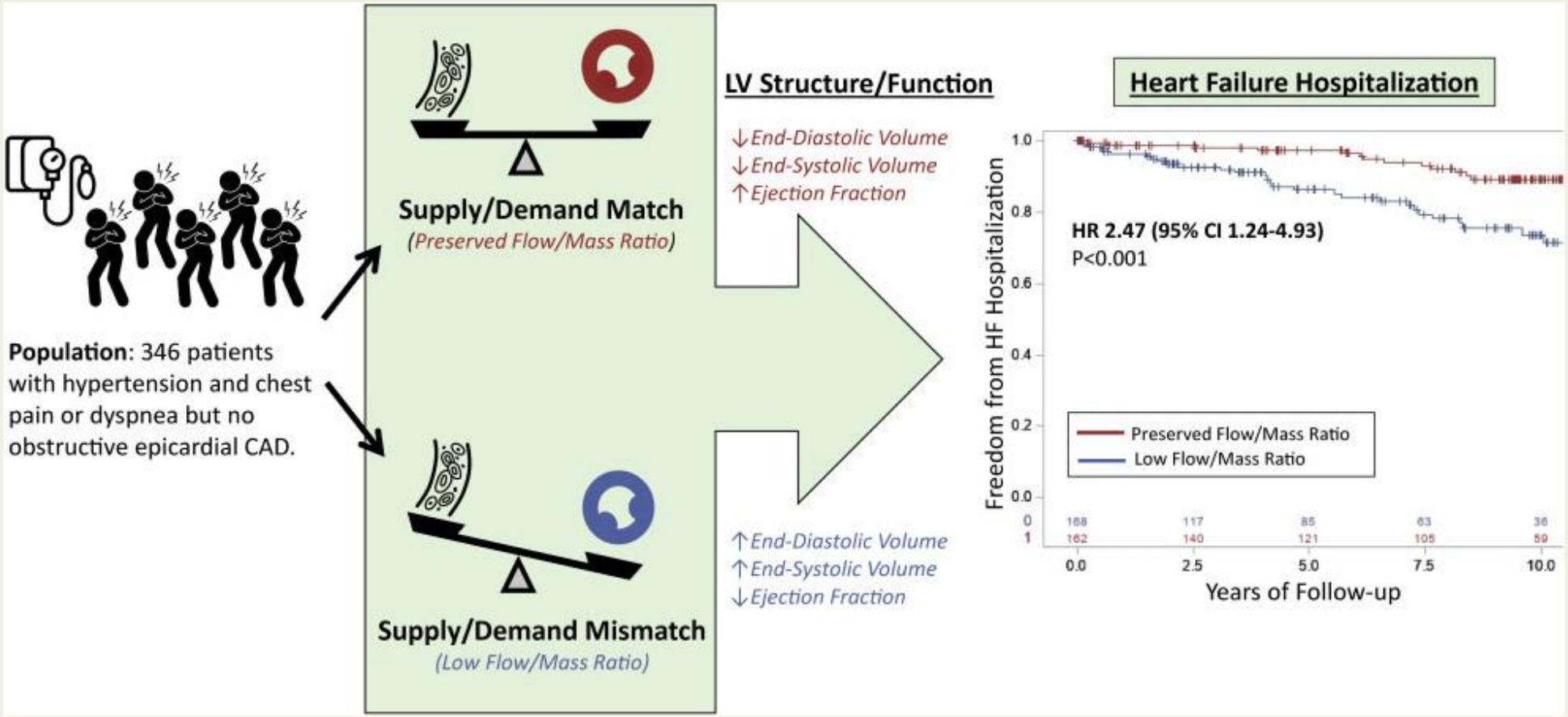
European Heart Journal (2022) **43**, 3323–3331
https://doi.org/10.1093/eurheartj/ehab610

CLINICAL RESEARCH
Hypertension

Low coronary flow relative to myocardial mass predicts heart failure in symptomatic hypertensive patients with no obstructive coronary artery disease

Jenifer M. Brown [1,2†], Wunan Zhou [2,3†], Brittany Weber [1,2], Sanjay Divakaran [1,2], Leanne Barrett [2], Courtney F. Bibbo[2], Jon Hainer [2], Viviany R. Taqueti [2], Sharmila Dorbala[1,2], Ron Blankstein[1,2], and Marcelo F. Di Carli[1,2*]

Graphical Abstract



Insufficient myocardial perfusion to match global metabolic demand, as measured by a myocardial perfusion to global left ventricular mass ratio, characterizes symptomatic patients with hypertension at risk of future heart failure and may help to understand the progression from hypertension to hypertensive heart disease. CAD, coronary artery disease; CI, confidence interval; LV, left ventricle; HR, hazard ratio.

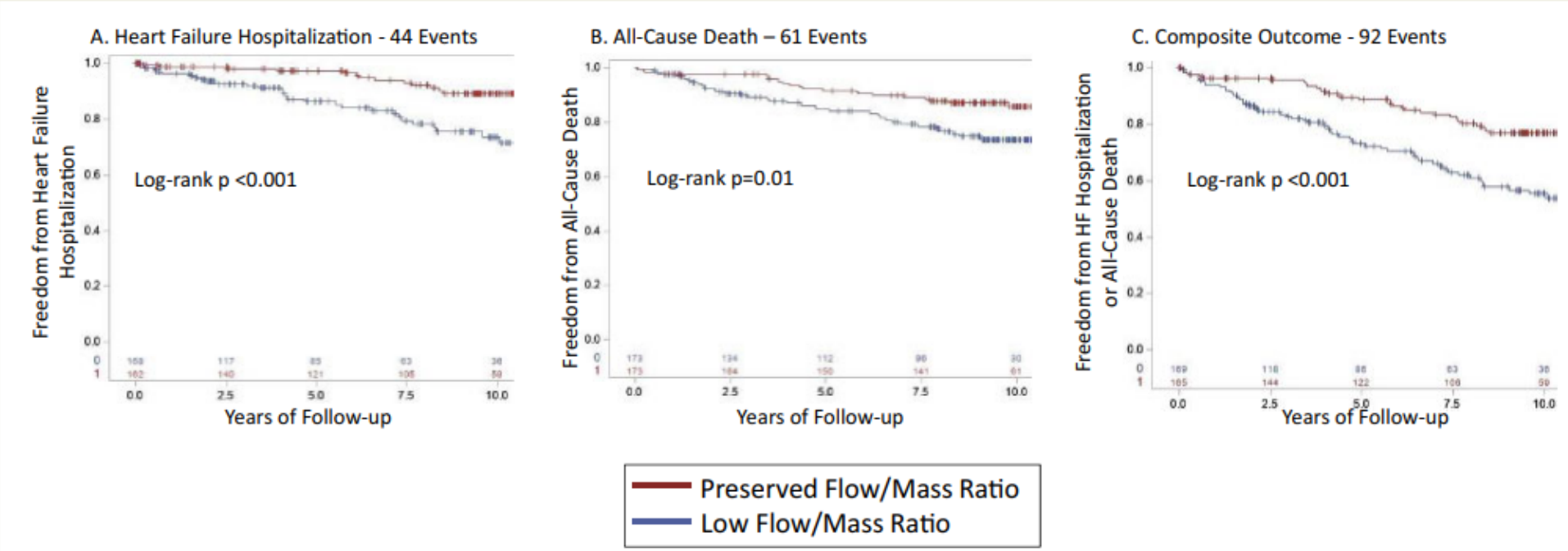
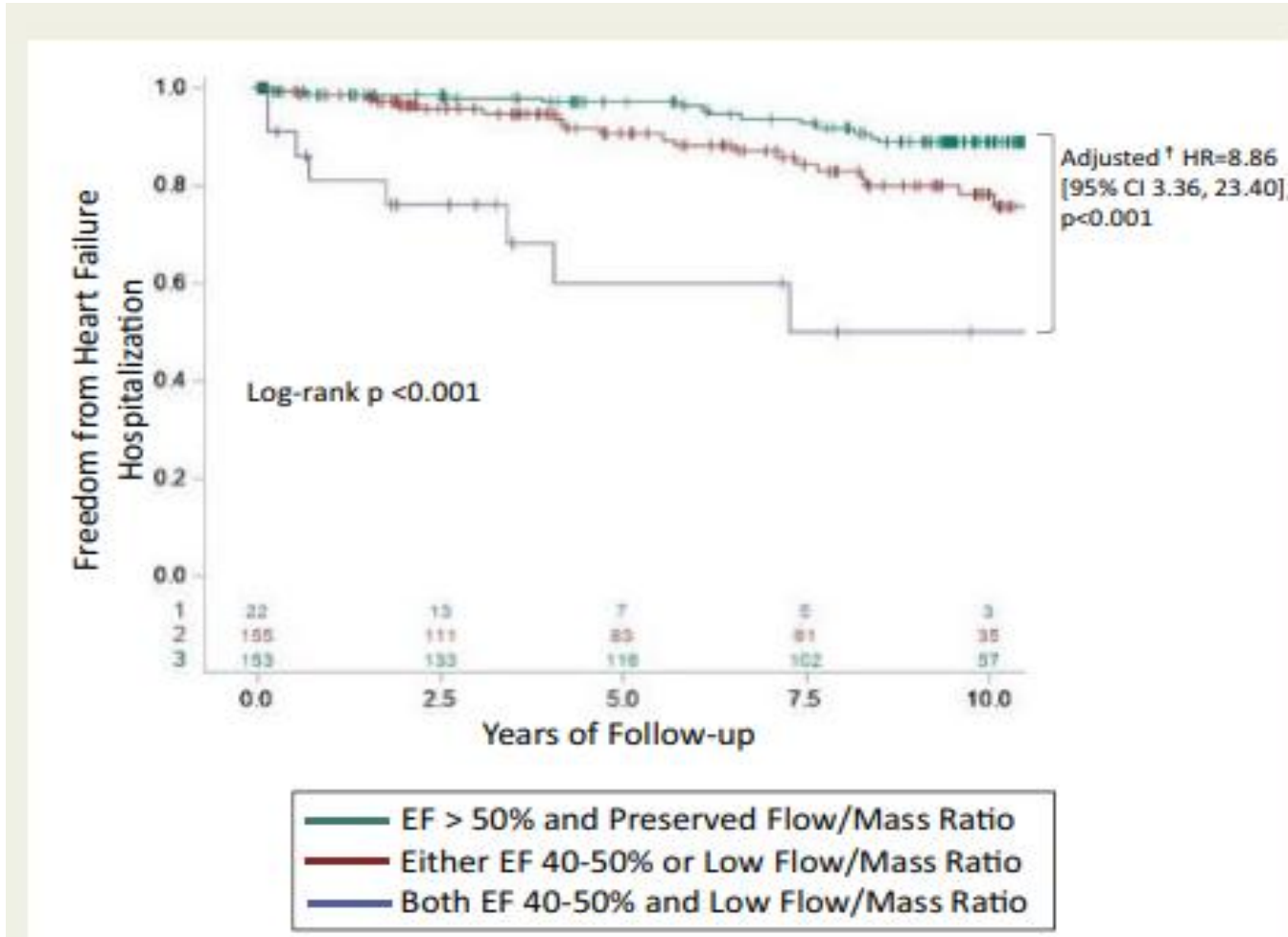


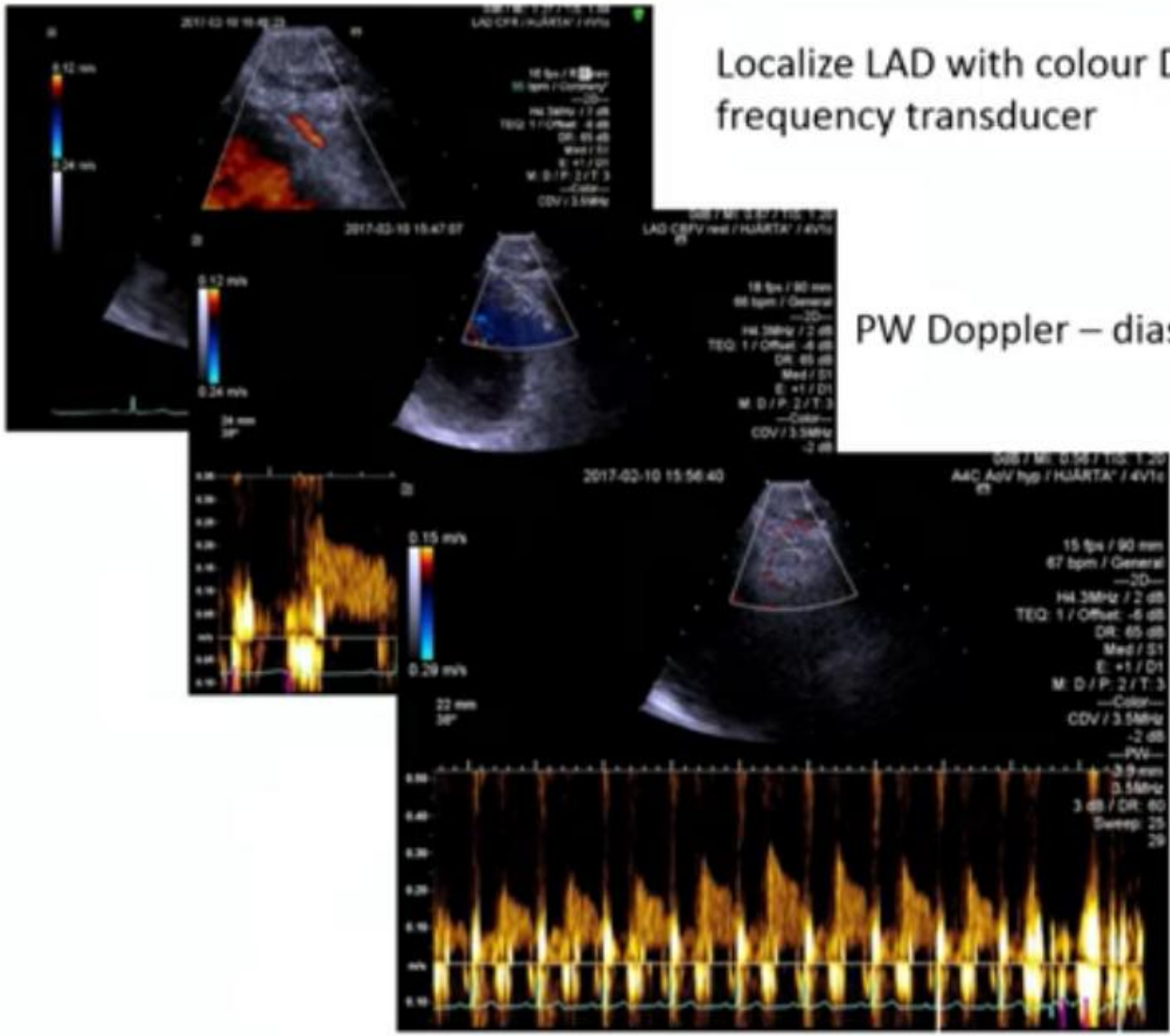
Figure 2 Kaplan–Meier survival curves are shown for heart failure hospitalization (*A*), all-cause death (*B*), and the composite of heart failure hospitalization and all-cause death (*C*), with patients categorized by preserved vs. low flow/mass ratio (≥ vs. <sex-specific median) over a median follow-up of 7.2 years for heart failure hospitalization, 8.9 years for death, and 7.3 years for the composite outcome.


Freedom from Heart Failure Hospitalization
1.0
0.8
0.6
0.4
0.2
0.0
Adjusted † HR=8.86
[95% CI 3.36, 23.40];
p<0.001
Log-rank p <0.001
1 22 13 7 5 3
2 155 111 83 61 35
3 153 133 116 102 57
0.0 2.5 5.0 7.5 10.0
Years of Follow-up
EF > 50% and Preserved Flow/Mass Ratio
Either EF 40-50% or Low Flow/Mass Ratio
Both EF 40-50% and Low Flow/Mass Ratio

Non-interventional methods

- Transthoracic Doppler echocardiography – TTDE
  - Well validated with prognostic studies
- Positron emission tomography – PET
  - Well validated with prognostic studies
- MRI
  - Not standardized for clinical use, no follow-up studies
- CT perfusion
  - Not standardized for clinical use, no follow-up studies
- Myocardial contrast echocardiography
  - Not standardized and no follow-up studies

How to do echo CFR?

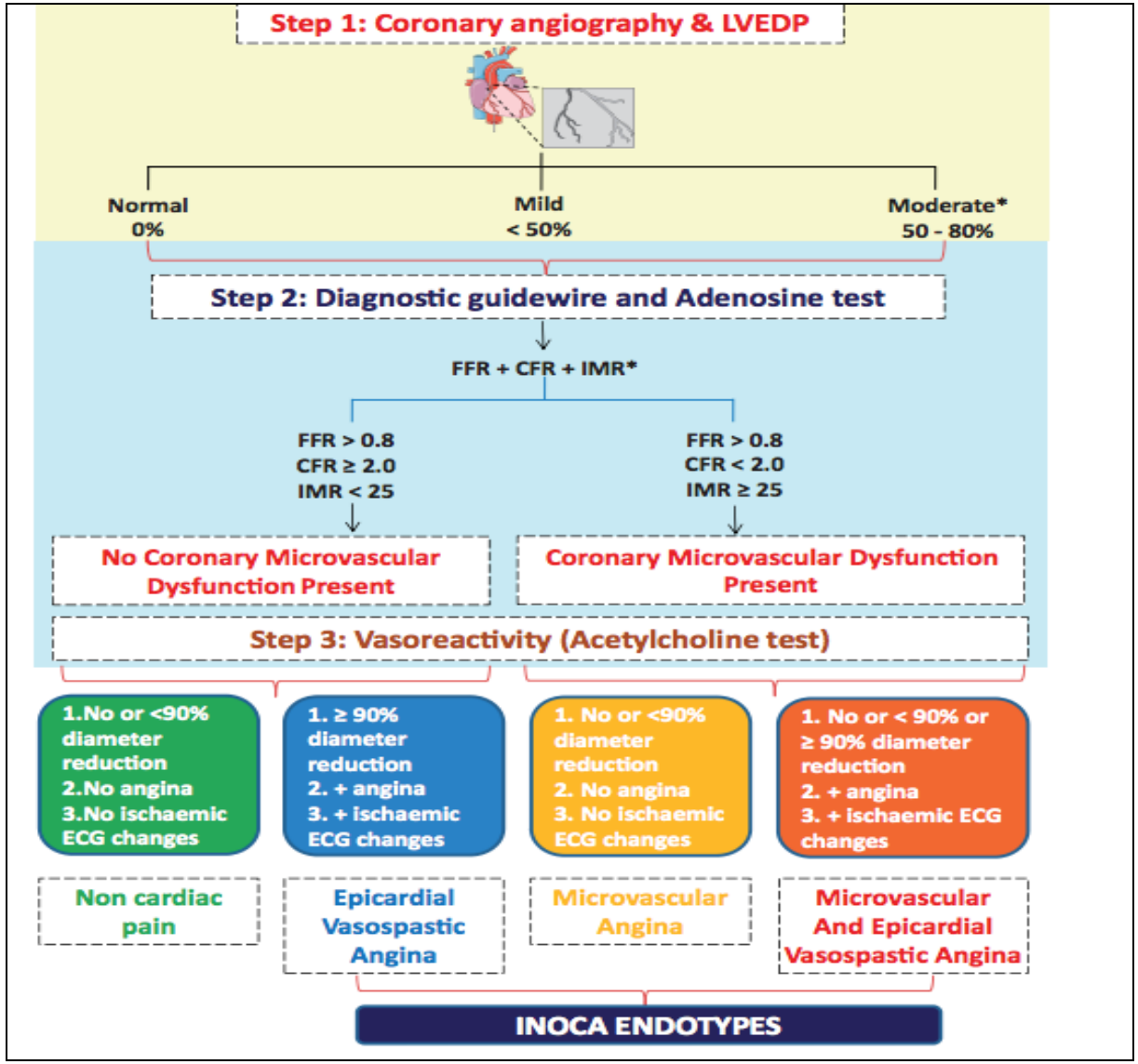


Localize LAD with colour Doppler – high frequency transducer

PW Doppler – diastolic flow

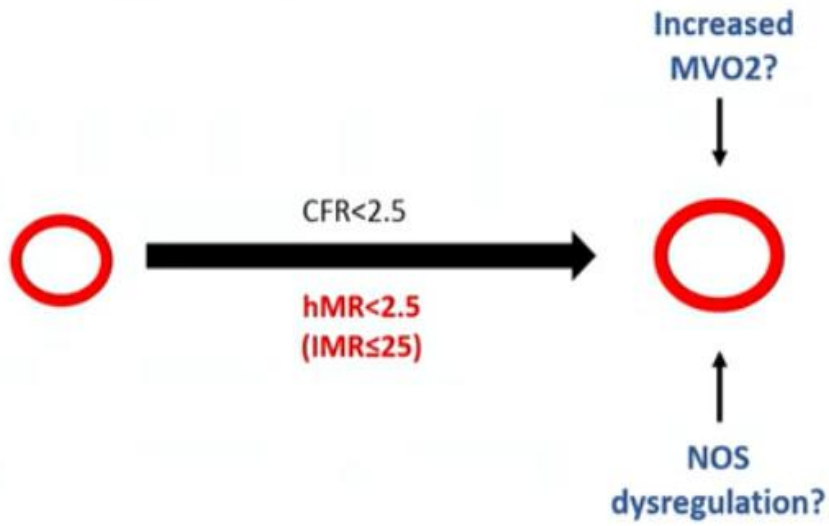
Induce maximal hyperemia with adenosine or dipyridamole

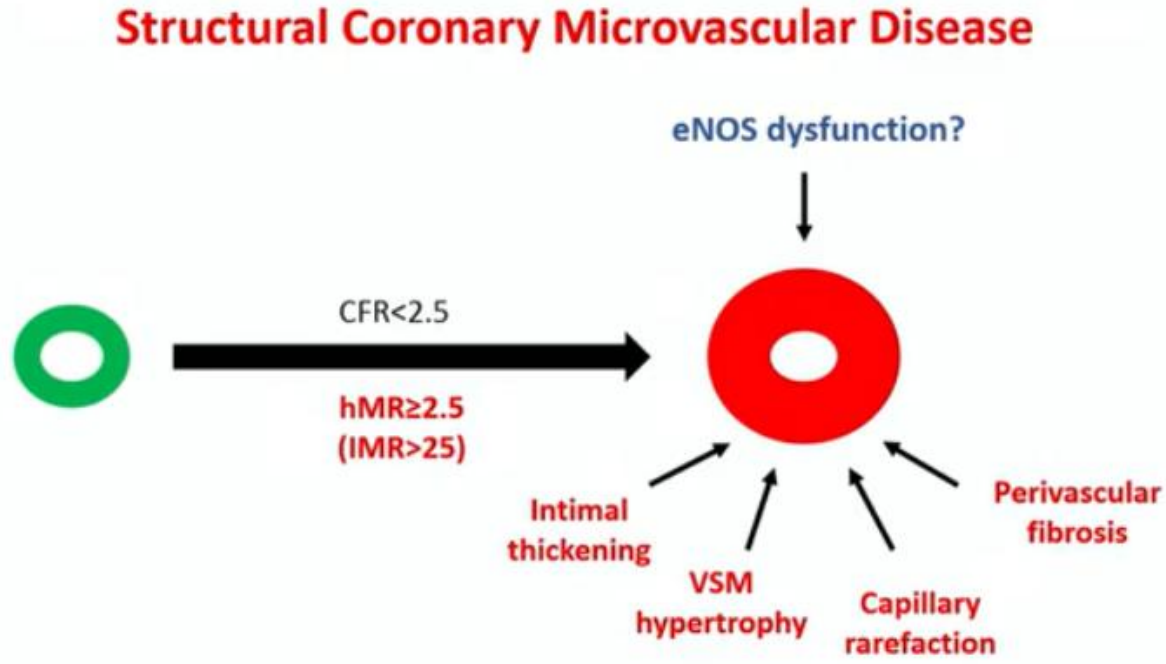
Invasive Evaluation of INOCA



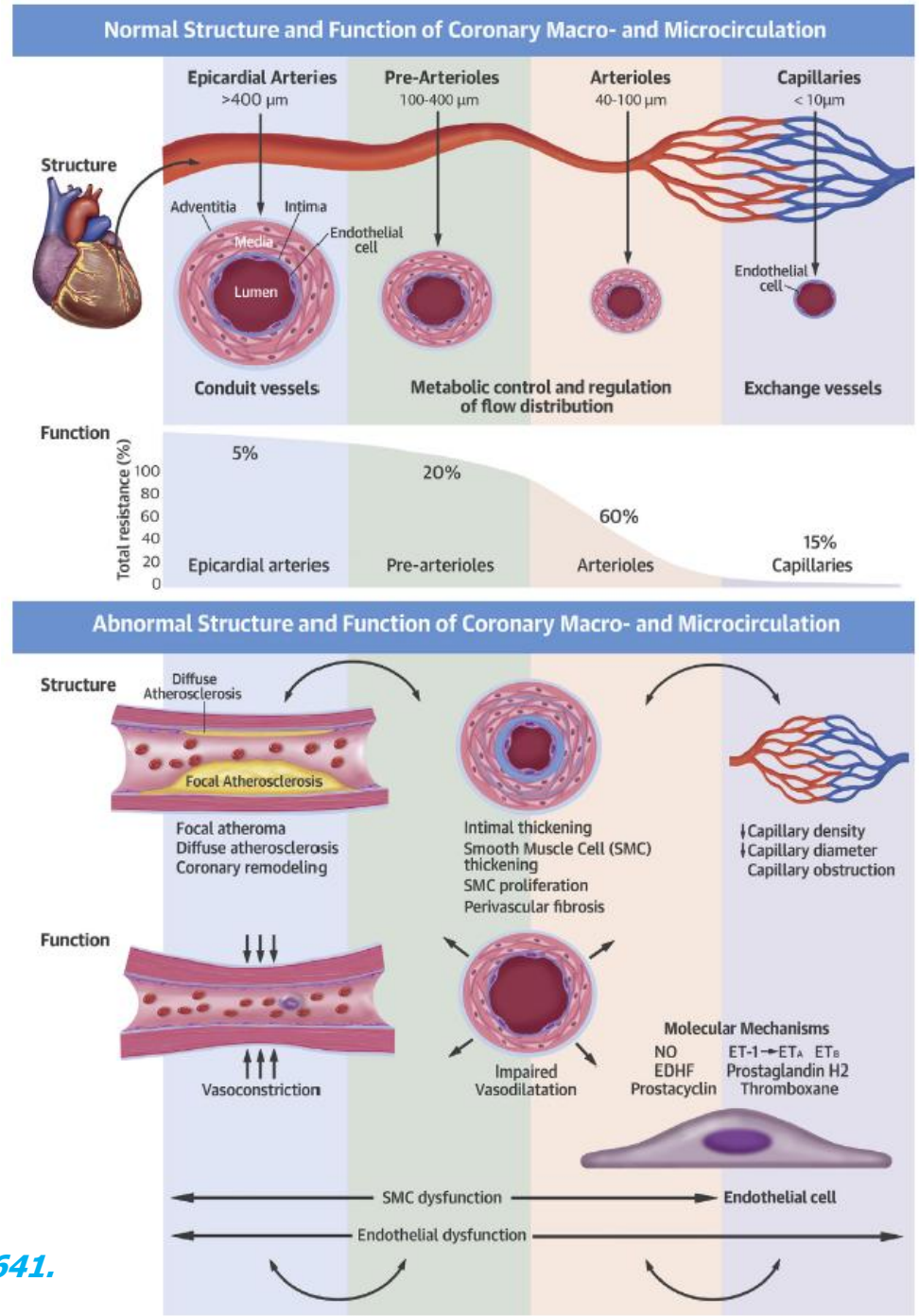
EAPCI Expert Consensus Document on INOCA. Eur Heart J 2020

INOCA Pathophysiology Simplified





Coronary *macro-* and *micro-* circulation



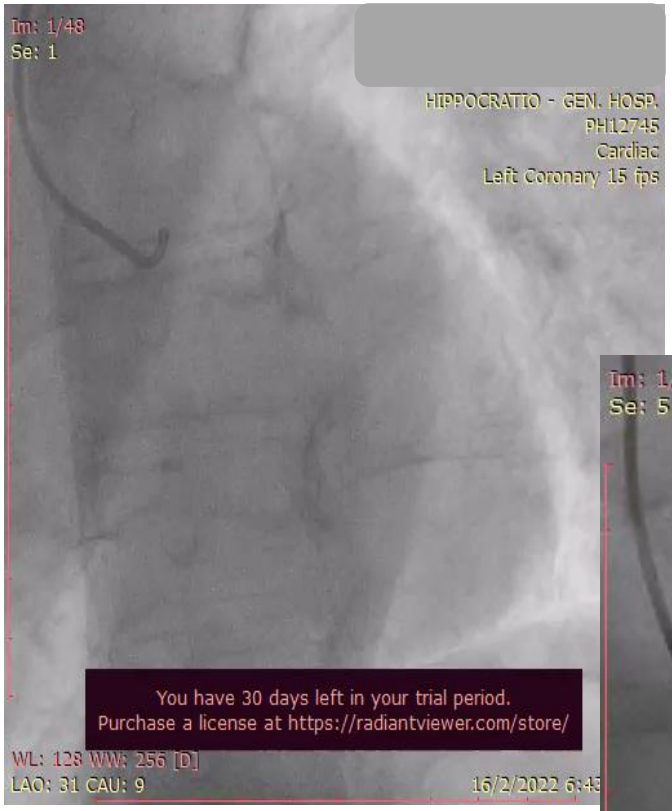
Taqueti VR, Di Carli MF. J Am Coll Cardiol. 2018;72:2625-2641.

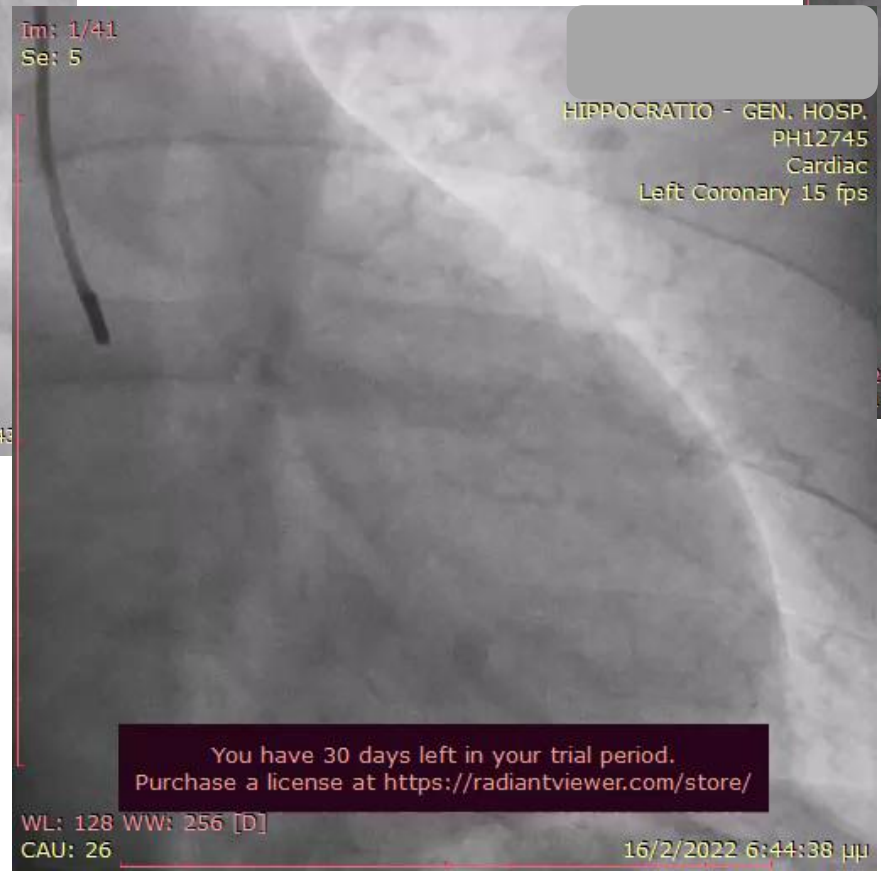
- Female 55 y

History

- Anxiety disorder
- Uncontrolled hypertension with 3 drugs
- Dyslipidemia
- Smoker
- Obese

- Dyspnea and chest pain on exertion
- **Stress Echo (+) for ischemia of the inferior wall**


Im: 1/48
Se: 1
HIPPOCRATIO - GEN. HOSP.
PH12745
Cardiac
Left Coronary 15 fps
You have 30 days left in your trial period.
Purchase a license at https://radiantviewer.com/store/
WL: 128 WW: 256 [D]
LAO: 31 CAU: 9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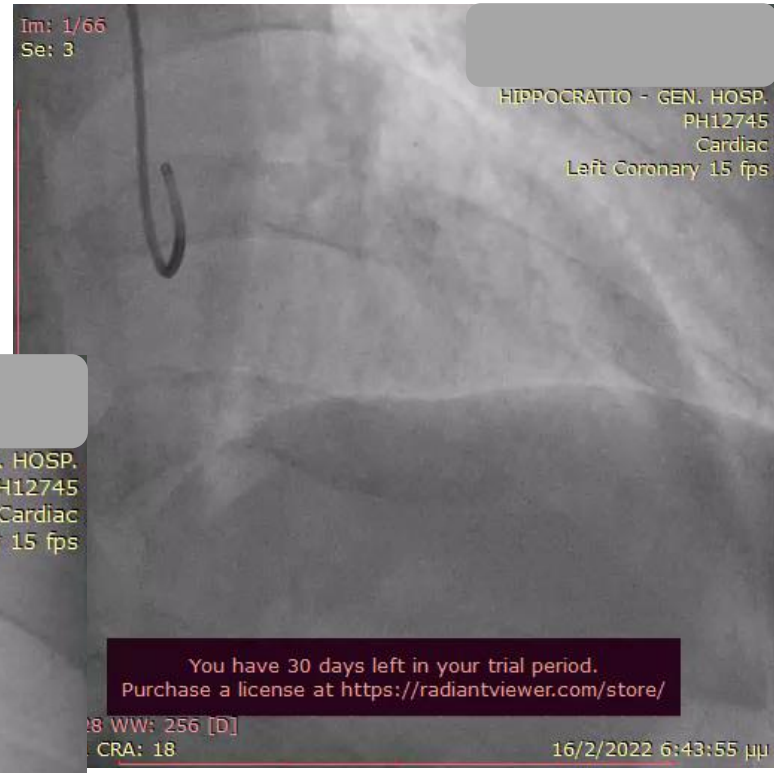
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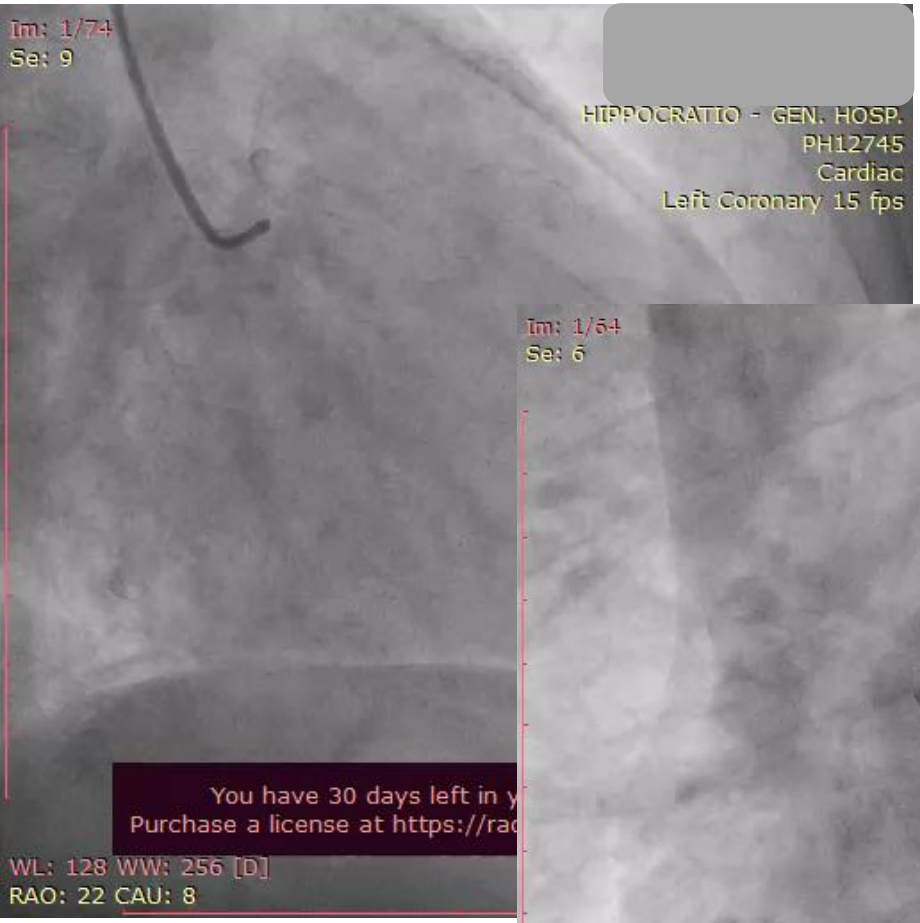
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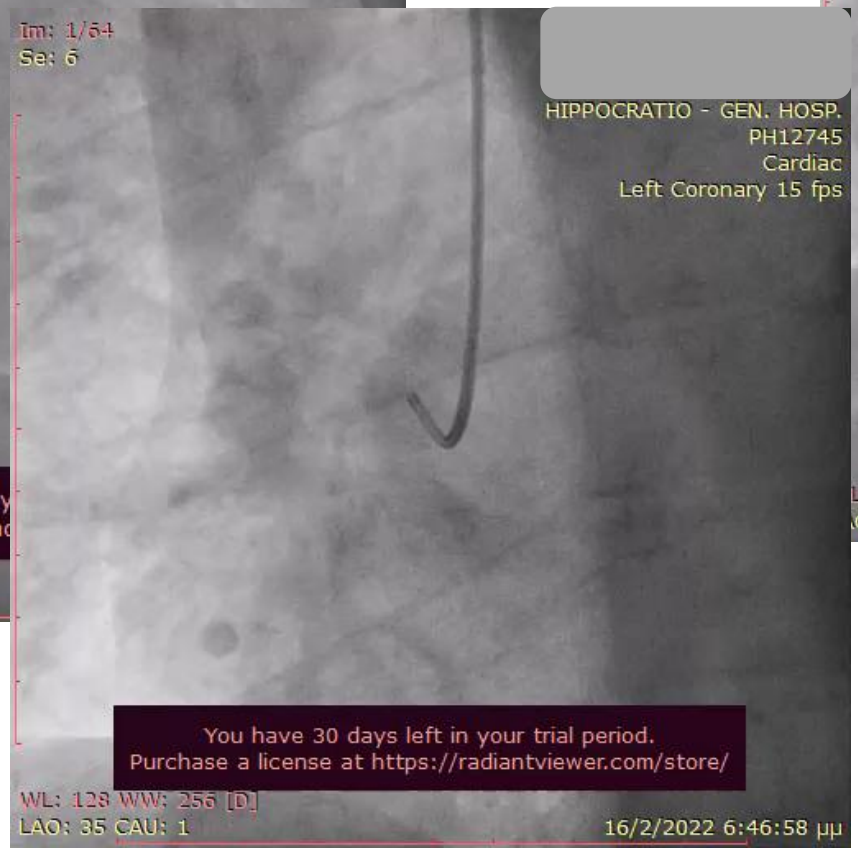
You have 30 days left in y
Purchase a license at https://rad
WL: 128 WW: 256 [D]
RAO: 22 CAU: 8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PH12745
Cardiac
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WL: 128 WW: 256 [D]
LAO: 35 CAU: 1
16/2/2022 6:46:58 μμ


Im: 1/57
Se: 7
HIPPOCRATIO - GEN. HOSP.
PH12745
Cardiac
Left Coronary 15 fps
You have 30 days left in your trial period.
Purchase a license at https://radiantviewer.com/store/
L: 128 WW: 256 [D]
O: 35 CAU: 1
16/2/2022 6:47:23 μμ

Measurement of coronary blood flow

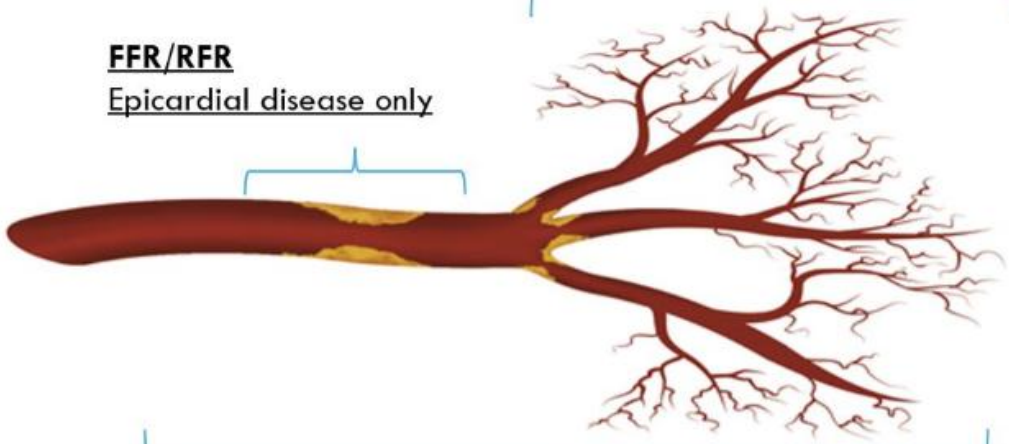
Microvascular Disease

- Hyperemia phase: IV adenosine 140 mcg/kg/min

Methods for assessing coronary circulation

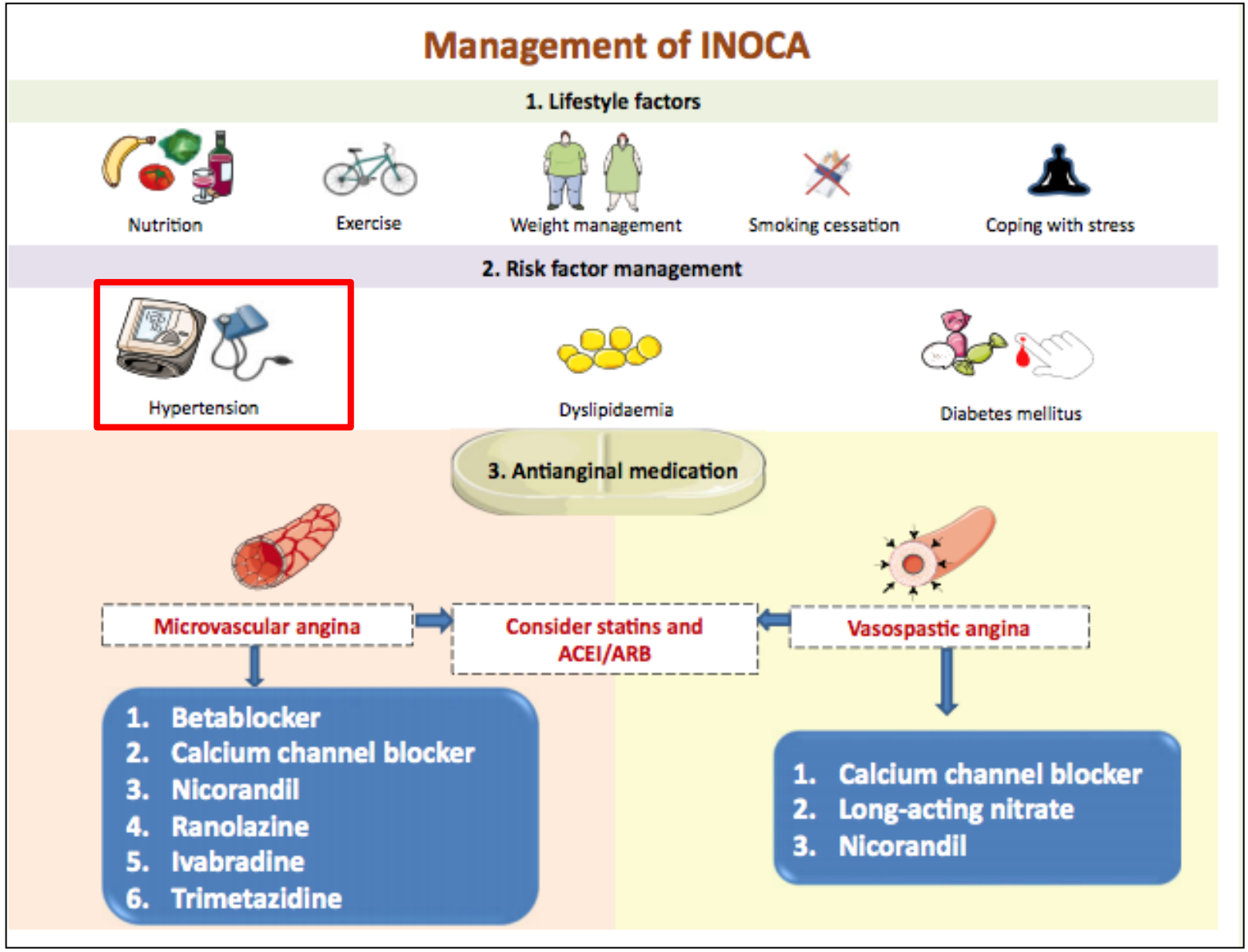
IMR = Resistance (au) — Micro-circulation only

FFR/RFR
Epicardial disease only



Absolute Flow/Resistance
Quantifiable assessment of microcirculatory Flow and Resistance in SI units

CFR = Flow at rest vs Flow at Hyperemia (au) — Affected by epicardial AND micro-circulatory disease



EAPCI Expert Consensus Document on INOCA. Eur Heart J 2020

Randomized trials in CMD

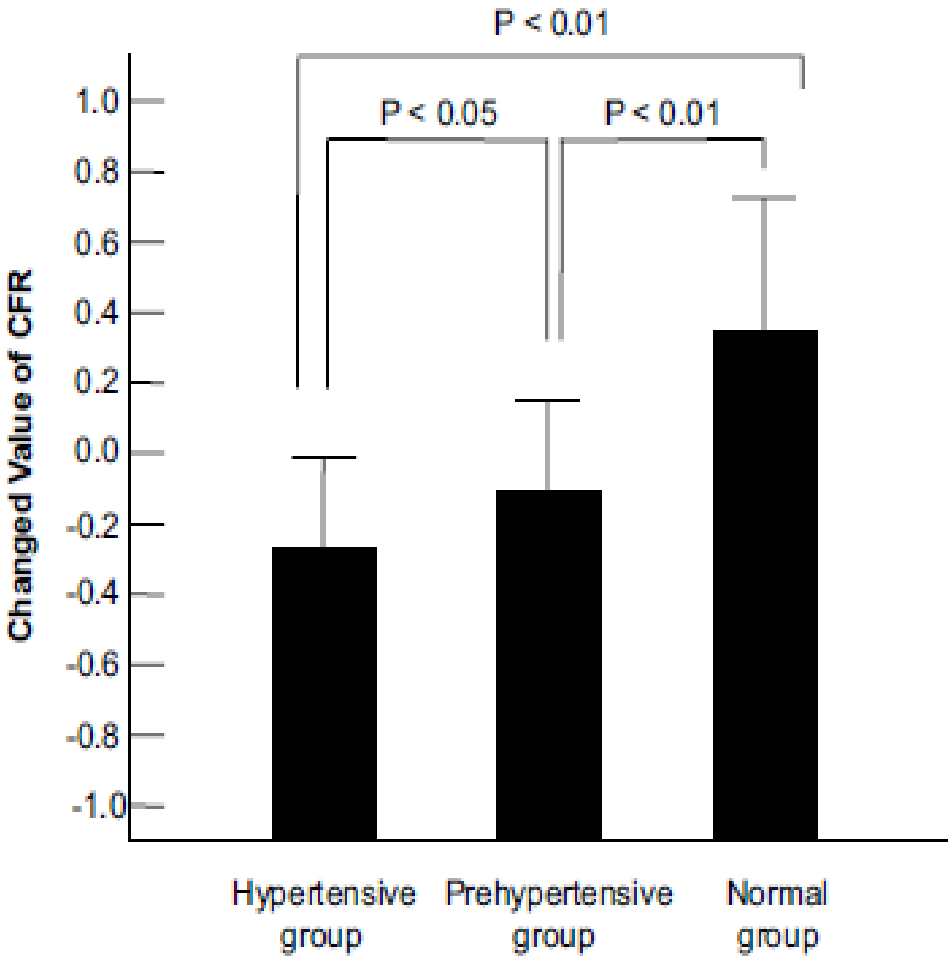
1985	Cannon	26 patients	syndrome x	calcium antagonist	placebo	improved exercise duration
1988	Romeo	30 patients	syndrome x	verapamil	acebutolol	improved exercise duration with both therapies
1999	Leonardo	16 patients	syndrome x	atenolol	trimetazidin	improved exercise duration with intervention
1994	Kaski	10 patients	reduced CFR	enalapril	placebo	improved exercise duration with intervention
2004	Pizzi	45 patients	syndrome x	ramipril/statin	placebo	improved exercise duration with intervention
2011	Laury	78 patients	NOCAD and CFR <3.0	quinalapril	placebo	improved CFR with intervention
1997	Chen	13 patients	microvascular angina	nicorandil	placebo	improved exercise duration with intervention
2011	Methta	20 patients	NOCAD, CMR with ischemia	ranolazine	placebo	less angina with intervention
2013	Villano	46 patients	NOCAD and CFR <2.5	ranolazine / ivabradine	placebo	improved exercise duration with ranolazine

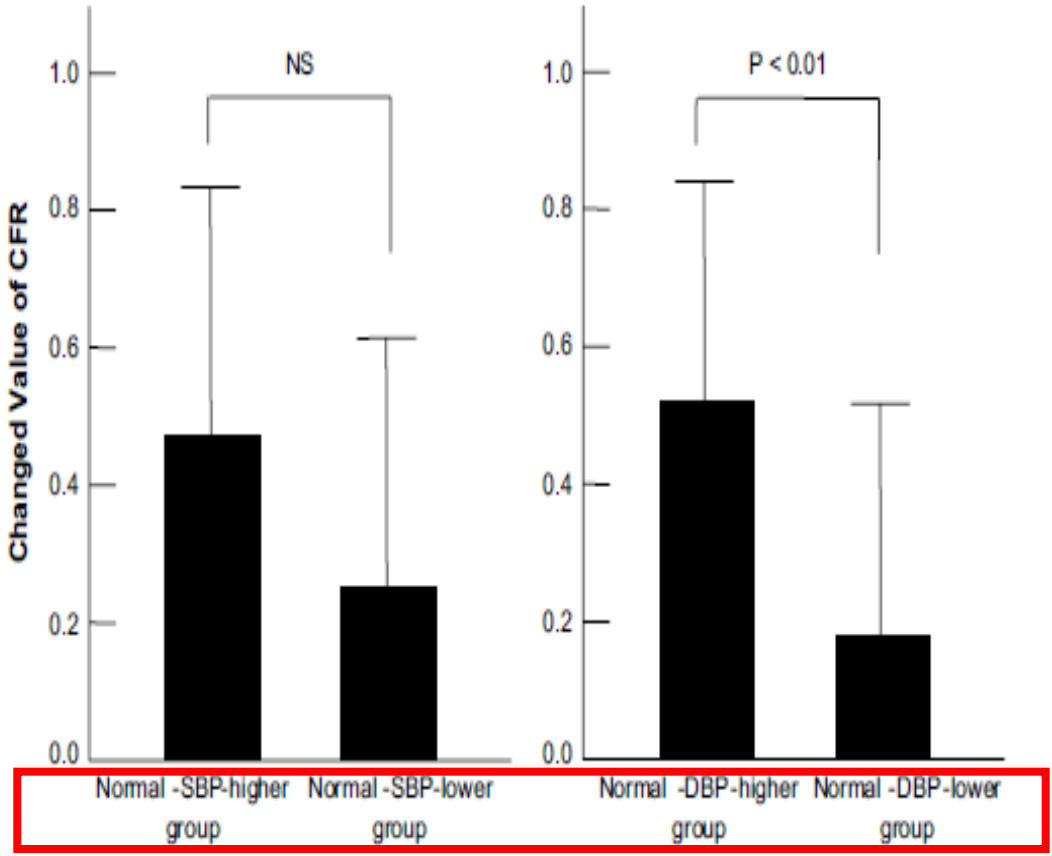
Drug interventions in small artery structure: Data so far

Reference	Drug	No. of patients	Basal M/L (%)	T M/L (%)	Δ M/L
	Diuretics	$n=33$			
Sihm *et al.* [40]	Hydrochlorotiazide	$n=25$	9.70	8.50	−1.20
Savoia *et al.* [47]	Eplerenone	$n=8$	8.75	7.50	−1.25
Mean			9.23	8.00	−1.23
SD			0.67	0.71	0.04
	Calcium-channel blockers	$n=45$			
Schiffrin *et al.* [38]	Nifedipine	$n=10$	7.52	5.71	−1.81
Sihm *et al.* [40]	Isradipine	$n=25$	10.90	8.80	−2.10
Schiffrin *et al.* [43]	Amlodipine	$n=10$	7.90	6.80	−1.10
Mean			8.77	7.10	−1.67
SD			1.85	1.57	0.51**
	ACE inhibitors	$n=79$			
Schiffrin *et al.* [34,35]	Cilazapril	$n=9$	7.64	5.64	−2.00
Sihm *et al.* [36]	Perindopril	$n=23$	9.70	7.50	−2.20
Thybo *et al.* [37]	Perindopril	$n=13$	7.94	5.96	−1.98
Rizzoni *et al.* [39]	Lisinopril	$n=14$	10.50	8.40	−2.10
Buus *et al.* [44]	Perindopril	$n=13$	8.05	6.84	−1.21
Rizzoni *et al.* [45]	Enalapril	$n=7$	11.70	9.20	−2.50
Mean			9.27	7.31	−1.97
SD			1.65	1.40	0.42***,#
	Angiotensin-receptor blockers	$n=42$			
Schiffrin *et al.* [41]	Losartan	$n=9$	8.40	6.70	−1.70
Schiffrin *et al.* [42]	Irbesartan	$n=11$	8.80	6.46	−2.34
Rizzoni *et al.* [45]	Candesartan	$n=8$	10.80	9.10	−1.70
Savoia *et al.* [46]	Valsartan	$n=14$	10.80	8.00	−2.80
Mean			9.70	7.57	−2.14
SD			1.28	1.23	0.54***
	β-blockers	$n=96$			
Schiffrin *et al.* [34,35]	Atenolol	$n=8$	8.23	8.00	−0.23
Thybo *et al.* [37]	Atenolol	$n=12$	7.14	6.79	−0.35
Schiffrin *et al.* [38]	Atenolol	$n=10$	7.52	7.32	−0.20
Schiffrin *et al.* [41]	Atenolol	$n=10$	8.30	8.80	0.50
Schiffrin *et al.* [42]	Atenolol	$n=11$	8.80	8.44	−0.36
Schiffrin *et al.* [43]	Atenolol	$n=9$	8.50	7.90	−0.60
Buus *et al.* [44]	Atenolol	$n=14$	8.05	7.65	−0.40
Savoia *et al.* [46]	Atenolol	$n=14$	10.70	10.00	−0.70
Savoia *et al.* [47]	Atenolol	$n=8$	8.75	7.50	−1.25
Mean			8.44	8.04	−0.40
SD			1.01	0.94	0.47

Agabiti-Rosei E, et al. J Hypertens 2009

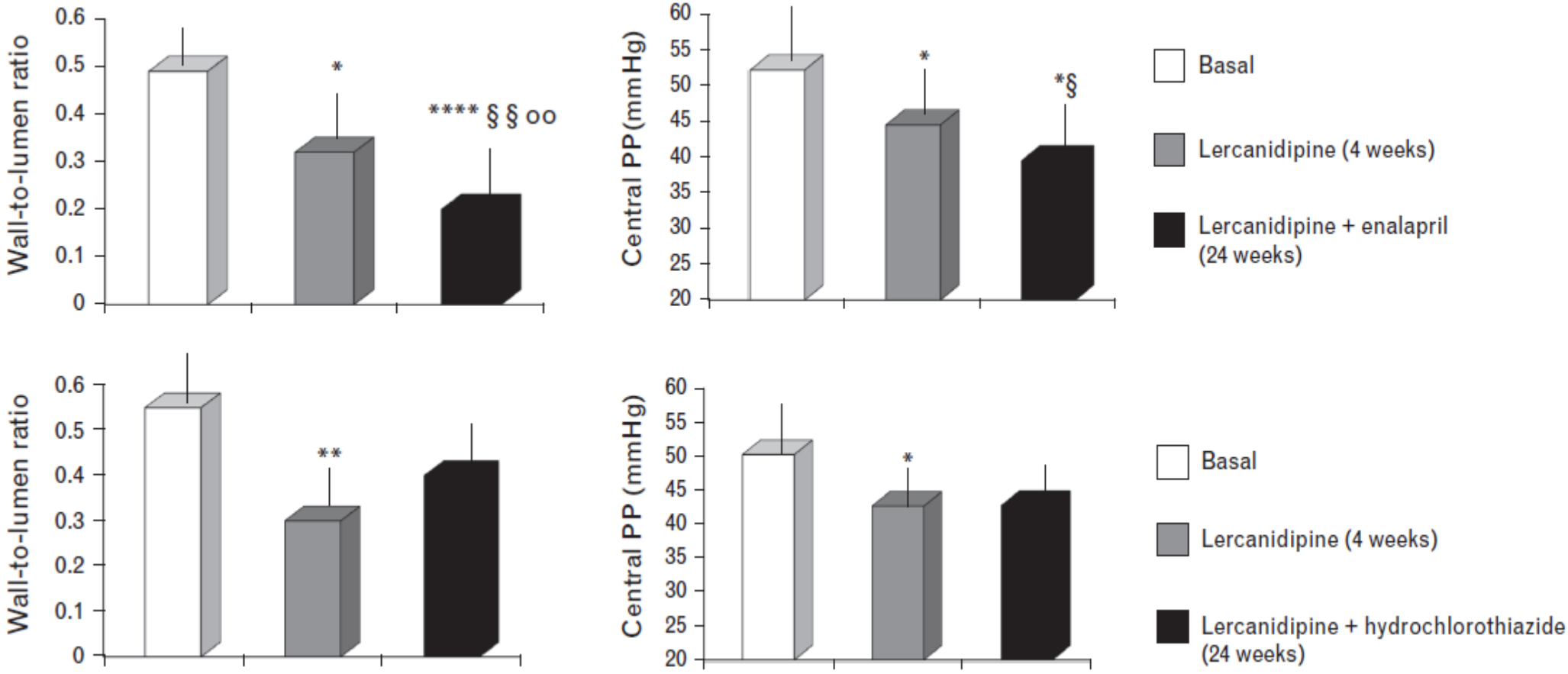
CFR and optimal BP control





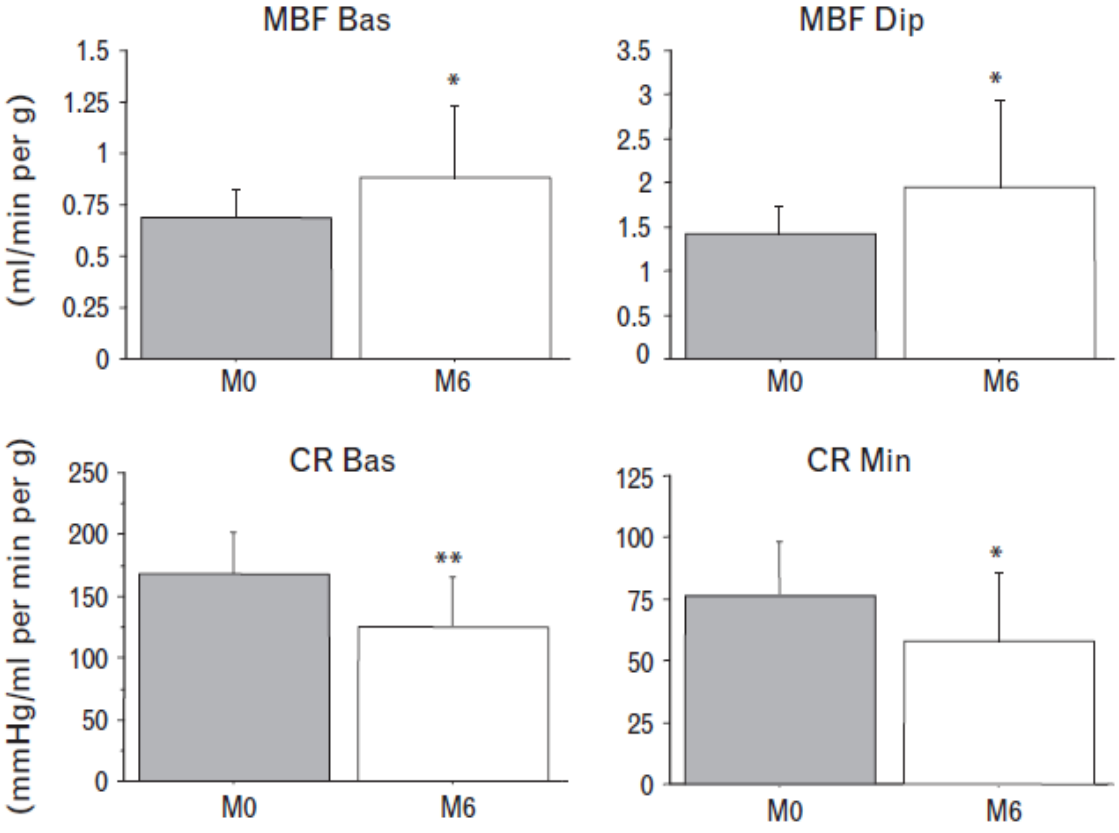
Mizuno R, et al. Hypertens 2012

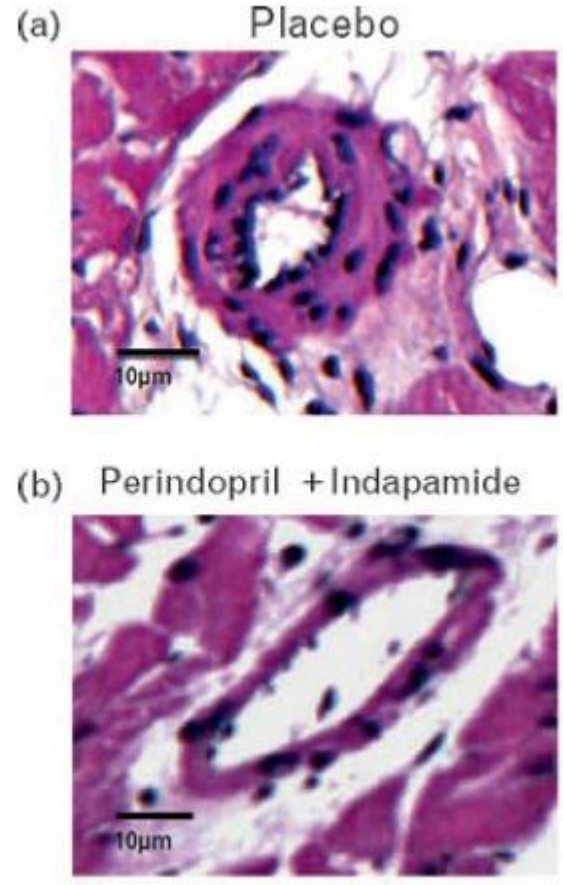
Antihypertensive therapy and microvascular structure in hypertension



De Ciuceis C et al. J Hypertens 2014

Antihypertensive therapy and microcirculation

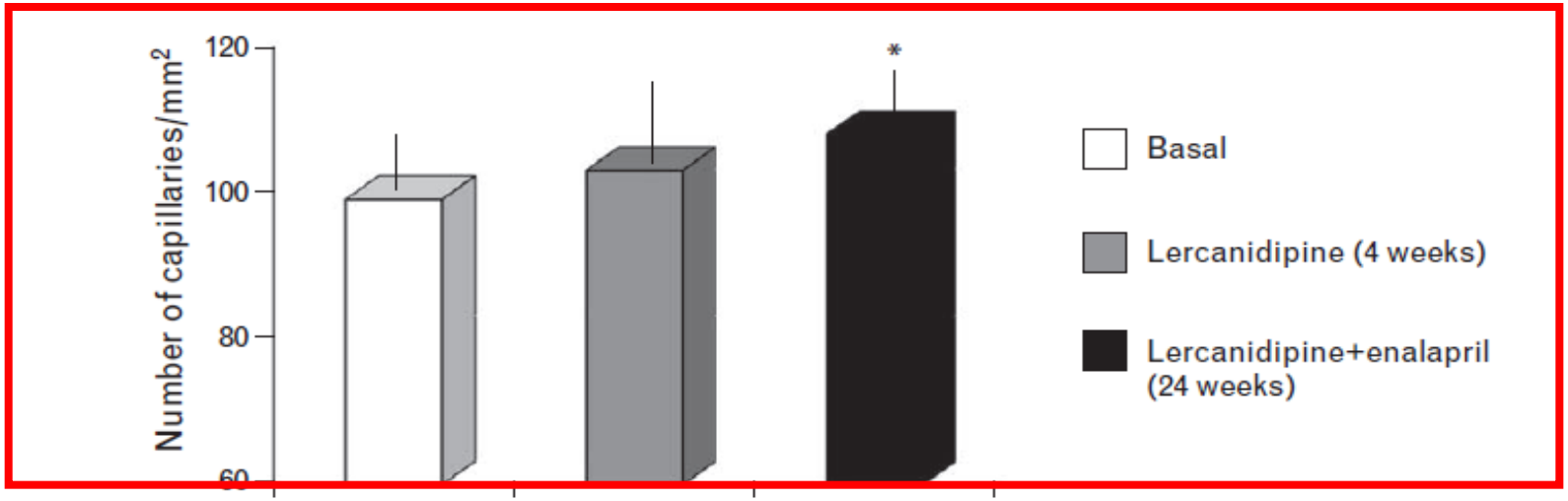


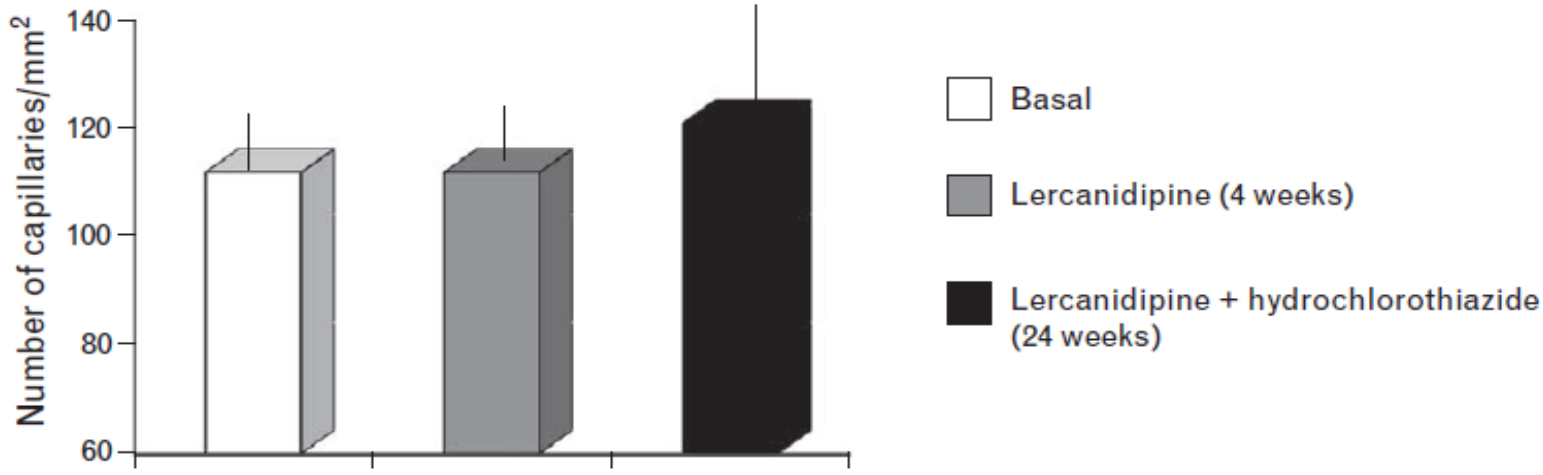


Indapamide+perindopril

Neglia D, et al. J Hypertens 2010

Effects on rarefaction





De Ciuceis C et al. J Hypertens 2014

Effects of antihypertensive combinations on SNS activity

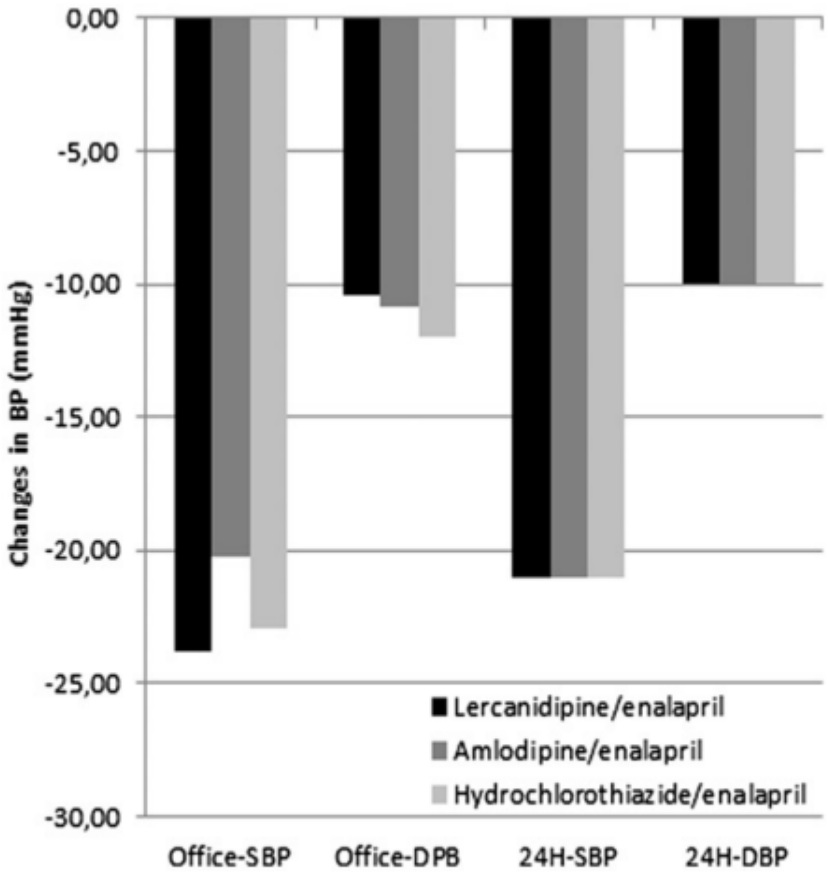


Figure 2. Changes in office and ambulatory blood pressure at 3 months. Abbreviations. BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.

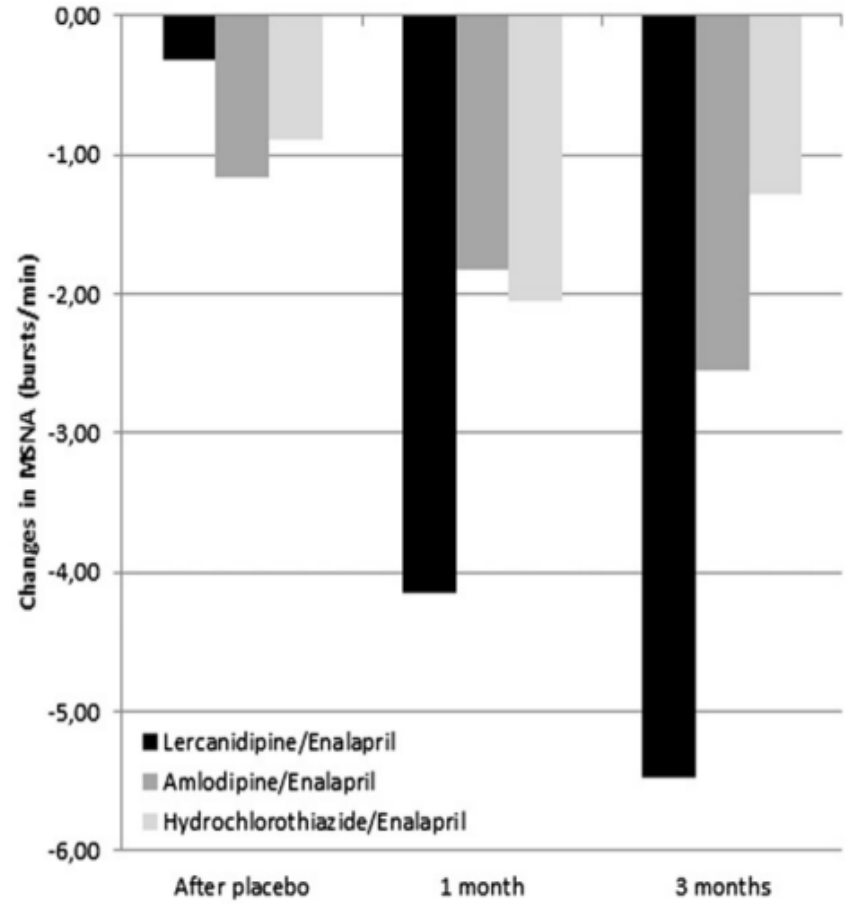
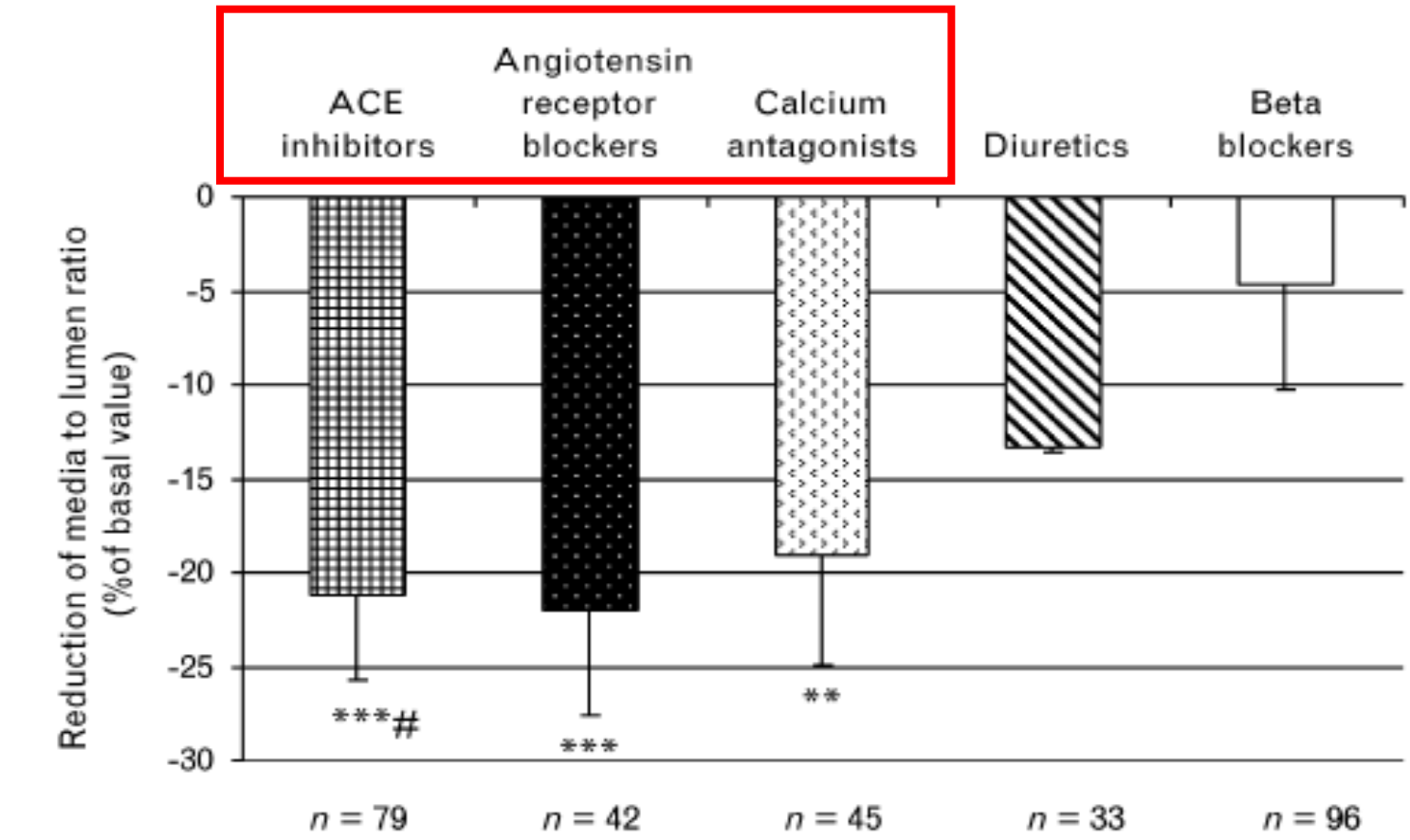


Figure 5. Changes in muscle sympathetic nerve activity (MSNA) from baseline.

K. Tsioufis, et al. Curr Med Res Opin 2016

Summary of effects



Agabiti-Rosei E, et al. J Hypertens 2009

ESC European Society of Cardiology

European Heart Journal - Cardiovascular Pharmacotherapy (2023) **0**, 1–17
https://doi.org/10.1093/ehjcvp/pvad053

REVIEW
Coronary artery disease

The effect of SGLT2 inhibitors on the endothelium and the microcirculation: from bench to bedside and beyond

Kyriakos Dimitriadis*, Eleni Adamopoulou, Nikolaos Pyrpyris, Athanasios Sakalidis, Ioannis Leontsinis, Eleni Manta, Emmanouil Mantzouranis, Eirini Beneki, Stergios Soulaidopoulos, Dimitrios Konstantinidis, Christos Fragkoulis, Konstantina Aggeli and Konstantinos Tsioufis

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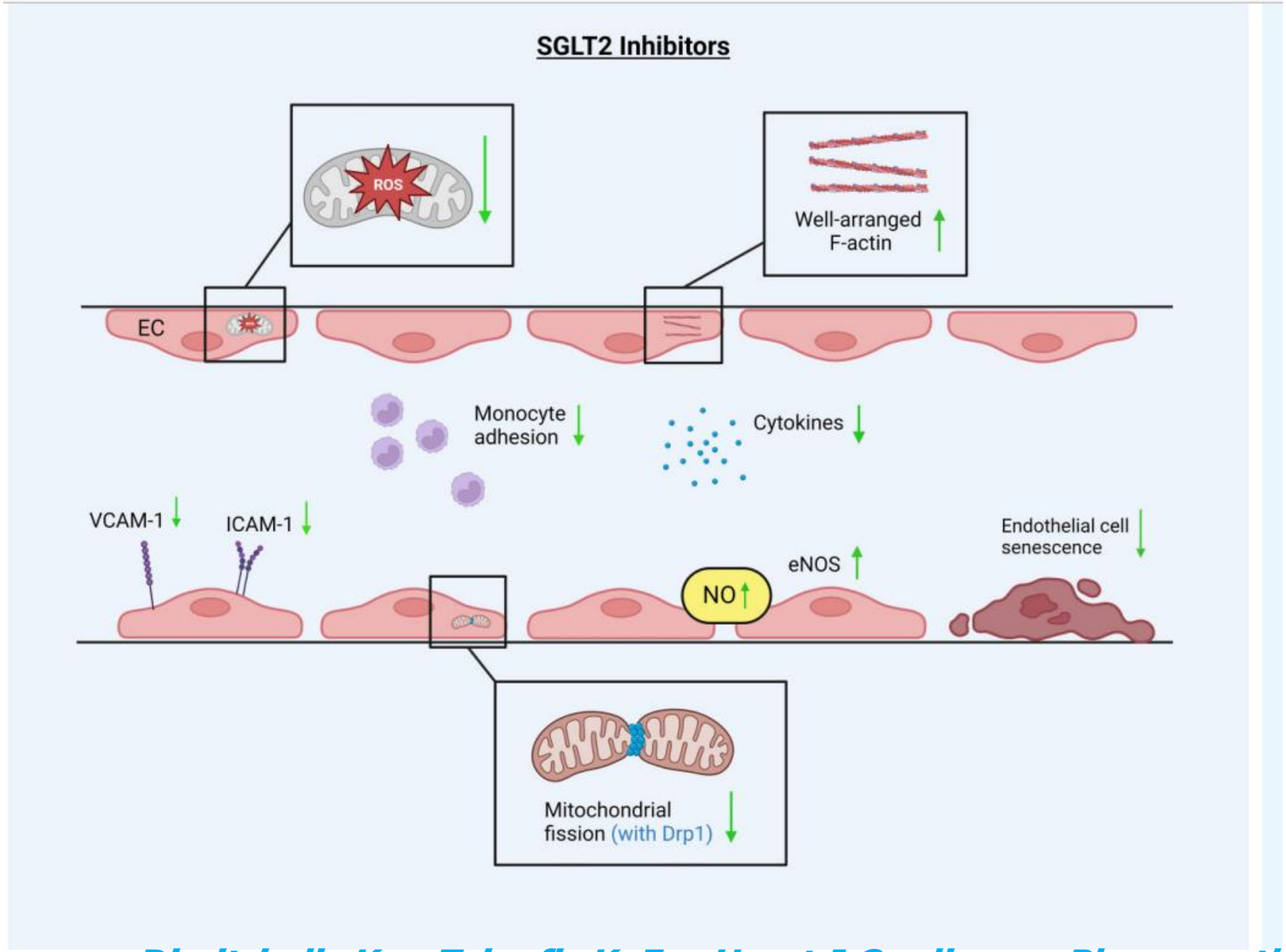
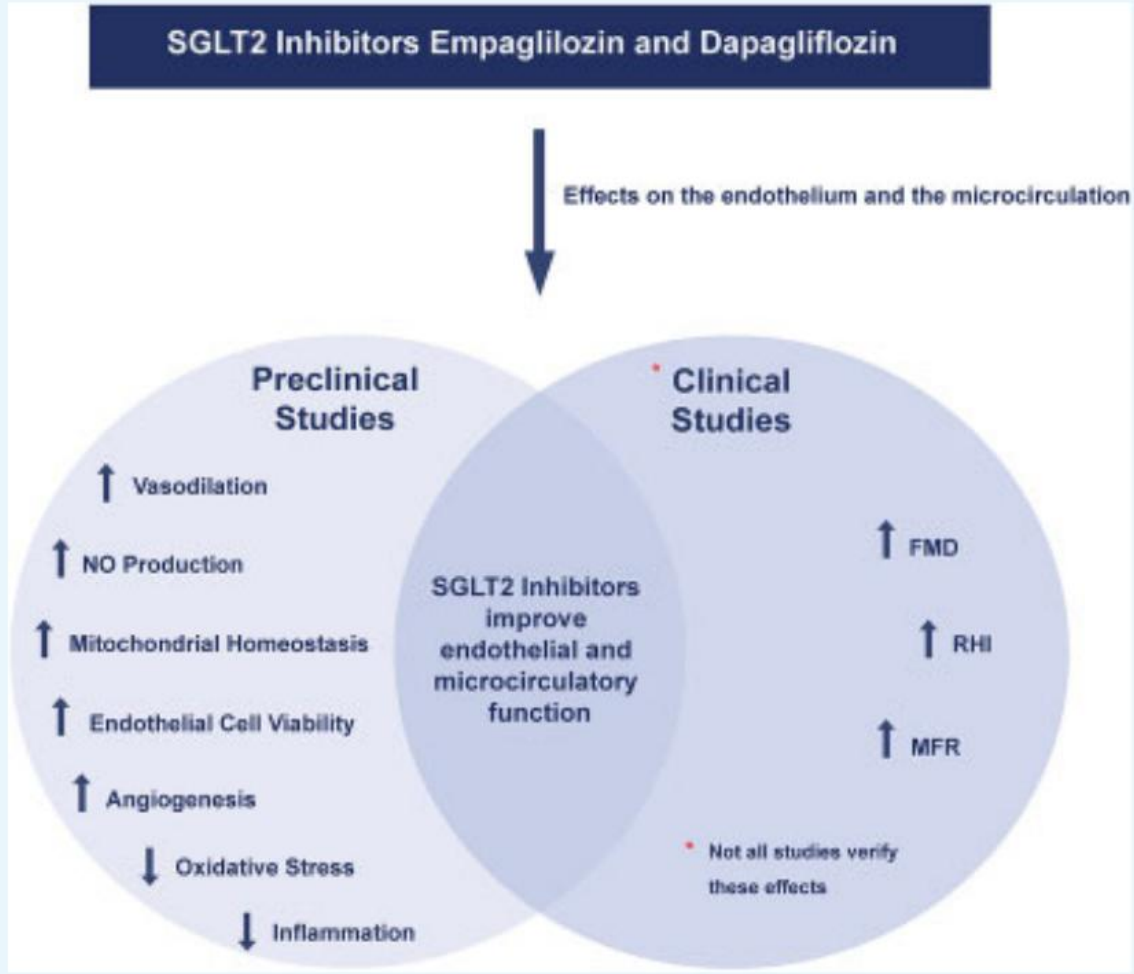
Received 5 May 2023; revised 22 June 2023; accepted 26 July 2023; online publish-ahead-of-print 27 July 2023

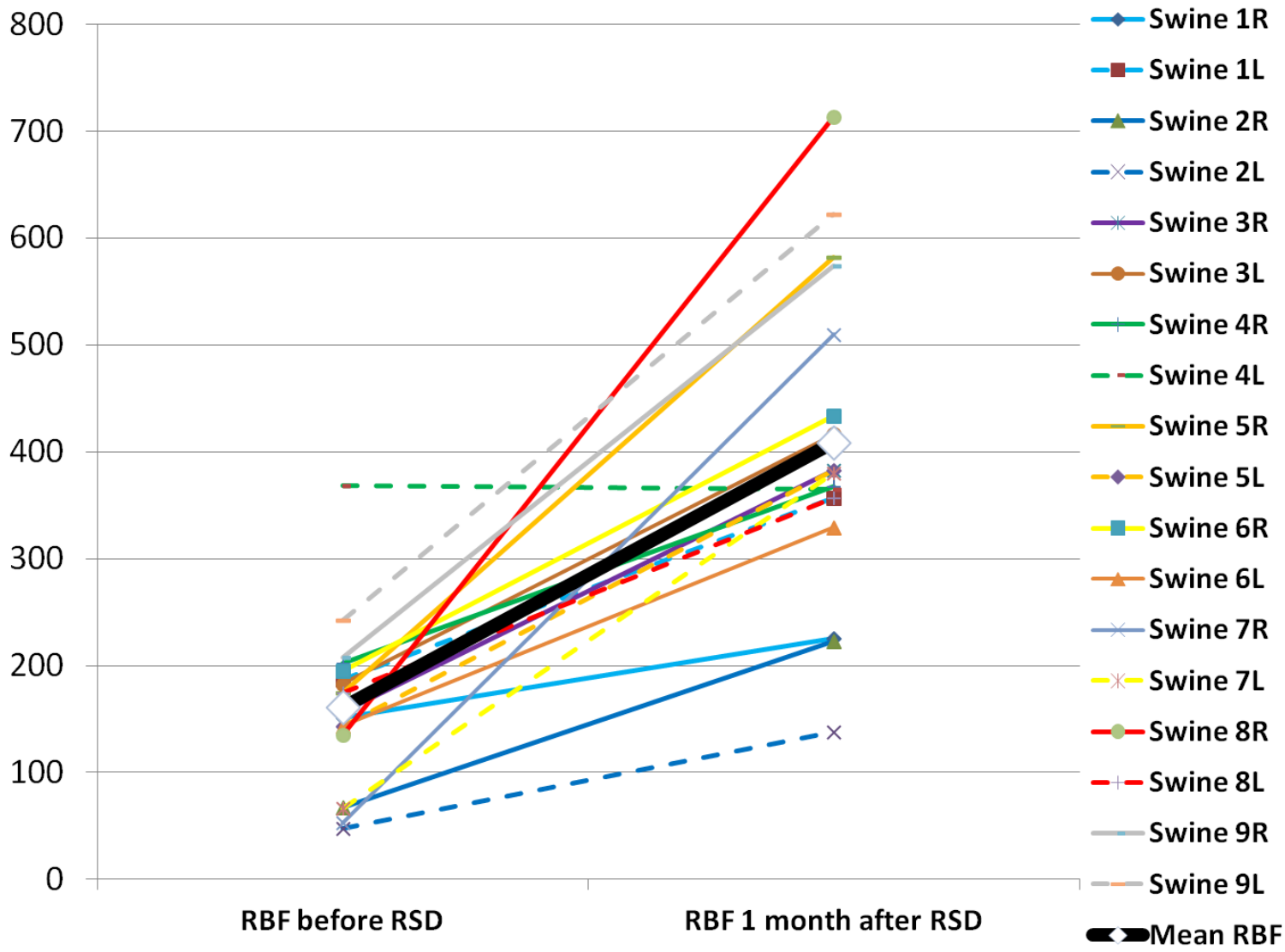


Dimitriadis K, …Tsioufis K. Eur Heart J Cardiovasc Pharmacother 2023



Dimitriadis K, …Tsioufis K. Eur Heart J Cardiovasc Pharmacother 2023

RDN and renal microcirculation in animal model



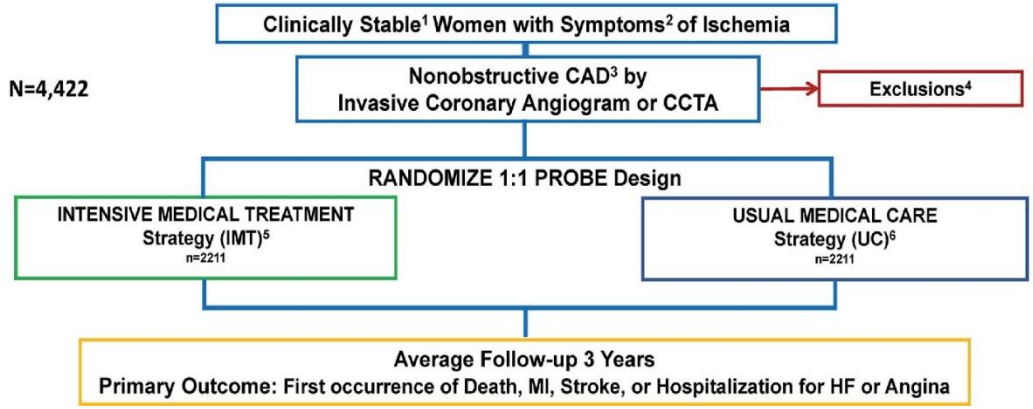
Tsioufis C, Papademetriou V, Dimitriadis K, et al. Int J Cardiol 2013

WOMEN'S ISCHEMIA TREATMENT REDUCES EVENTS IN NON-OBSTRUCTIVE CAD

WARRIOR (NCT #03417388)

Women's IschemiA TReatment Reduces Events In Non-ObstRuctiveCAD

Congressionally Directed Medical Research Programs
CDMRP
Department of Defense



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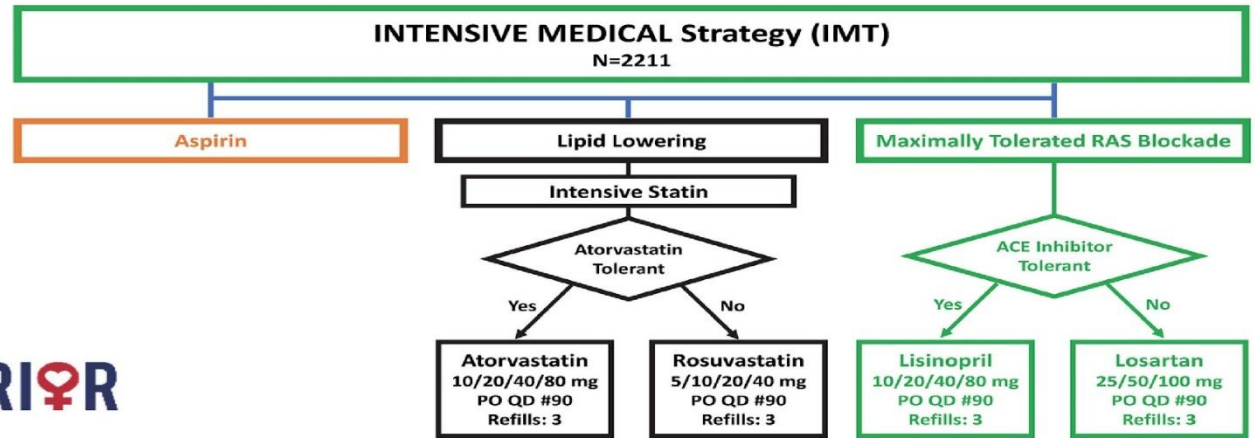
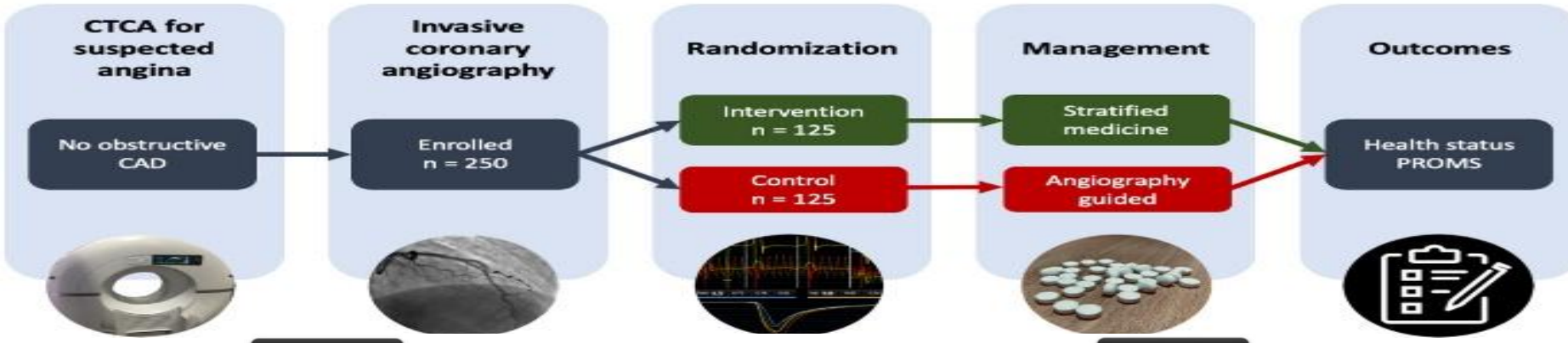


WARRIOR

The BHF CORONARY-CTCA Trial

The BHF CORonary Microvascular Function and CT Coronary Angiography Trial: Rationale and Design



SETTING | **EXCLUSION**

COMMUNITY

Screen CTCA referrals in 3 hospitals → 45%: no history of angina

RADIOLOGY DEPARTMENT

Angina (typical or atypical) → 10%: no angina; 25%: decline to participate

Enrolment with informed consent → 30%: obstructive CAD; <20%: relevant incidental findings

No obstructive CAD or alternative explanation for angina → 20%: declined angiography

CATHETER LABORATORY

Coronary angiogram &
Tests of coronary vascular function
Coronary guidewire – FFR, IMR, CFR
Pharmacological tests – ACh (10^{-4}, 10^{-5}, 10^{-6} M), ACh 100µg, GTN 300µg
n = 250

Intervention group n = 125

Control group n = 125

COMMUNITY

Patient reported health status at 6 and 12 months
Electronic record linkage for long-term follow up

Integrated approach to INOCA

Referral outpatient clinical program

Second opinion by the expert team
Standardised medical treatment
Personalised medical treatment
Multi Disciplinary Consultation

INOCA expert team

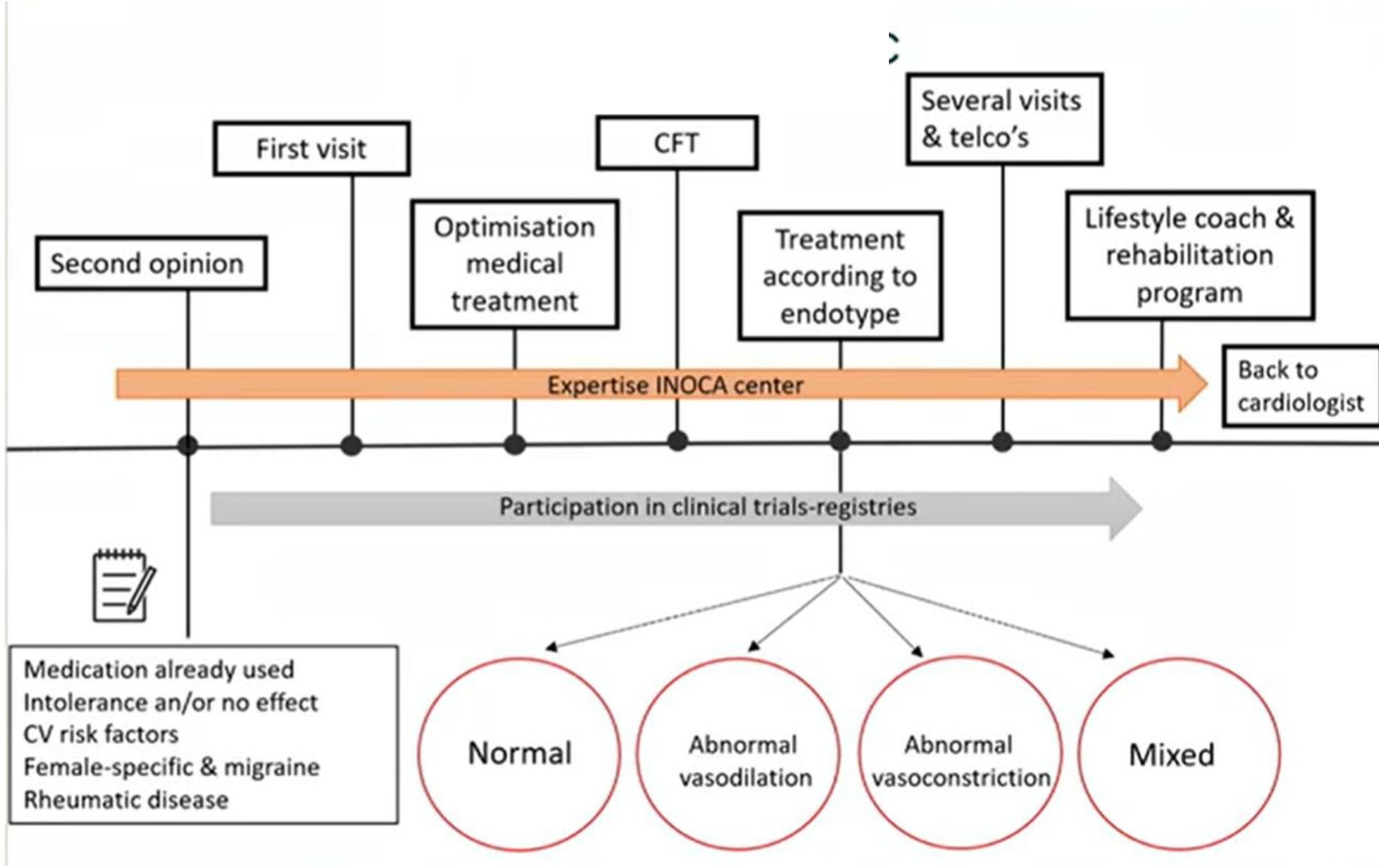
Interventional cardiologists
(Imaging) cardiologists
Nurse specialist
Physiotherapist & psychologist
Research team incl. PhD students

Invasive diagnostic procedures

Experienced cathlab team
Standardised protocol
Measurements vasospasm-CFR-HMR
Endotyping patients

Educational program

Referring centers and trainees
ESC INOCA concensuspaper 2020
Dutch guideline INOCA 2020
Latest results studies
Medical treatment
Lifestyle


Second opinion
First visit
Optimisation medical treatment
CFT
Treatment according to endotype
Several visits & telco's
Lifestyle coach & rehabilitation program
Back to cardiologist
Expertise INOCA center
Participation in clinical trials-registries
Medication already used
Intolerance an/or no effect
CV risk factors
Female-specific & migraine
Rheumatic disease
Normal
Abnormal vasodilation
Abnormal vasoconstriction
Mixed

Conclusions

- MD should be evaluated in the setting of hypertension
- MD is related to worst prognosis, HF pathophysiology and INOCA in hypertension
- Diagnostic interventional approach is key to successful diagnosis and phenotyping
- Research is needed to address modern optimal management in this high-risk hypertension setting, including INOCA pts
- The new “targeting” of MD equals “targeting” better prognosis in hypertension

ΣΑΣ ΕΥΧΑΡΙΣΤΩ ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ...

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