

NOVELTIES IN CORONARY PHYSIOLOGY

Where Are We ?



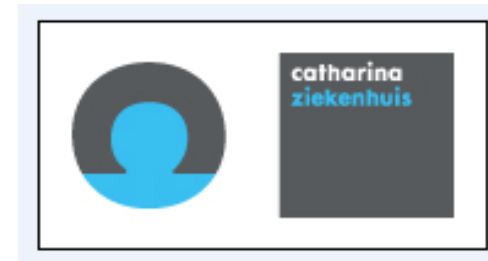
Madrid Microcirculation Meeting - 4th Edition

Madrid Microcirculation Meeting 4th Edition
november 29th & 30th 2023



CATHARINA-ZIEKENHUIS

Nico H. J. Pijls, MD, PhD
Catharina Hospital,
Eindhoven, The Netherlands





MMM Madrid Microcirculation Meeting - 4th Edition - Hospital Universitario de La Princesa

We are here in Madrid (2022)

Conflicts of Interest:

- Institutional Research Grants: Abbott
- Consulting relationships and fees: Abbott, Coroventis
- Equity: ASML, General Electric, Philips, Heartflow
- SAB: Heartflow
- Patents pending in the field of the coronary microcirculation and aortic valve stenosis



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Novelties in Coronary Physiology: Where Are We

- Absolute flow related novelties: true resting microvascular resistance ($R_{\mu,rest}$) and MRR
- Distinguish between functional and structural Microvascular Disease
- Standardized protocols for invasive assessment of MVD
- PPG (Pressure Pullback Gradient)
- New insights in NHPR (iFR vs FFR) and changes in guidelines
- Angiographic assessment of different indices
- EuroCraft Registry
- Non-invasive assessment of coronary physiology and MVD: PET/CT (Heartflow) or Hybrid Approaches:
MASTER-PACT Study



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Novelties in Coronary Physiology: Where Are We

- 15 years ago, every interested cardiologist and every center had his/its own protocol for investigation of the coronary microcirculation:

→ great variability in accumulation of data and different studies hard to compare

- Several standardized protocols have been made now and are implemented in the guidelines (ACC/AHA & ESC)

→ comparability of data and increased knowledge, larger studies (multicenter), accumulation of knowledge.



Accepted protocols consist now of:

Testing for vasospastic angina (acetylcholine), followed by

→ ***FFR, CFR, IMR by bolusthermodilution , followed by or replaced by***

→ ***absolute flow and resistance at rest and at hyperemia & MRR by continous thermodilution***

(guidelines will be adapted)

Novelties in Coronary Physiology: Where Are We

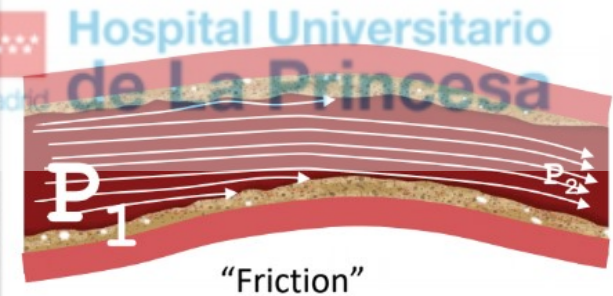
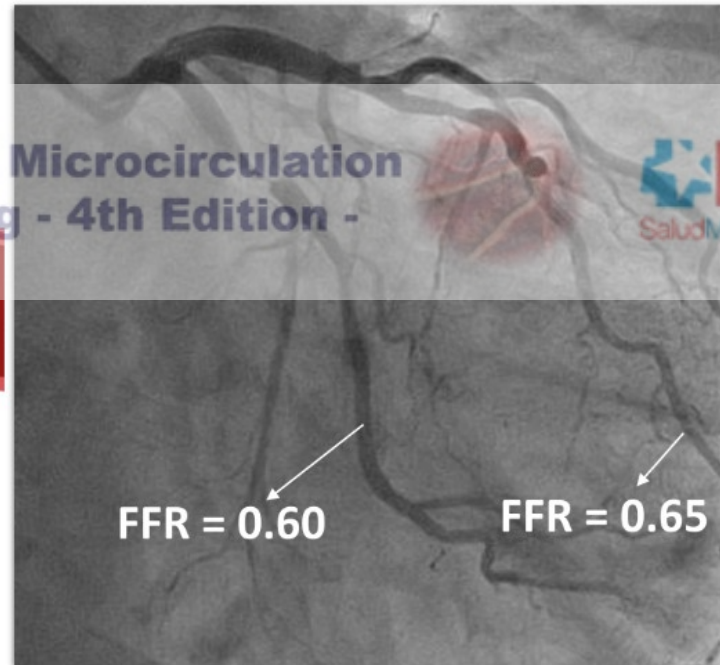
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Focal versus Diffuse Atherosclerosis



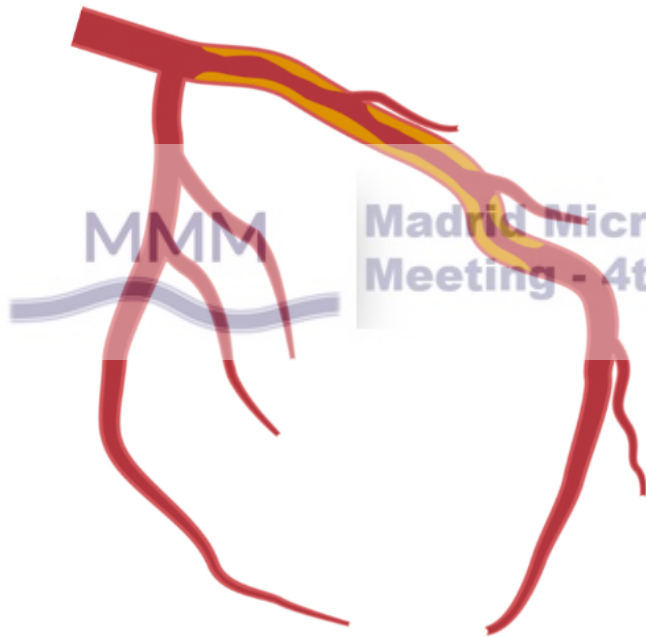
$$\Delta P = fQ + sQ^2$$



$$\Delta P = fQ + sQ^2$$



Diagnosis of Diffuse Disease



No standardized criteria



Relies on visual assessment



Low interobserver reproducibility



Cannot be detected by angiography

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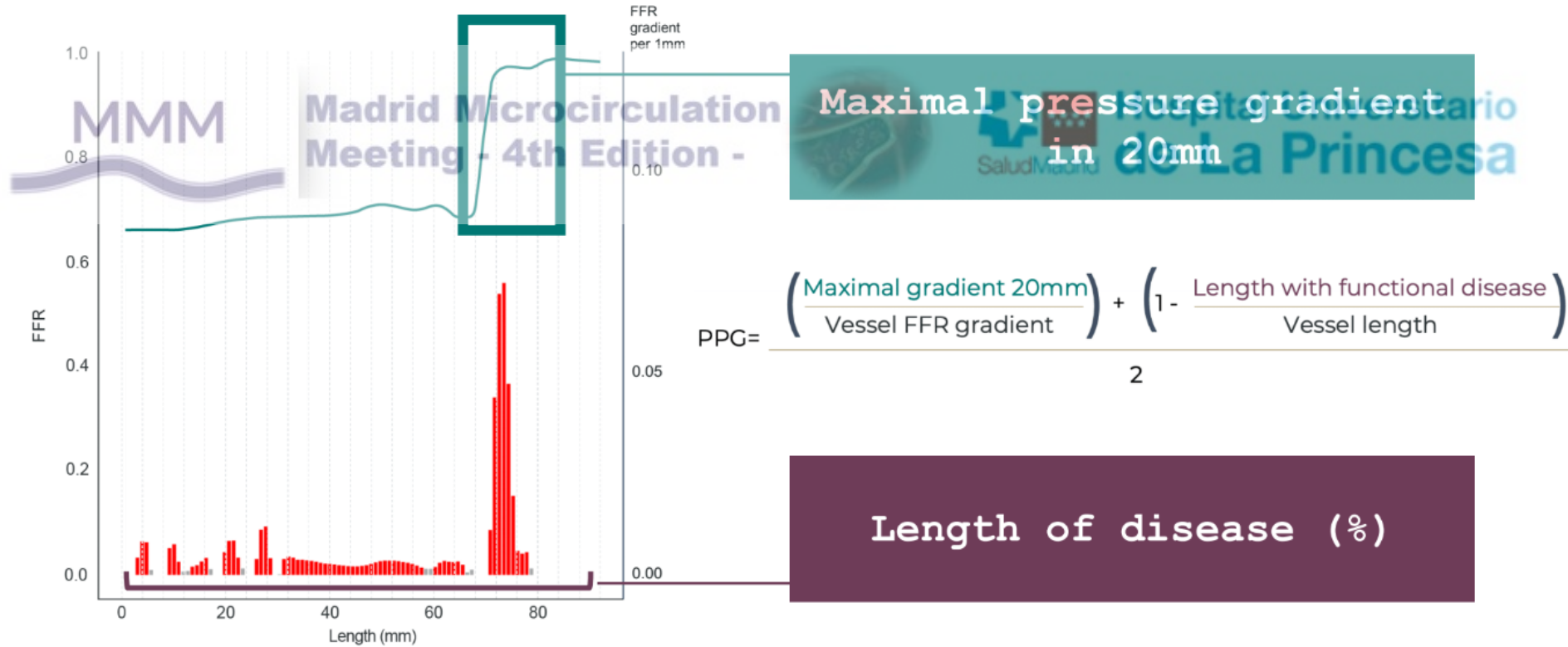
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For “physiologists” : hyperemic pull-back recording under fluoroscopy
or:
Resting pullback recording on Philips console

Principles of Pressure Pullback Gradient (PPG)

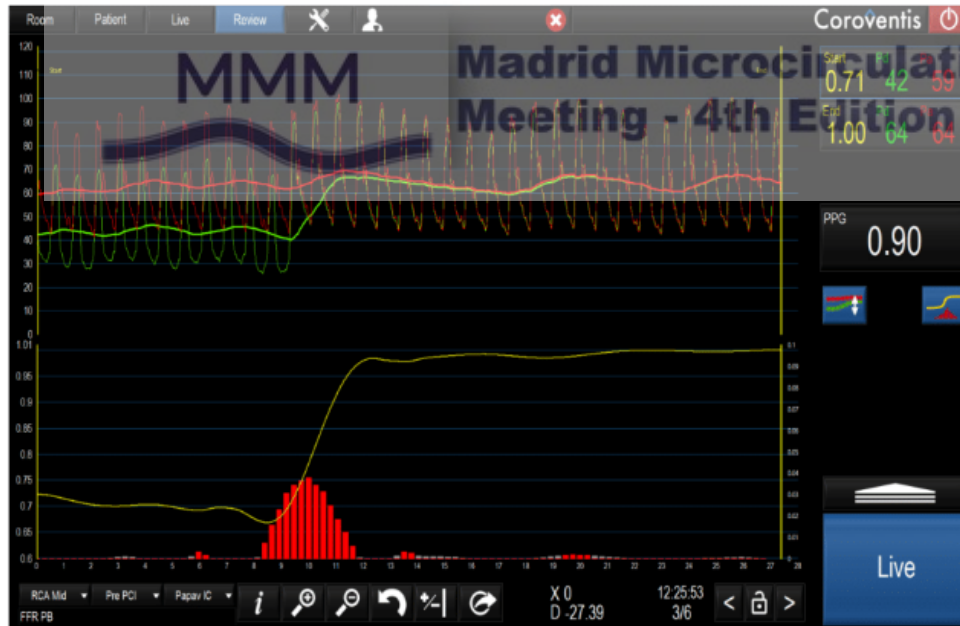


PPG 'focality' and diffuseness



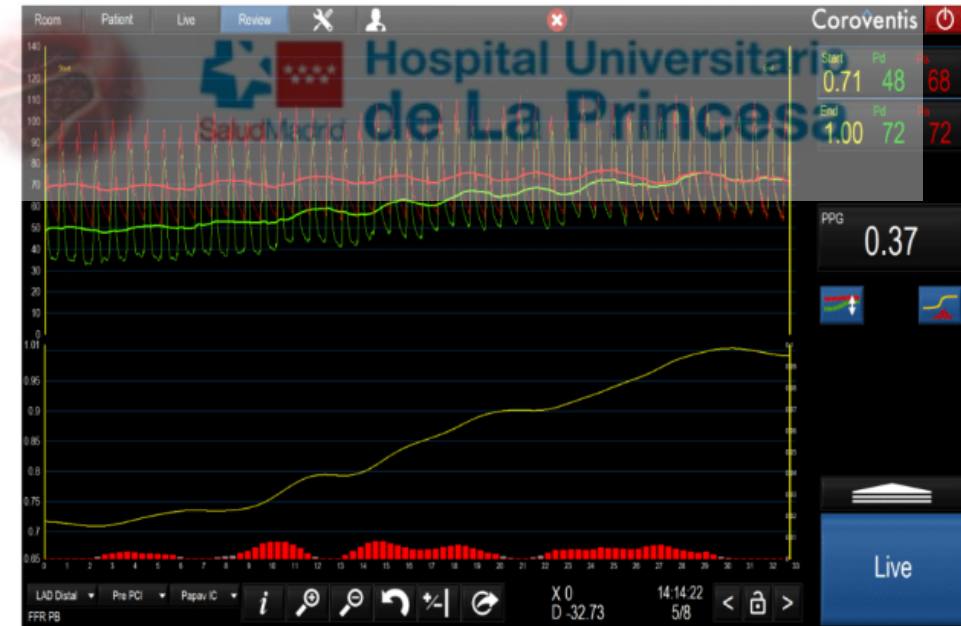
1. Does this patient need to be treated?
2. How can this lesion be treated?

Focal



PPG close to 1 → focal disease

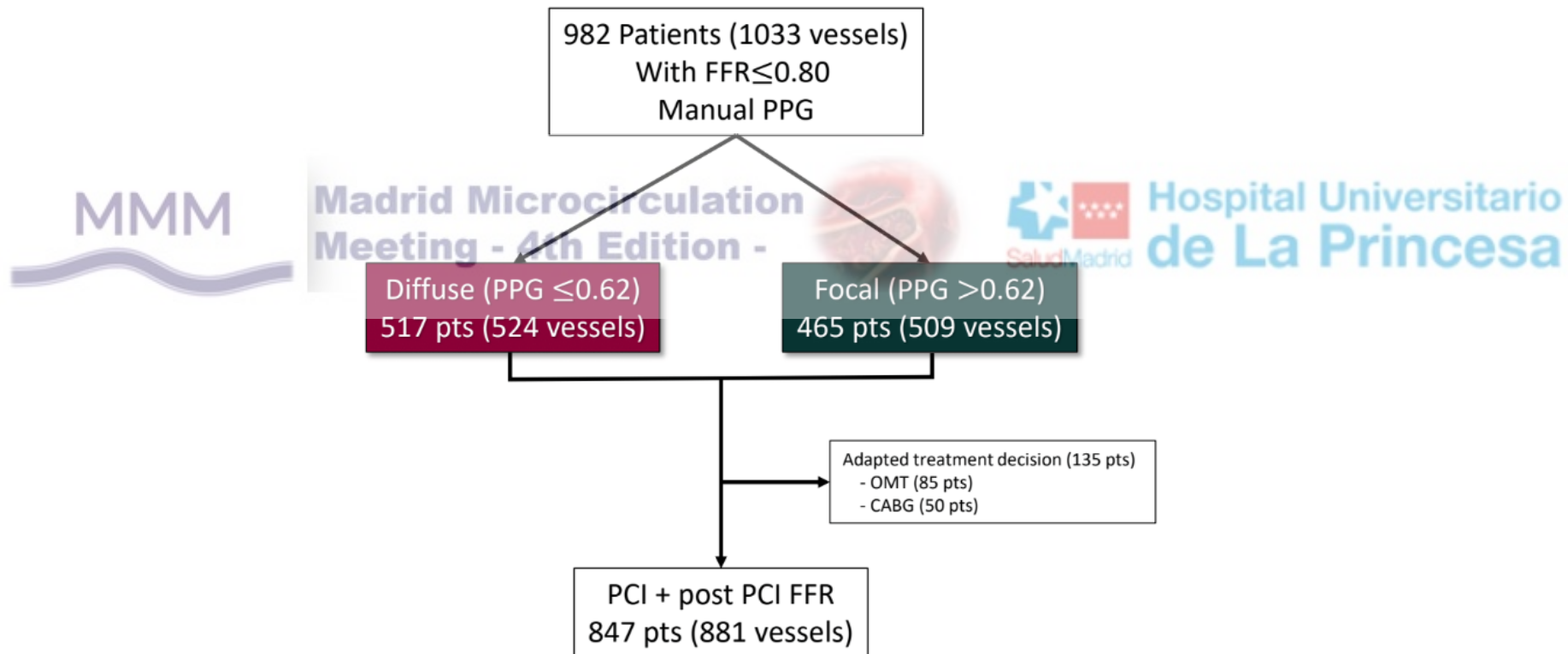
Diffuse



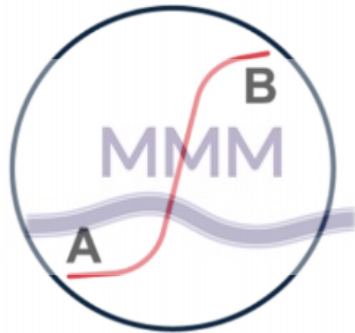
PPG close to 0 → diffuse disease

$$1 > \text{PPG} > 0$$

PPG-Global Registry



PPG-Global Registry Conclusions



Patients with focal disease defined by PPG achieved higher final FFR values after PCI compared to those with diffuse disease.



PPG before intervention predicted post-PCI FFR with excellent accuracy.



The systematic measurement of PPG in patients already planned to undergo PCI changed revascularization decisions in one out of seven patients



Periprocedural myocardial infarction was lower in focal than in diffuse disease.

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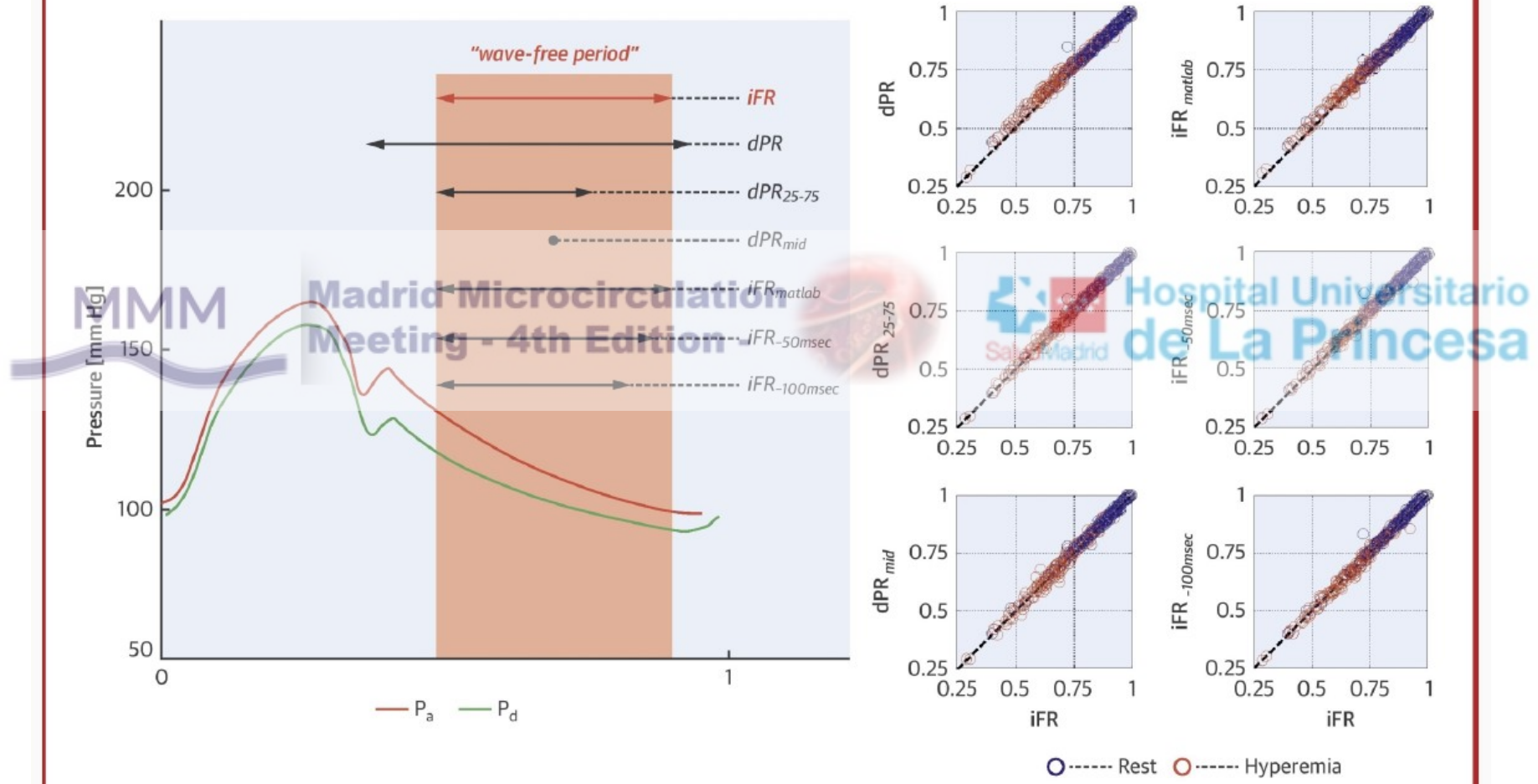


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CENTRAL ILLUSTRATION: Correlations and AUC Values >0.99 for All Resting Pd/Pa Ratios Over Different Periods in Diastole Compared With iFR as the Reference Standard



van't Veer, M. et al. J Am Coll Cardiol. 2017;70(25):3088-96.

HYPEREMIA (FFR) vs NHPR (iFR, dPR, RFR, etc)

DEFINE-FLAIR

Davies, NEJM 2017

SWEDE-HEART

Gotberg, NEJM 2017



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VS

FAME

Tonino, NEJM 2009

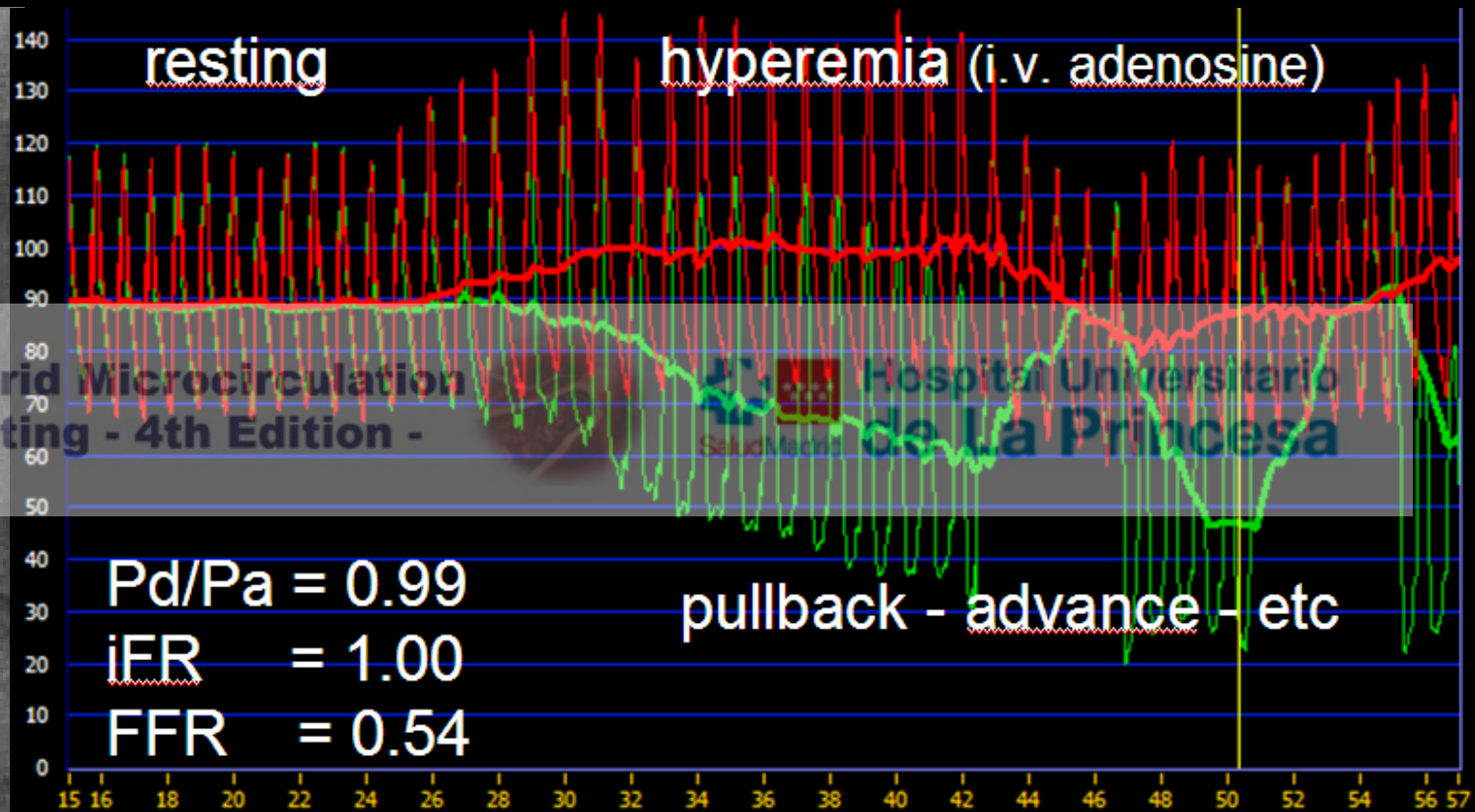
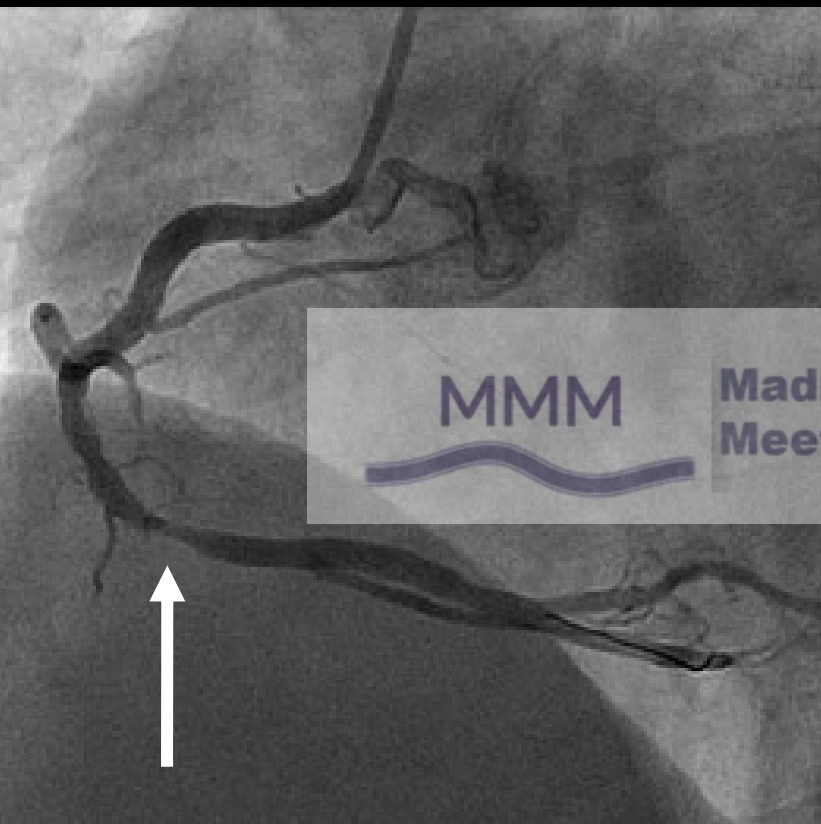
VERIFY

Berry, JACC 2012

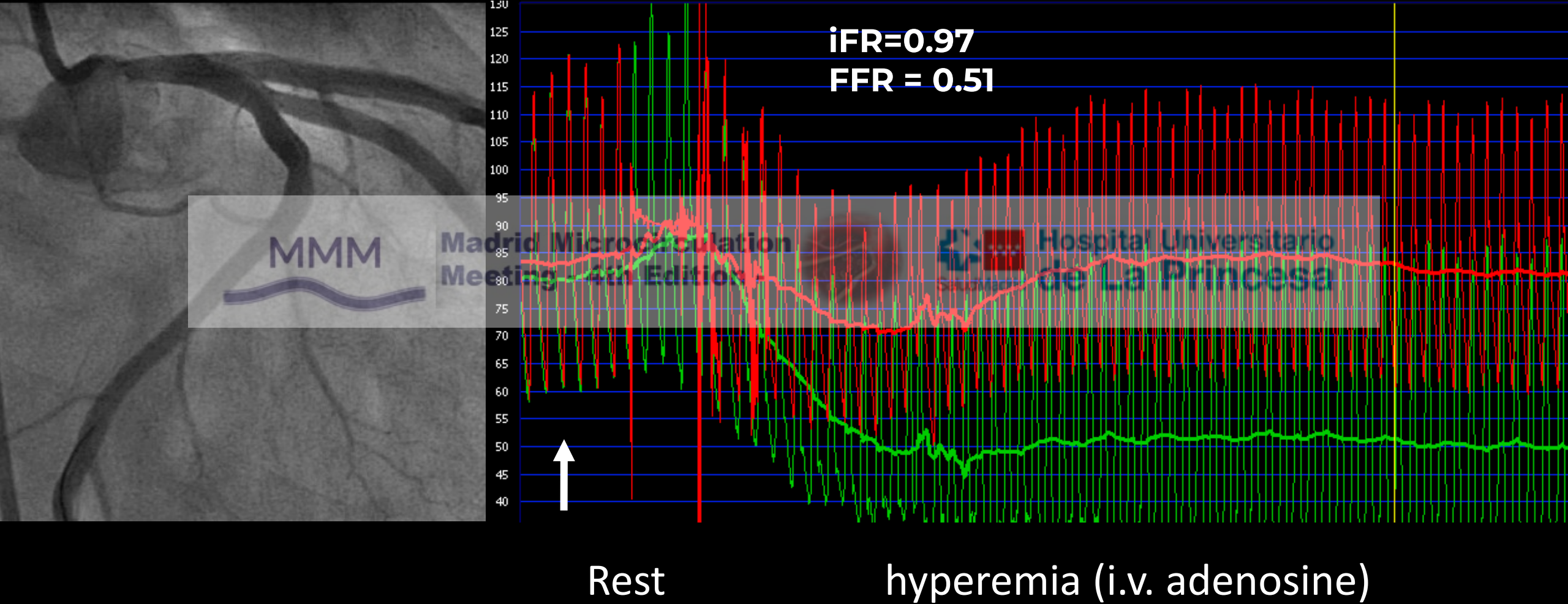
Non-inferiority of NHPR's was investigated in 2 RCT'S:
DEFINE-FLAIR study and SWEDE-HEART:

- low-risk populations (*not all-comers as claimed, but selective group of low-risk pat*)
- single vessel disease in 58% of patients
- no PCI at all-in 45% of patients
- average number of stents 0.7
- ***Studies claimed to be “physiology-guided” but first an angiographic assessment was made and only if visual lesion severity was < 70%, iFR or FFR was measured***
 - ➔ Almost 50% of all stents were placed without physiologic measurement, just by eye-balling
 - ➔ Many false-negative iFR excluded from analysis ***by design*** of the study

Young male, large RCA, focal lesion 70%



Middle-aged woman, short 50% LM stenosis



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Not surprisingly, iFR was found to be non-inferior to FFR in these populations at one year, which could be expected merely by the design of the studies and the low-risk populations investigated.

Nevertheless, the results of the Define-Flair and Swede-Heart Studies (“iFR is non-inferior to FFR at 1 year”) in these selected low-risk populations) were **extrapolated to all patients in the cathlab** (including MVD, LM, bifurcations, etc) and taken-over in the Guidelines without additional proof.

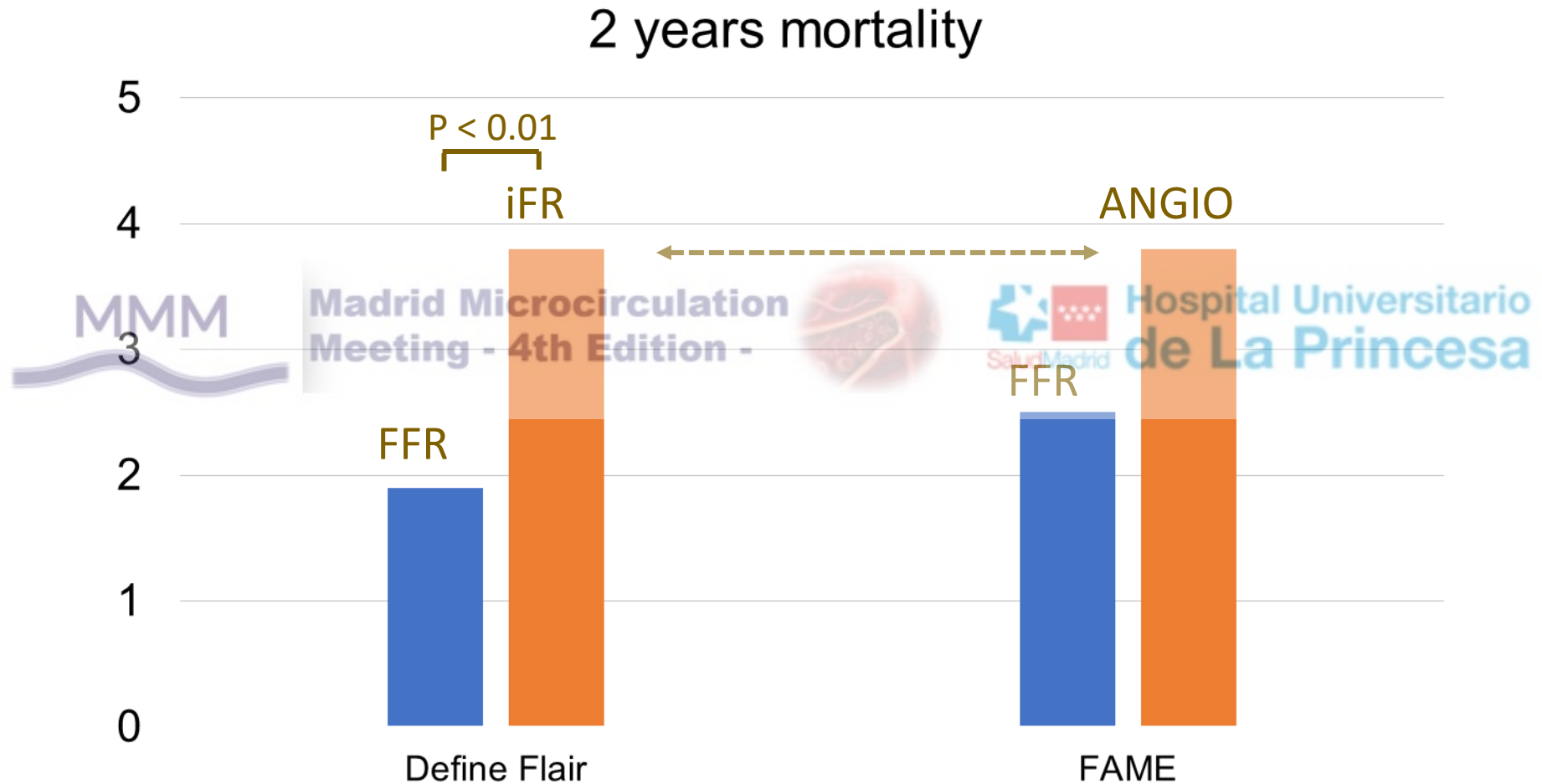


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2-year-mortality with iFR- guidance in low-risk
DEFINE-FLAIR population, was as high as in
angio-guided group in complex FAME population



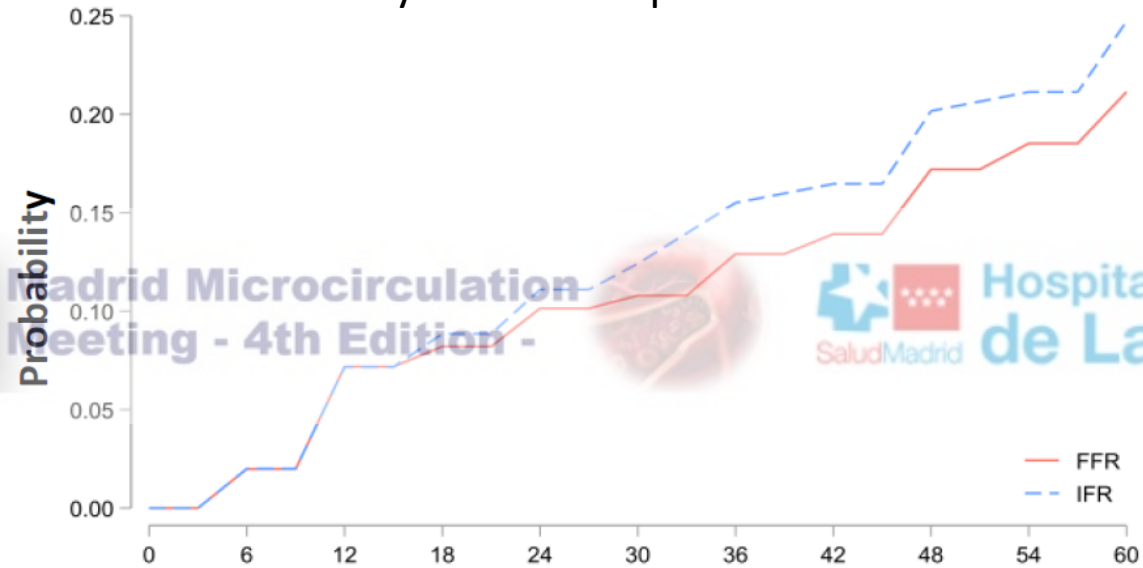
adapted from Davies J, TCT 2019; Van Nunen, Lancet 2015;386;1853-1860

MACE

Meta-analysis Define-Flair and SwedeHeart

iFR 21.5 %
FFR 18.6 %
HR 1.18 95% CI[1.04; 1.34]

5-year follow-up



No. at risk	0	6	12	18	24	30	36	42	48	54	60
FFR	2257	2164	2037	1910	1849	1789	1773	1726	1703	1631	1339
iFR	2254	2149	2011	1873	1824	1757	1731	1670	1647	1574	1275



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Instantaneous Wave Free Ratio vs. Fractional Flow Reserve

Nov 06, 2023

Authors: Eftekhari A, Holck EN, Westra J, et al.

Citation: [Instantaneous Wave Free Ratio vs. Fractional Flow Reserve and 5-Year Mortality: IFR SWEDEHEART and DEFINE FLAIR. Eur Heart J. 2023;44:4376-4384.](#)

Summary By: [Debabrata Mukherjee, MD, FACC](#)

Quick Takes

- iFR-guided revascularization is associated with an increase in the composite of MACE (all-cause mortality, MI, or unplanned revascularization) and all-cause mortality alone compared to FFR-guided revascularization.
- Based on the current data, FFR-guided strategy should be the preferred option in proximal lesions in large coronary arteries with a large perfusion territory.
- Pending additional data, it is prudent to use nonhyperemic pressure indices judiciously and consider FFR-guided revascularization the gold standard strategy for intracoronary pressure measurement.

Quick Takes

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- Pending additional data, it is prudent to use nonhyperemic pressure indices judiciously and consider FFR-guided revascularization the gold standard strategy for intracoronary pressure measurement.

Similar statement in Editorial in Europ Heart J November 2023

And call to change the guidelines (ACC & ESC)

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True FFR on horizontal axis; FFR by Angio on vertical axis

Ninomiya et al: JACC CVI 2023 *on-line*:

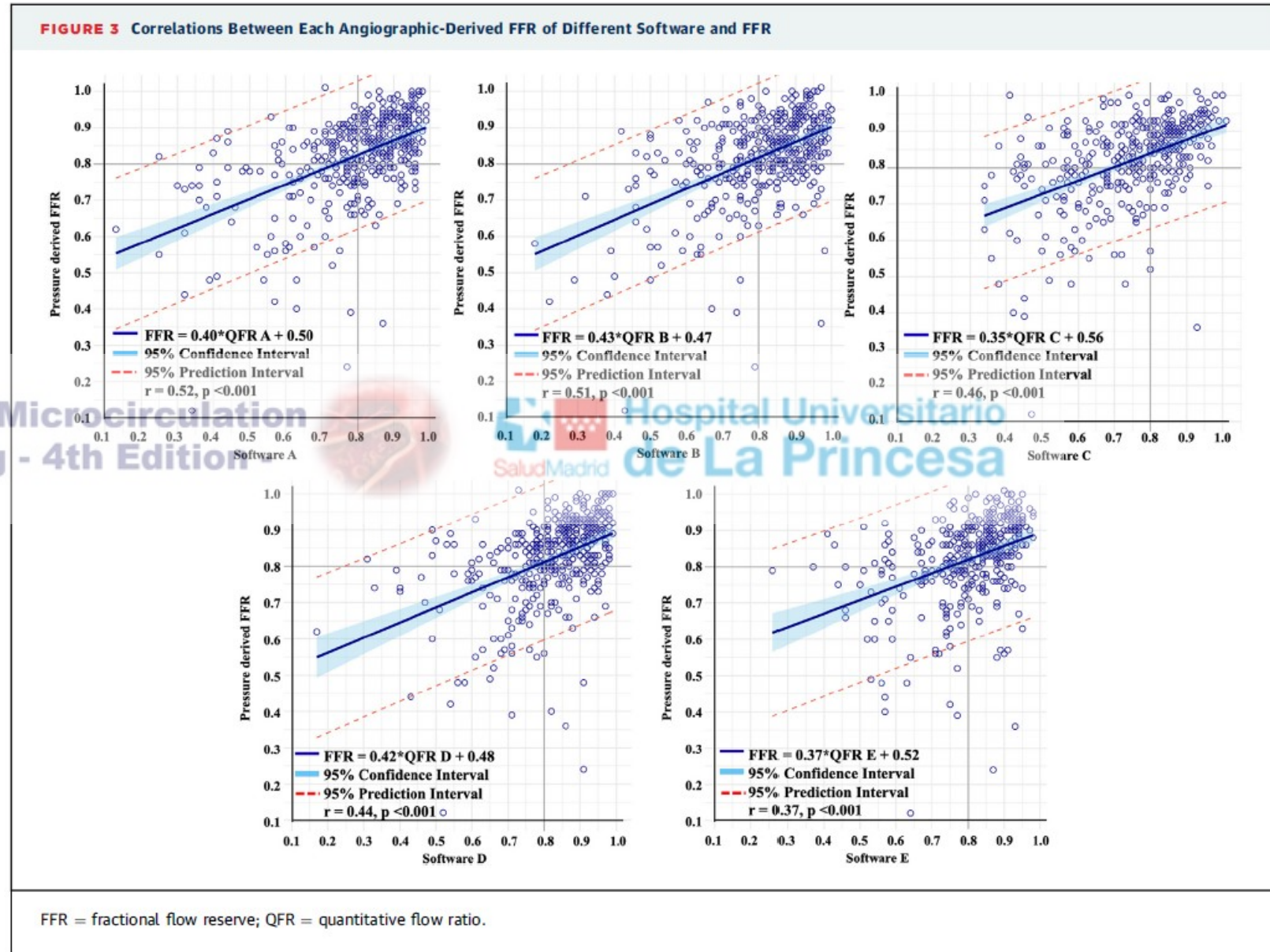
Blinded comparison of 5 FFR-angio

vendors versus Pressurewire-derived FFR

1. Accuracy of FFR-angio far below vendor-sponsored study claims
2. FFR-angio by far not accurate enough to justify clinical use
3. FFR by wire remains gold standard

My personal opinion:

IMR-angio and MRR-angio will even be worse



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EuroCRAFT Registry

European Coronary microcirculatory Resistance and Absolute Flow Trial

- Large European Registry collecting patients undergoing physiologic measurements including continuous thermodilution with absolute Q and R_{μ} at rest and at hyperemia, FFR, absolute CFR, and MRR

MMM

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- Directed by CORE-Aalst, supported by Hexacath
- Goal is 700 patients; included so far ~ 175
- 7 centers active (Aalst, Eindhoven, La Princesa, Basildon, Cadiz, Copenhagen, Lausanne) and 3 on the list (San Carlos, Imperial, Mainz)
- Completion foreseen early 2025
- *Good and motivated centers using the technique are wellcome to join*

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The End



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FAME-study (N= 1000)
(Tonino, NEJM 2009:360:213-224)

DEFINE FLAIR (N= 2492)
Davis, NEJM 2017, March 17th

Hypothesis

FFR-guided PCI in MVD is superior to standard, angio-guided PCI

Instantaneous Flow Ratio (iFR) or NHPR are non-inferior to FFR with respect to outcome

Primary Endpoint

Death, MI, revascularization at 1,2, 5 y

Death, MI, revascularization at 1,2, 5 y

Design

RCT in all-comers

RCT "all-comers"

Population

Moderate/high risk: 4 stenoses, 3 stents

low risk population:

- **56% Single vessel disease**
- **no PCI at all in 45% of all patients**

Strong points



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rather high-risk, all-comers, 91% DES



Weak points

- **50% of lesions in iFR/FFR group had no physiologic measurement performed**
- **exclusion of many false-negatives by design**

Outcome

FFR-guided PCI superior to angio-guided PCI, also for all individual endpoints

equipoise for FFR guidance vs iFR guidance at 1 year
Significant higher mortality in IFR group at 2 years

Applicability for average population

High: reduction of all adverse events with 30% at 1, 2, and 5 years

Caveat. Mistrust negative iFR/ NHPR in proximal focal lesions and in high-risk patients