



New Assessment of coronary stenosis: the instantaneous wave free ratio (iFR)

Flavio Ribichini
Università di Verona,
Italy





Flavio Ribichini,

I have no conflict of interest related to this talk

I use of FFR since 1998 in Italy.

I am an FFR believer and iFR researcher

Using Pressure to Get Flow

- Coronary pressure is simple to measure
- Flow velocity is more challenging

Fundamental Equation for relating Pressure and Flow:

$$P = Q \times R$$

Pressure = Flow x Resistance

or

$$\Delta P \approx \Delta Q \times R$$

Change in Pressure = Change in Flow x Constant Resistance

When **Resistance is Constant**, changes in Pressure are proportional to changes in Flow

MEASUREMENT OF FRACTIONAL FLOW RESERVE TO ASSESS THE FUNCTIONAL SEVERITY OF CORONARY-ARTERY STENOSES

NICO H.J. PIJLS, M.D., PH.D., BERNARD DE BRUYNE, M.D., KATHINKA PEELS, M.D.,
PEPIJN H. VAN DER VOORT, M.D., HANS J.R.M. BONNIER, M.D., PH.D., JOZEF BARTUNEK, M.D.,
AND JACQUES J. KOOLEN, M.D., PH.D.

Abstract *Background.* The clinical significance of coronary-artery stenoses of moderate severity can be difficult to determine. Myocardial fractional flow reserve (FFR) is a new index of the functional severity of coronary stenoses that is calculated from pressure measurements made during coronary arteriography. We compared this index with the results of noninvasive tests commonly used to detect myocardial ischemia, to determine the usefulness of the index.

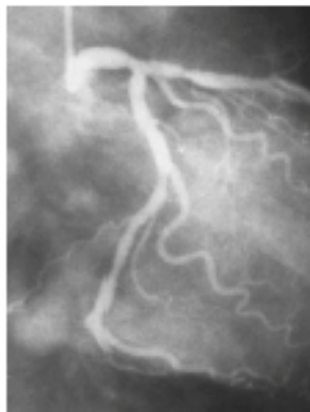
Methods. In 45 consecutive patients with moderate coronary stenosis and chest pain of uncertain origin, we performed bicycle exercise testing, thallium scintigraphy, stress echocardiography with dobutamine, and quantitative coronary arteriography and compared the results with measurements of FFR.

Results. In all 21 patients with an FFR of less than 0.75, reversible myocardial ischemia was demonstrated

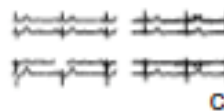
unequivocally on at least one noninvasive test. After coronary angioplasty or bypass surgery was performed, all the positive test results reverted to normal. In contrast, 21 of the 24 patients with an FFR of 0.75 or higher tested negative for reversible myocardial ischemia on all the noninvasive tests. No revascularization procedures were performed in these patients, and none were required during 14 months of follow-up. The sensitivity of FFR in the identification of reversible ischemia was 88 percent, the specificity 100 percent, the positive predictive value 100 percent, the negative predictive value 88 percent, and the accuracy 93 percent.

Conclusions. In patients with coronary stenosis of moderate severity, FFR appears to be a useful index of the functional severity of the stenoses and the need for coronary revascularization. (N Engl J Med 1996;334:1703-8.)

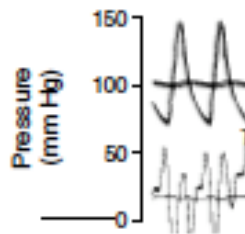
©1996, Massachusetts Medical Society.



A

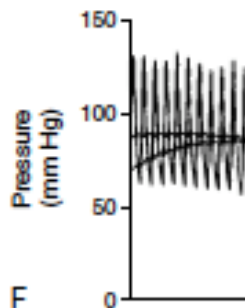


C

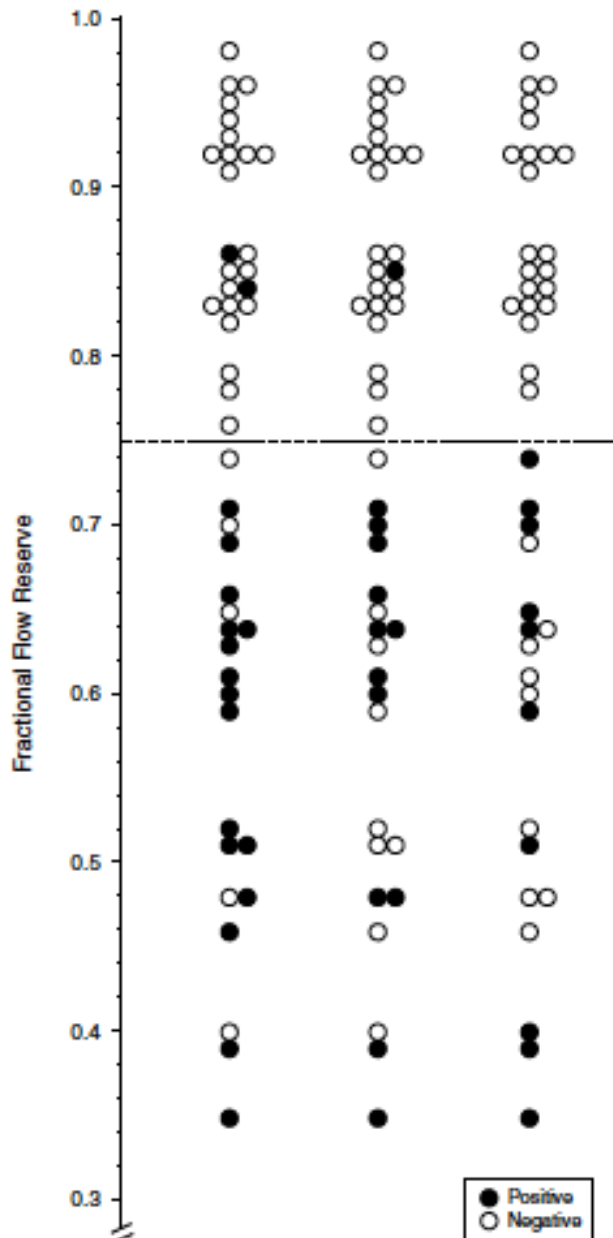


D

V



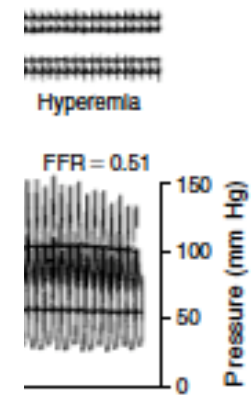
F



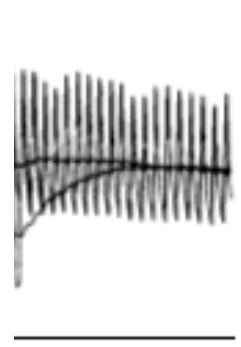
● Positive
○ Negative



C

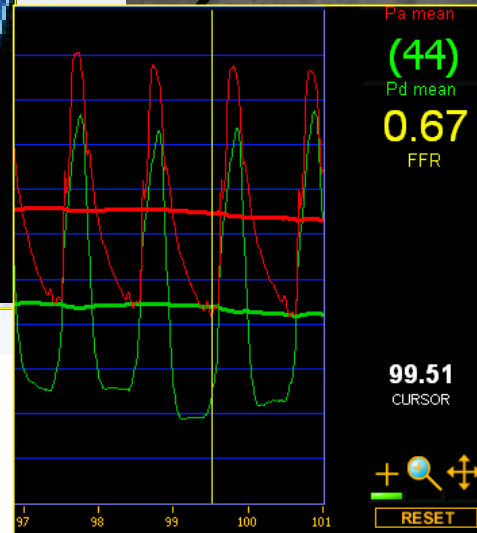
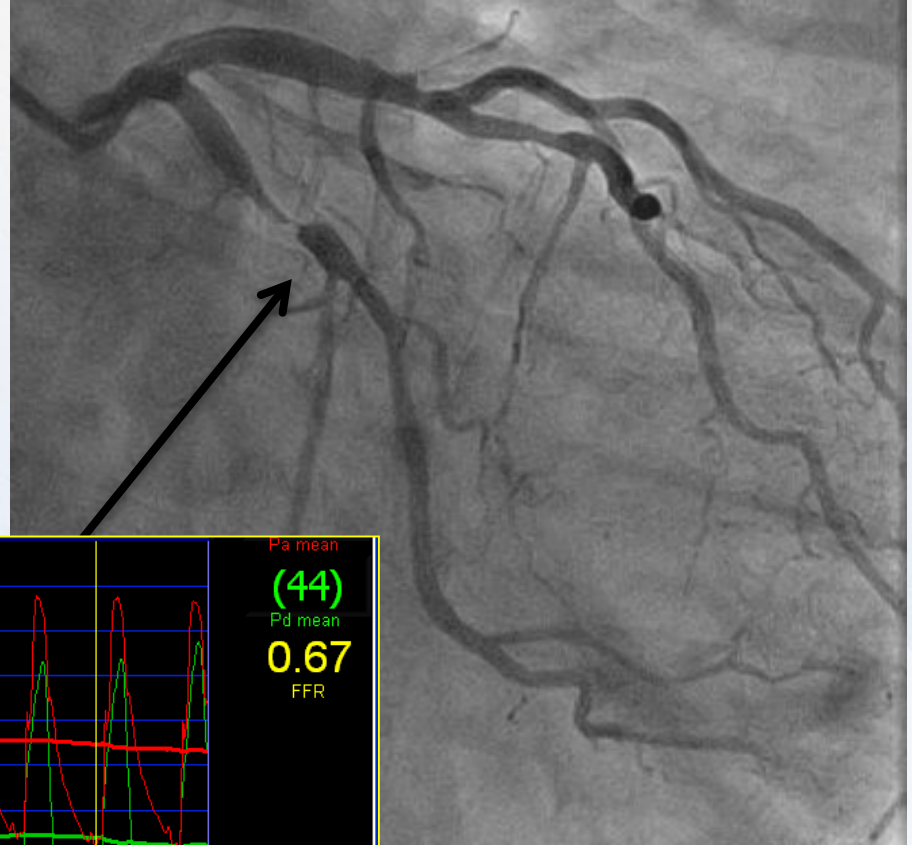
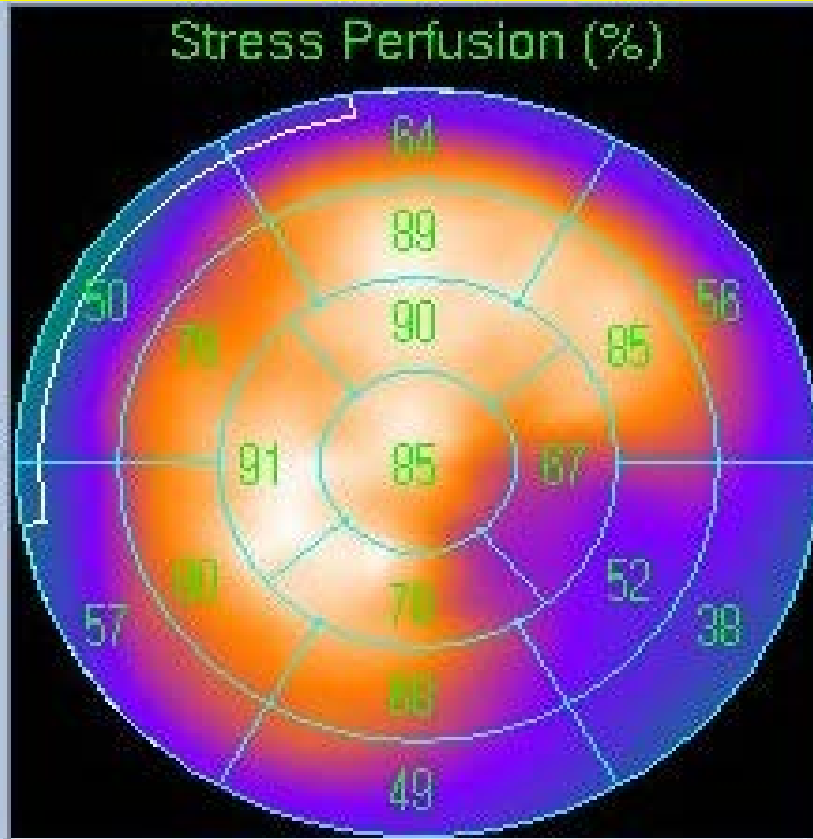


Hyperemia

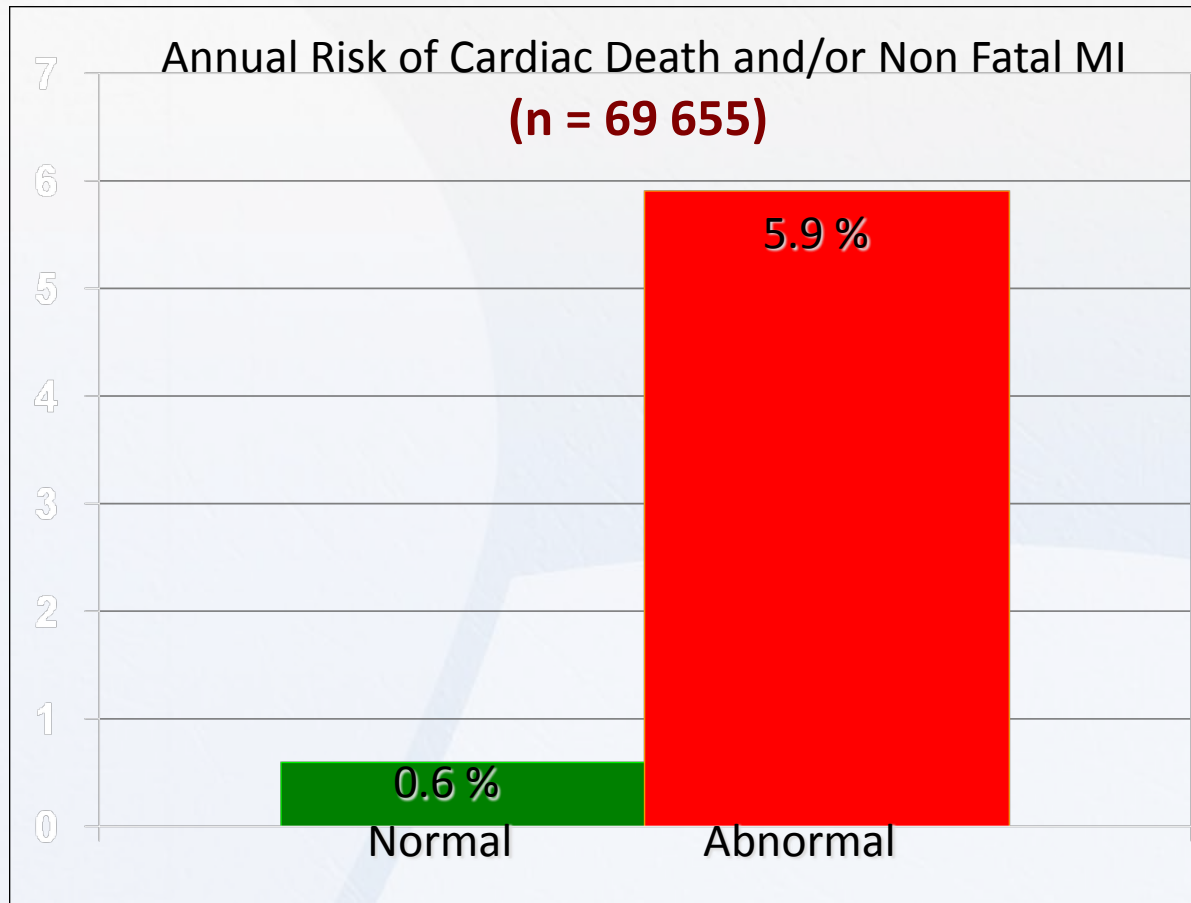


F

- 67-year-old male
- Risk Factors
 - ✓ Ex-smoker (stopped 3 years ago)
 - ✓ Total cholesterol (240 mg/dL)
- Chest pain suggestive for angina
- Normal Resting ECG



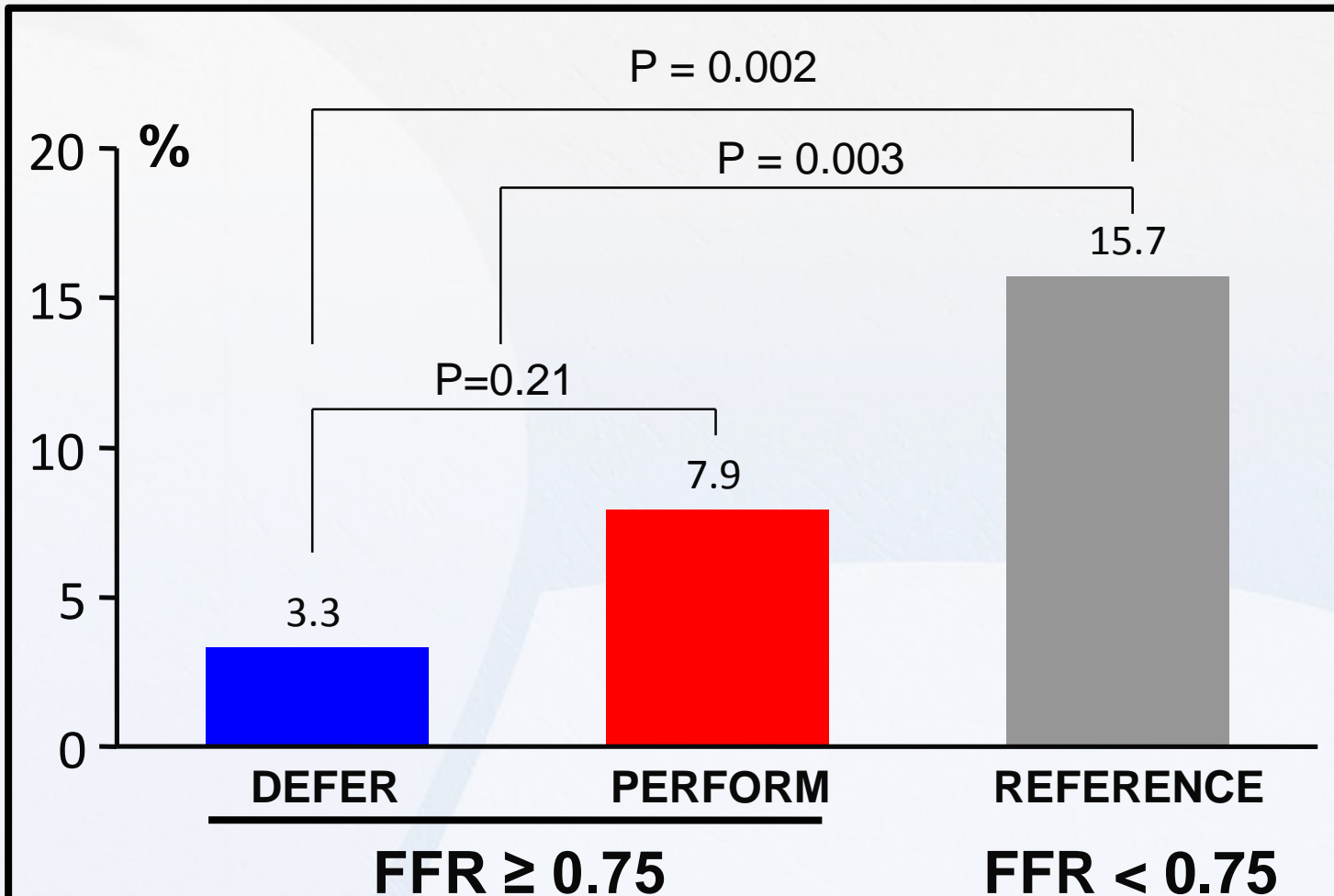
Prognostic Value of Gated Myocardial Perfusion SPECT



DEFER: Clinical Outcome at 5 Years

NHJ Pijls et al JACC 2007

Rate of Death/MI after 5 years





ORIGINAL ARTICLE

Use of the Instantaneous Wave-free Ratio or Fractional Flow Reserve in PCI

J.E. Davies, S. Sen, H.-M. Dehbi, R. Al-Lamee, R. Petraco, S.S. Nijjer, R. Bhindi, S.J. Lehman, D. Walters, J. Sapontis, L. Janssens, C.J. Vrints, A. Khashaba, M. Laine, E. Van Belle, F. Krackhardt, W. Bojara, O. Going, T. Härle, C. Indolfi, G. Niccoli, F. Ribichini, N. Tanaka, H. Yokoi, H. Takashima, Y. Kikuta, A. Erglis, H. Vinhas, P. Canas Silva, S.B. Baptista, A. Alghamdi, F. Hellig, B.-K. Koo, C.-W. Nam, E.-S. Shin, J.-H. Doh, S. Brugaletta, E. Alegria-Barrero, M. Meuwissen, J.J. Piek, N. van Royen, M. Sezer, C. Di Mario, R.T. Gerber, I.S. Malik, A.S.P. Sharp, S. Talwar, K. Tang, H. Samady, J. Altman, A.H. Seto, J. Singh, A. Jeremias, H. Matsuo, R.K. Kharbanda, M.R. Patel, P. Serruys, and J. Escaned

iFR[®]
instant wave-Free I



ORIGINAL ARTICLE

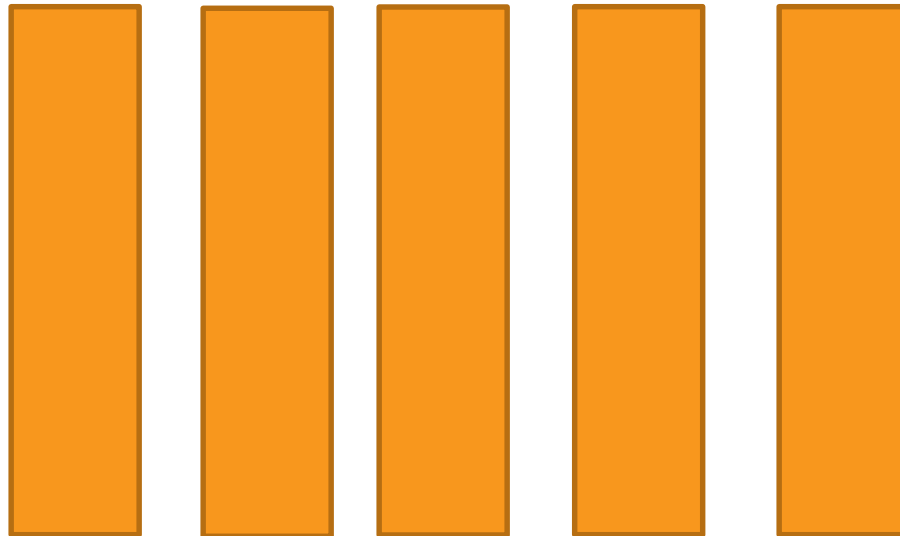
Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI

M. Götzberg, E.H. Christiansen, I.J. Gudmundsdottir, L. Sandhall, M. Danielewicz, L. Jakobsen, S.-E. Olsson, P. Öhagen, H. Olsson, E. Omerovic, F. Calais, P. Lindroos, M. Maeng, T. Tödt, D. Venetsanos, S.K. James, A. Käregren, M. Nilsson, J. Carlsson, D. Hauer, J. Jensen, A.-C. Karlsson, G. Panayi, D. Erlinge, and O. Fröbert, for the iFR-SWEDEHEART Investigators*



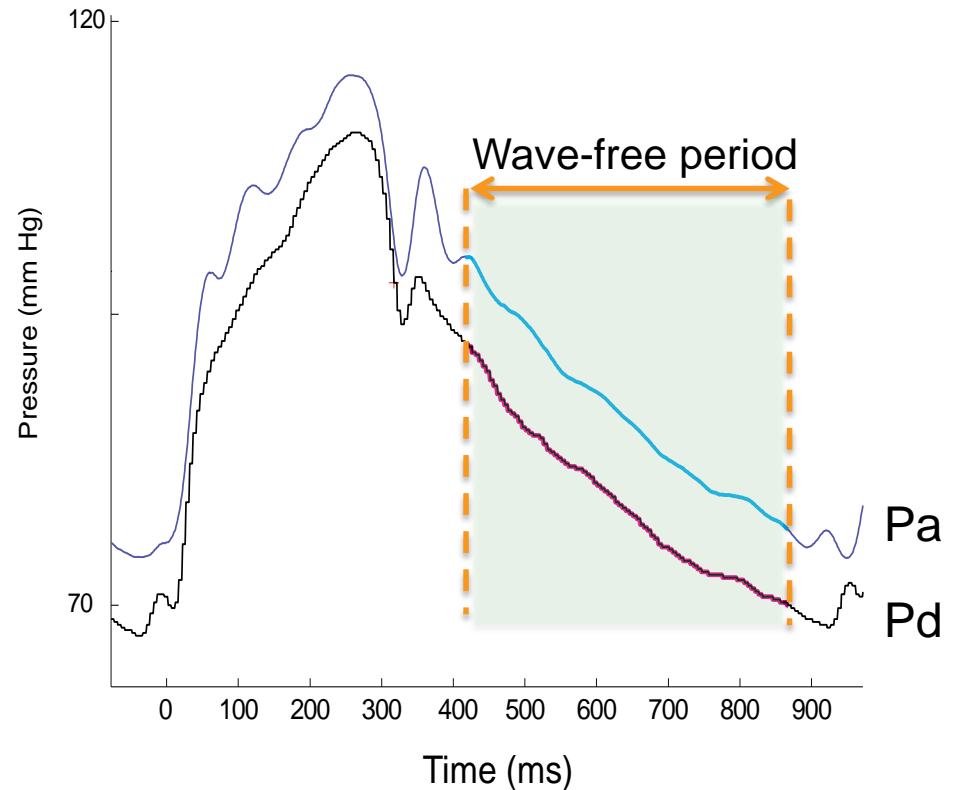
Resistance is Constant in the Wave-Free Period

Resistance is Constant in the Wave-Free Period



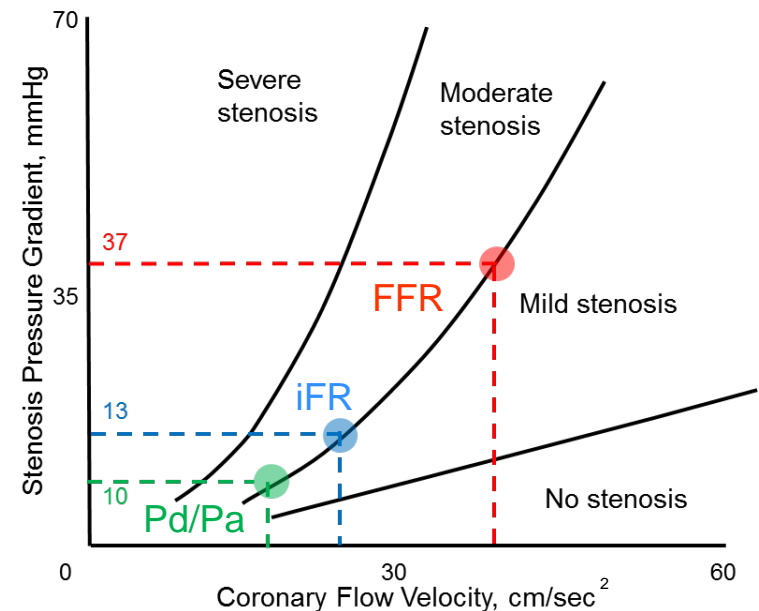
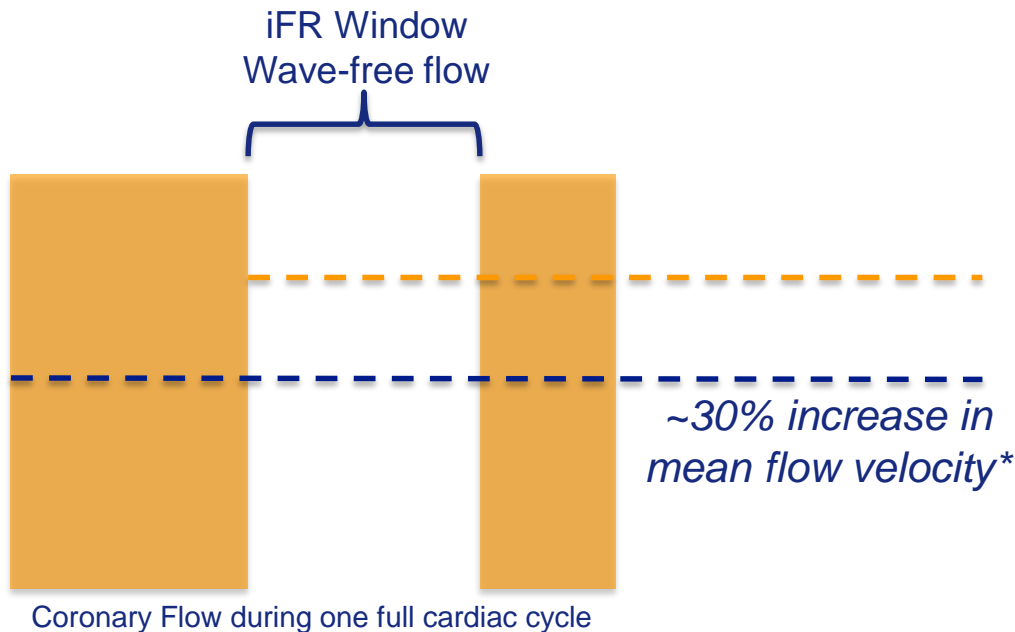
Introduction of the iFR Modality

Definition: Instantaneous pressure ratio, across a stenosis during the wave-free period, when **resistance is naturally constant** and minimized in the cardiac cycle



iFR Window Maximizes Flow Velocity

- iFR Flow is ~30% higher which amplifies the signal vs. Pd/Pa alone¹



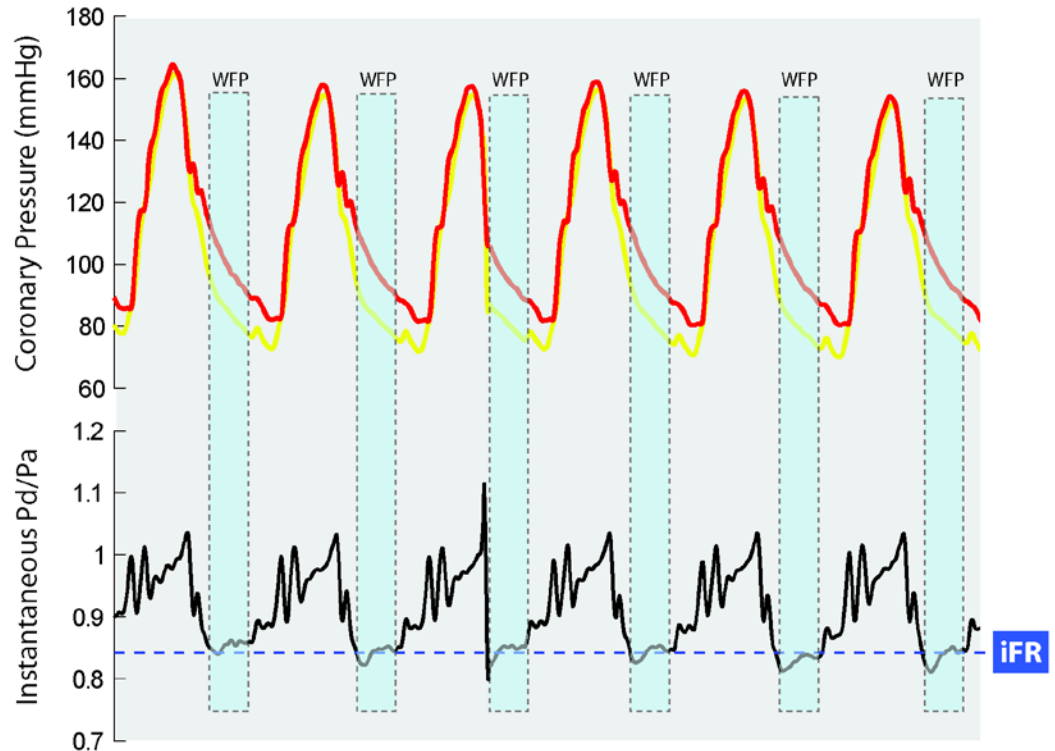
- Bigger pressure drop = better classification of stenosis severity

1. Sen et al. Instantaneous Wave-Free Ratio and FFR Are Equivalent (Results from CLARIFY). JACC Vol. 61, No. 13, 2013. April 2, 2013: 1409-20.

2. Adapted from Gould, K. Pressure-flow characteristics of coronary stenoses in unanesthetized dogs at rest and during coronary vasodilation Circulation research 1978;43:242-253

The Meaning of 'Instantaneous'

- Instantaneous Pd/Pa varies during the cardiac cycle
- The measurement is stable at any *instantaneous* point during the iFR window



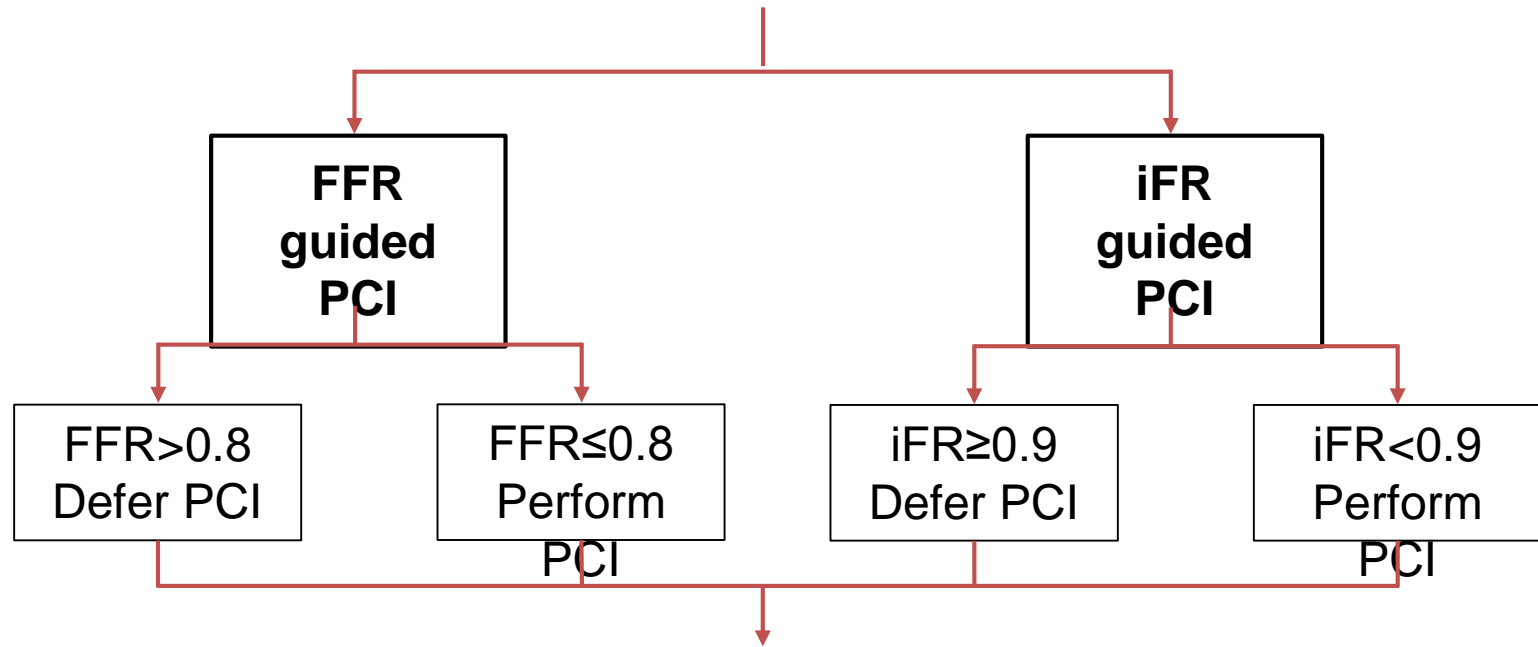
DEFINE FLAIR

Functional Lesion Assessment of Intermediate stenosis to guide Revascularisation

Intermediate lesion requiring physiological assessment

In ACS : intermediate *non-culprit* lesion

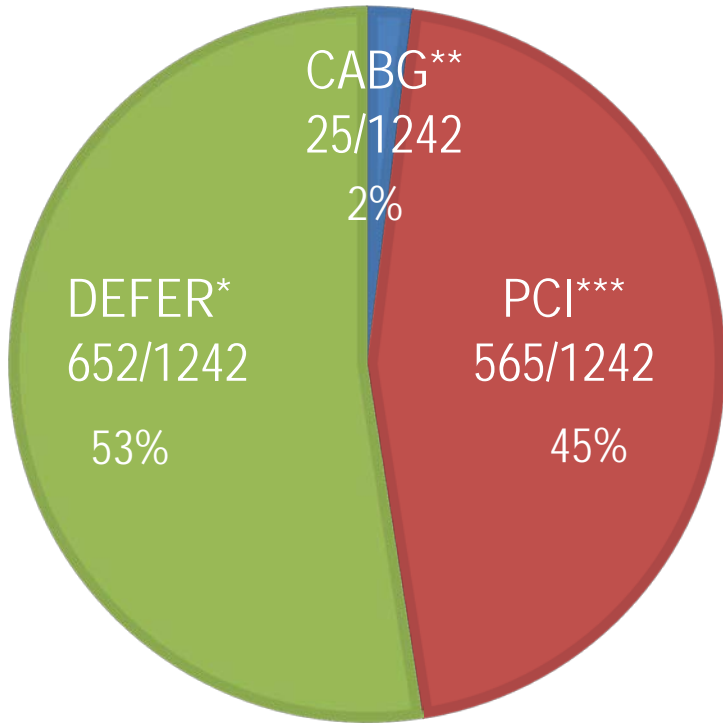
N=2500, 1:1 Randomisation



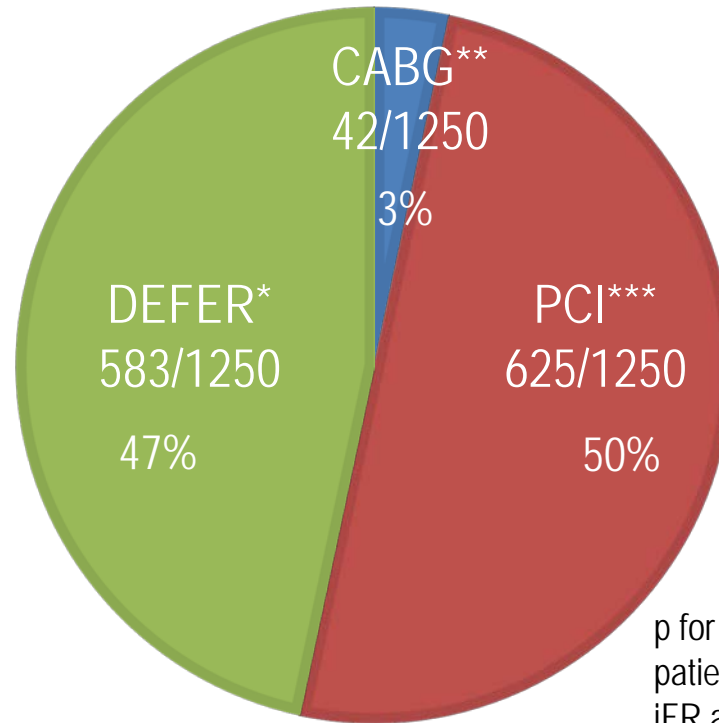
30 day, 1, 2 and 5yr follow-up

Treatment allocation with iFR and FFR

iFR



FFR



Significantly less revascularization with iFR

p for comparison between patients randomized to iFR and FFR

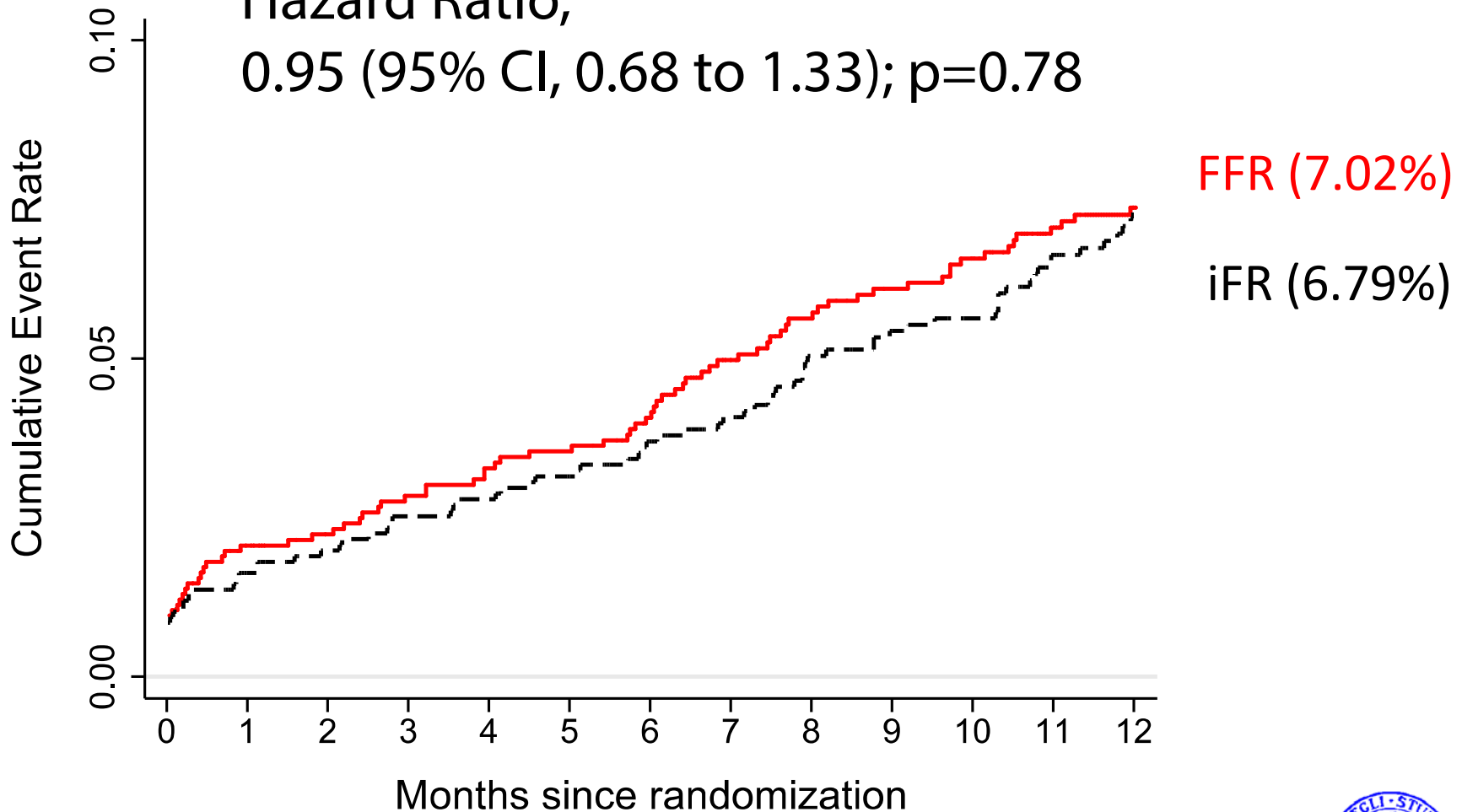
DEFER* p=0.003
 CABG** p=0.04
 PCI*** p=0.02



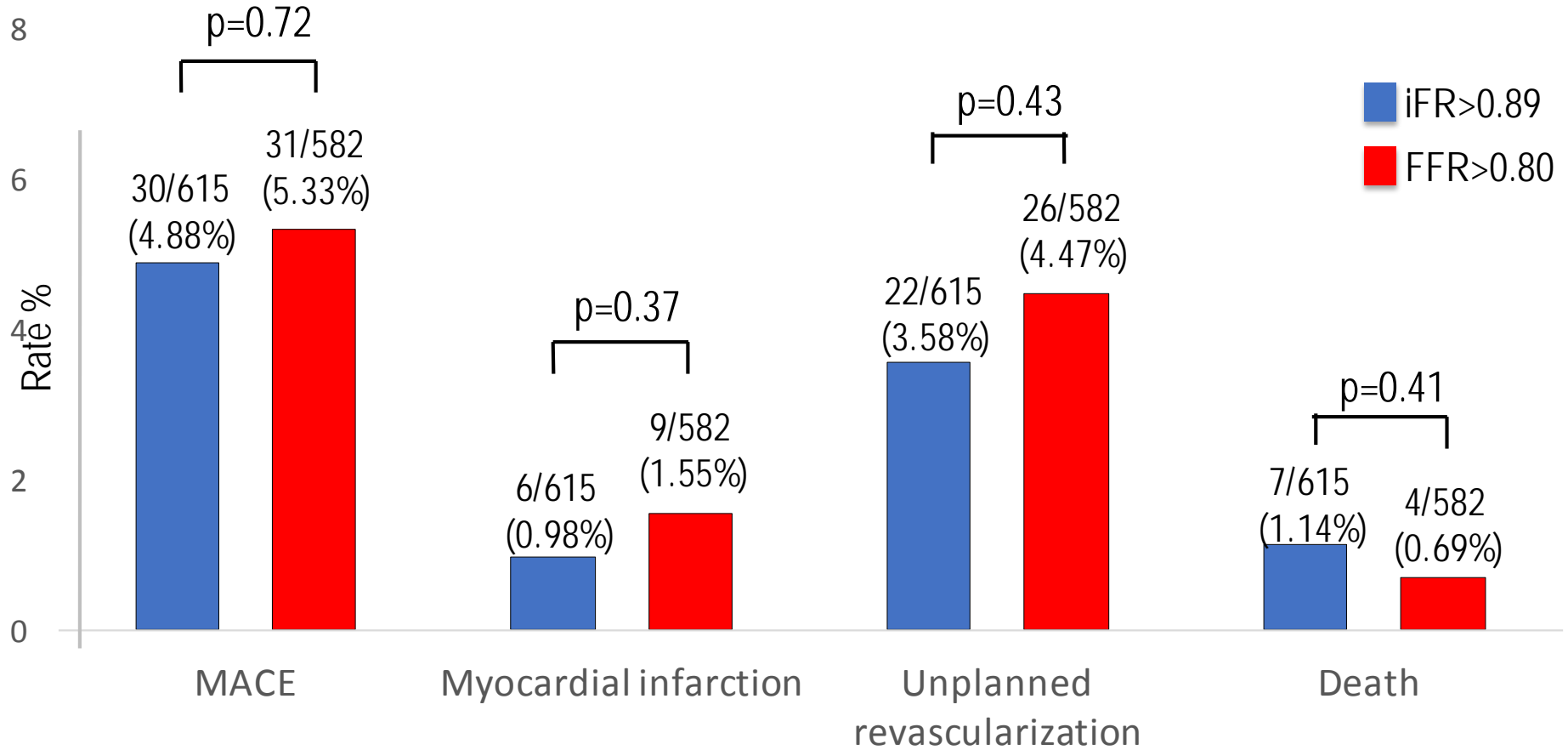
Primary Endpoint (MACE)

Death, MI, unplanned Revascularization

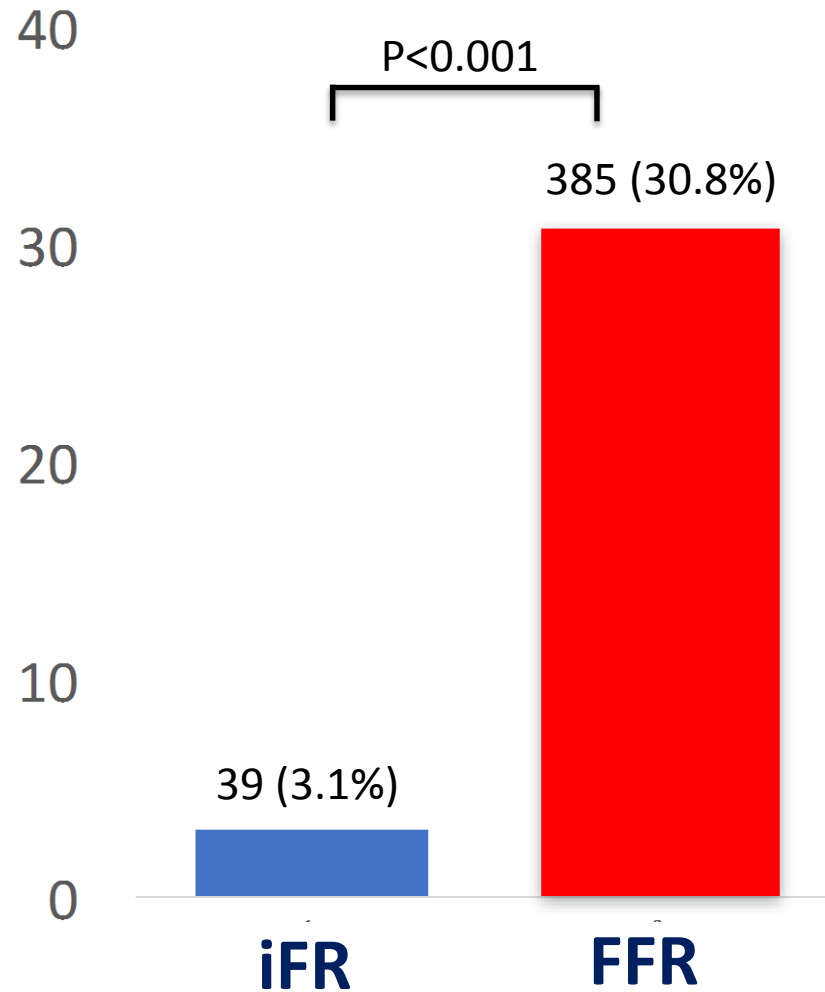
Hazard Ratio,
0.95 (95% CI, 0.68 to 1.33); p=0.78



Event Rates in Deferred Patients



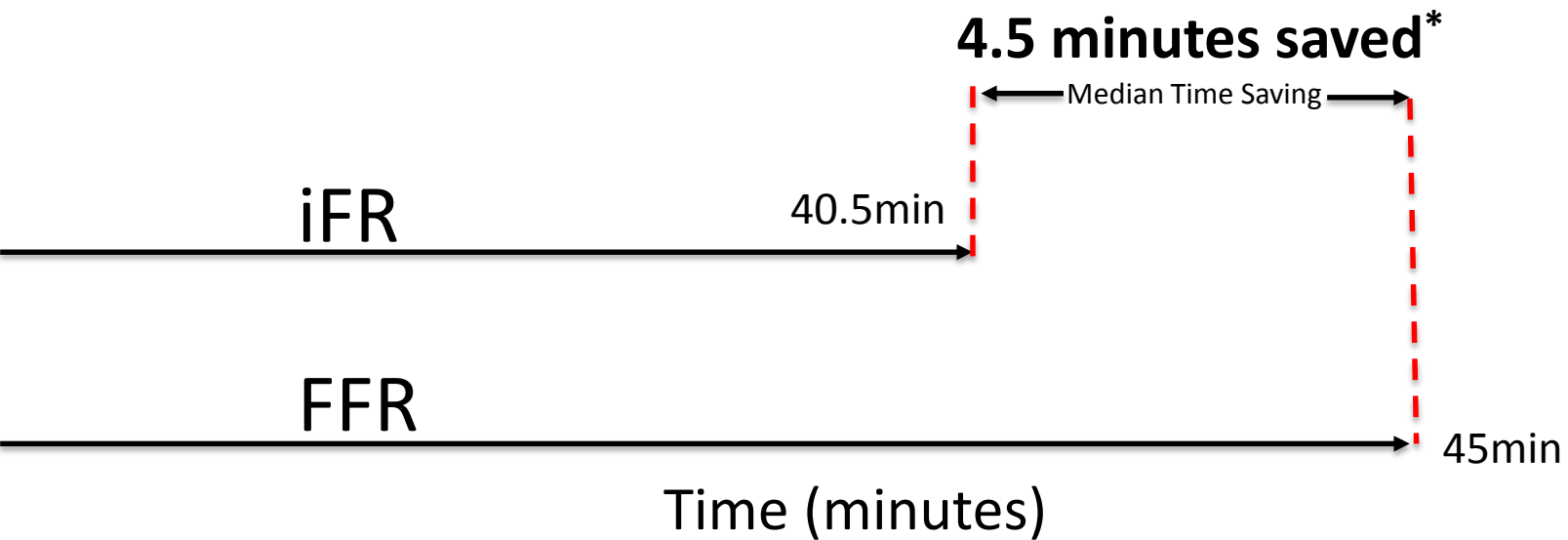
10-fold Fewer Procedural Symptoms



	iFR	FFR
Dyspnea	13 (1.0%)	250 (20.0%)
Chest pain	19 (1.5%)	90 (7.2%)
Rhythm disturbance	2 (0.2%)	60 (4.8%)
Hypotension	4 (0.3%)	13 (1.0%)
Vomiting / Nausea	1 (0.1%)	11 (0.9%)
Bronchospasm/VT	1 (0.1%)	8 (0.6%)
Other	4 (0.3%)	38 (3.0%)



iFR Guided Revascularization Reduces Procedure Time



* Threshold for reduction in median time ($p=0.001$)



iFR-Swedeheart



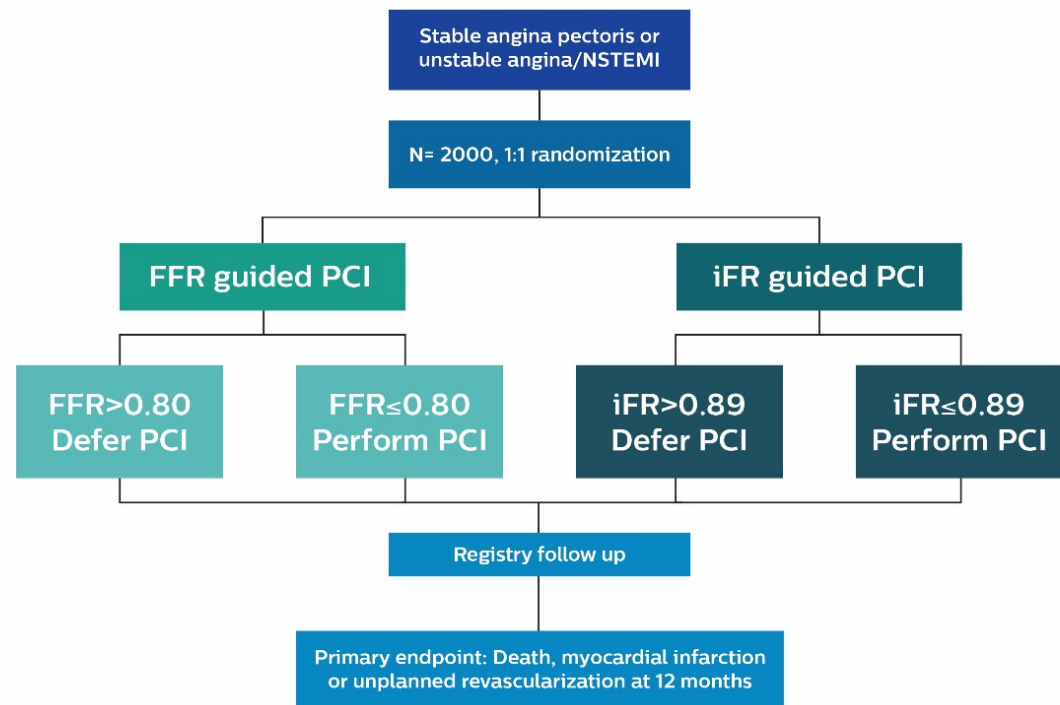
Primary objective

- Assess safety and efficacy of decision-making on coronary revascularisation based on iFR vs FFR
- Assess if iFR is non-inferior to FFR when used to guide treatment of coronary stenosis with PCI

Primary endpoint

- Major adverse cardiac events (MACE) rate in the iFR and FFR groups at 30 days, 1 and 2 years.
- MACE (combined endpoint of death, non-fatal MI, or unplanned revascularisation)

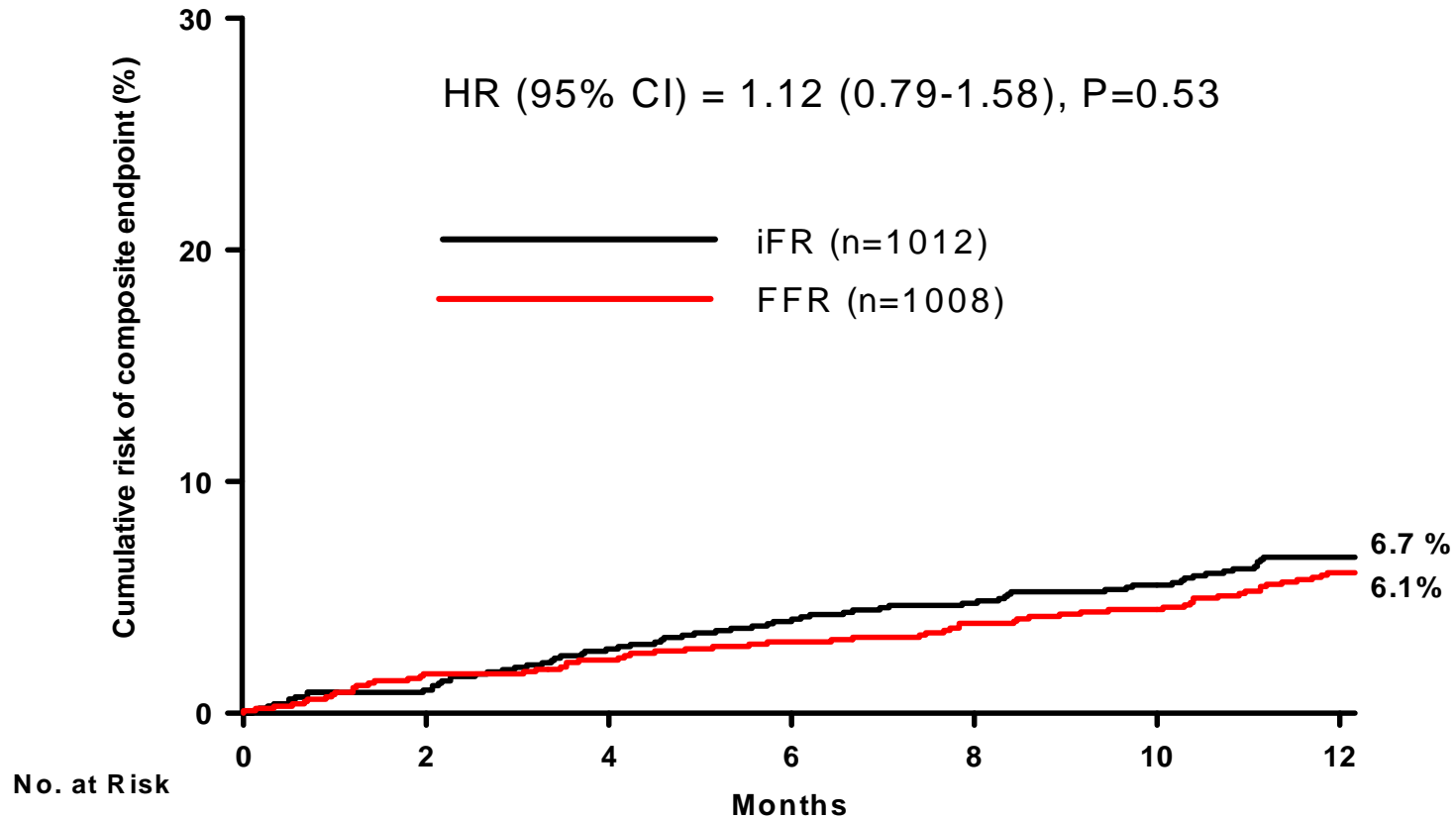
iFR Swedeheart



Primary Endpoint at 12 months



(Death, MI, Unplanned revascularization)



iFR	1012	1002	984	971	963	956	944
FFR	1007	990	984	976	968	961	946

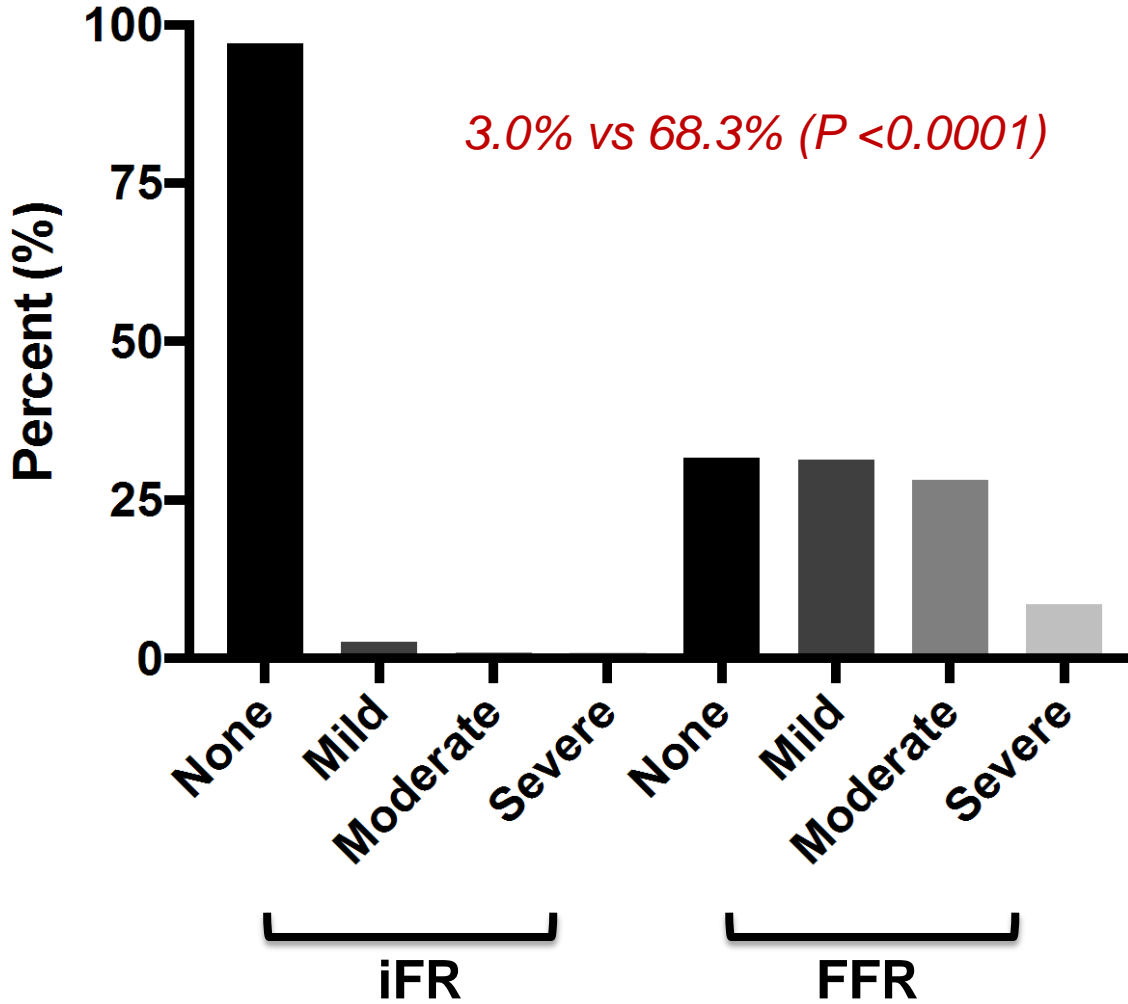


Secondary Endpoints at 12 months

	iFR (N=1012)	FFR (N=1007)	Hazard Ratio (95% CI)	P Value
All cause death - no. (%)	15 (1.5)	12 (1.2)	1.25 (0.58-2.66)	0.57
Myocardial infarction - no. (%)	22 (2.2)	17 (1.7)	1.29 (0.68-2.44)	0.42
Unplanned revascularization - no. (%)	47 (4.6)	46 (4.6)	1.04 (0.69-1.57)	0.84
Target lesion revascularization (TLR) - no. (%)	29 (2.9)	27 (2.7)	1.21 (0.70-2.07)	0.49
Restenosis - no. (%)	19 (1.9)	18 (1.8)	1.05 (0.55-2.01)	0.87
Stent thrombosis - no. (%)	1 (0.1)	2 (0.2)		

No significant differences between iFR and FFR in any of the endpoints

Chest Discomfort During Procedure

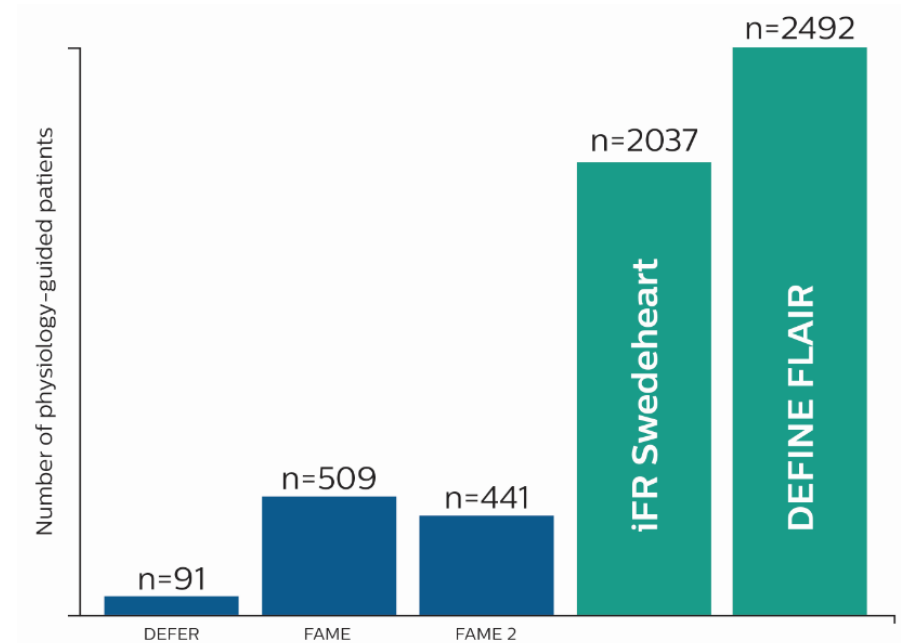


I.v. adenosine 69%
I.c. adenosine 31%



Combined iFR FFR data

- DEFINE FLAIR and iFR Swedeheart are the new landmark physiology studies
- **4500+** patients, more than twice the combined patient population of previous landmark physiology studies
 - DEFINE FLAIR: n = 2492 patients
 - iFR Swedeheart: n = 2037 patients
- **2** prospective, randomized, controlled trials
- Published in New England Journal of Medicine

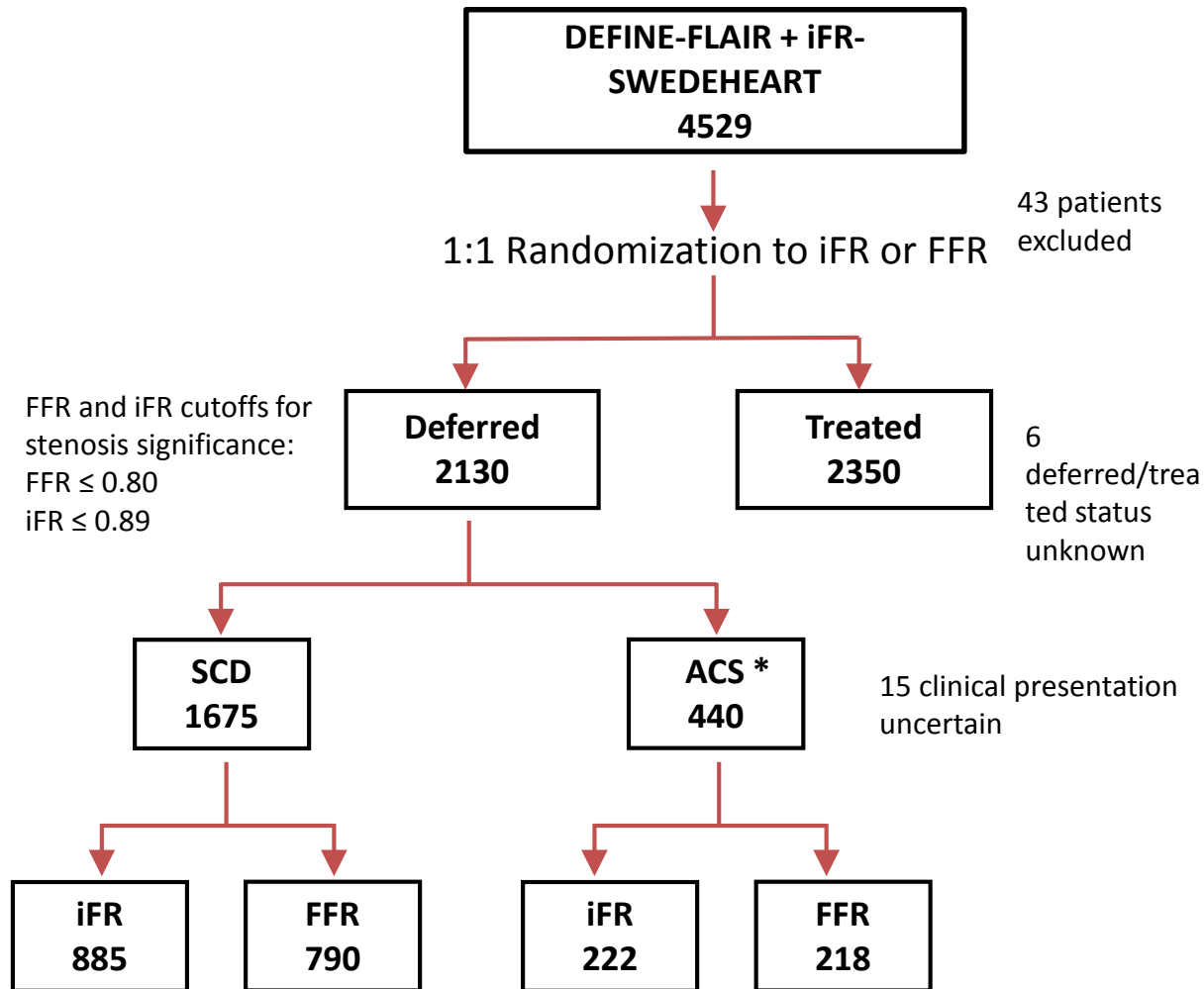


The **NEW ENGLAND**
JOURNAL of MEDICINE

Escaned J EuroPCR 2017



Study population



* In ACS, only non-culprit vessels were evaluated with pressure guidewires



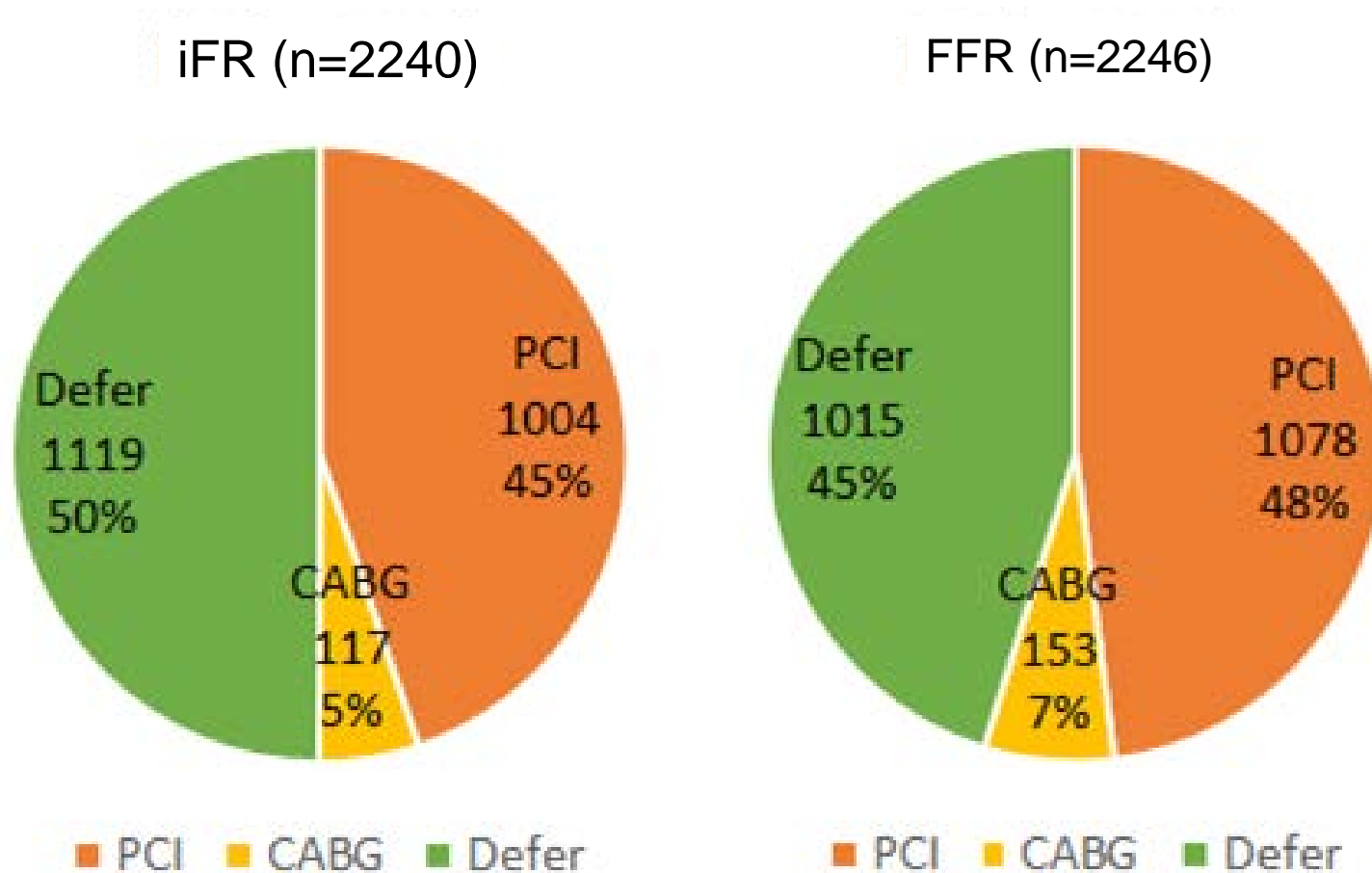
Patient characteristics in the deferred and treated groups

	Deferred	Treated	P value
Number of patients	2130	2350	
Age (yr), mean (sd)	66.3 (10.3)	66.3 (10.1)	0.72
Male, N (%)	1493 (70.1)	1887 (80.3)	<0.01
Diabetes mellitus, N (%)	494 (23.2)	696 (29.6)	<0.01
Previous myocardial infarction, N (%)	644 (30.2)	746 (31.7)	0.51
Previous PCI, N (%)	1207 (56.7)	1411 (60.0)	0.03

Deferred patients had a lower cardiovascular risk profile than treated patients



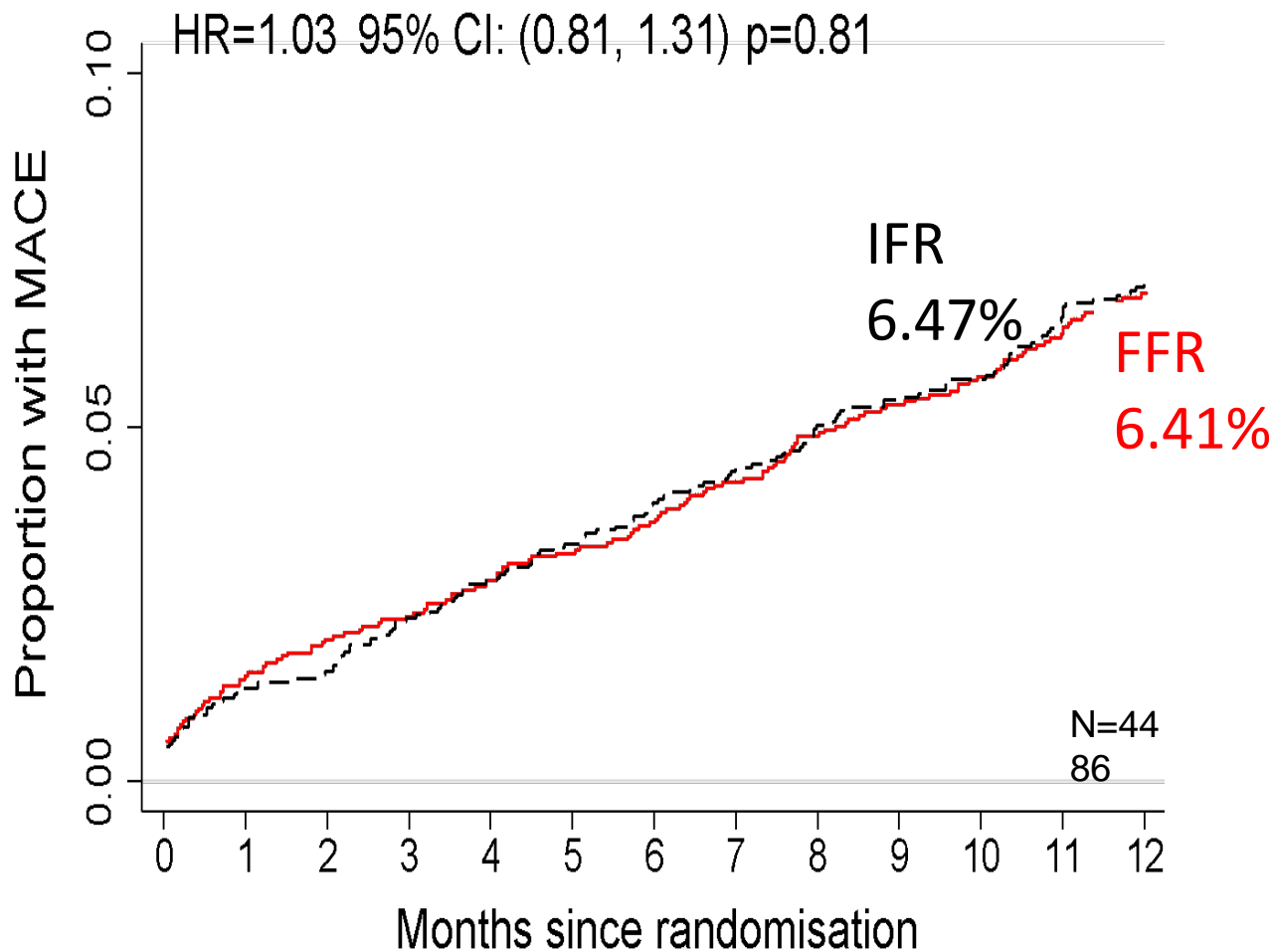
Treatment allocations with iFR and FFR



Significantly less revascularisation based on iFR interrogation ($P < 0.01$)



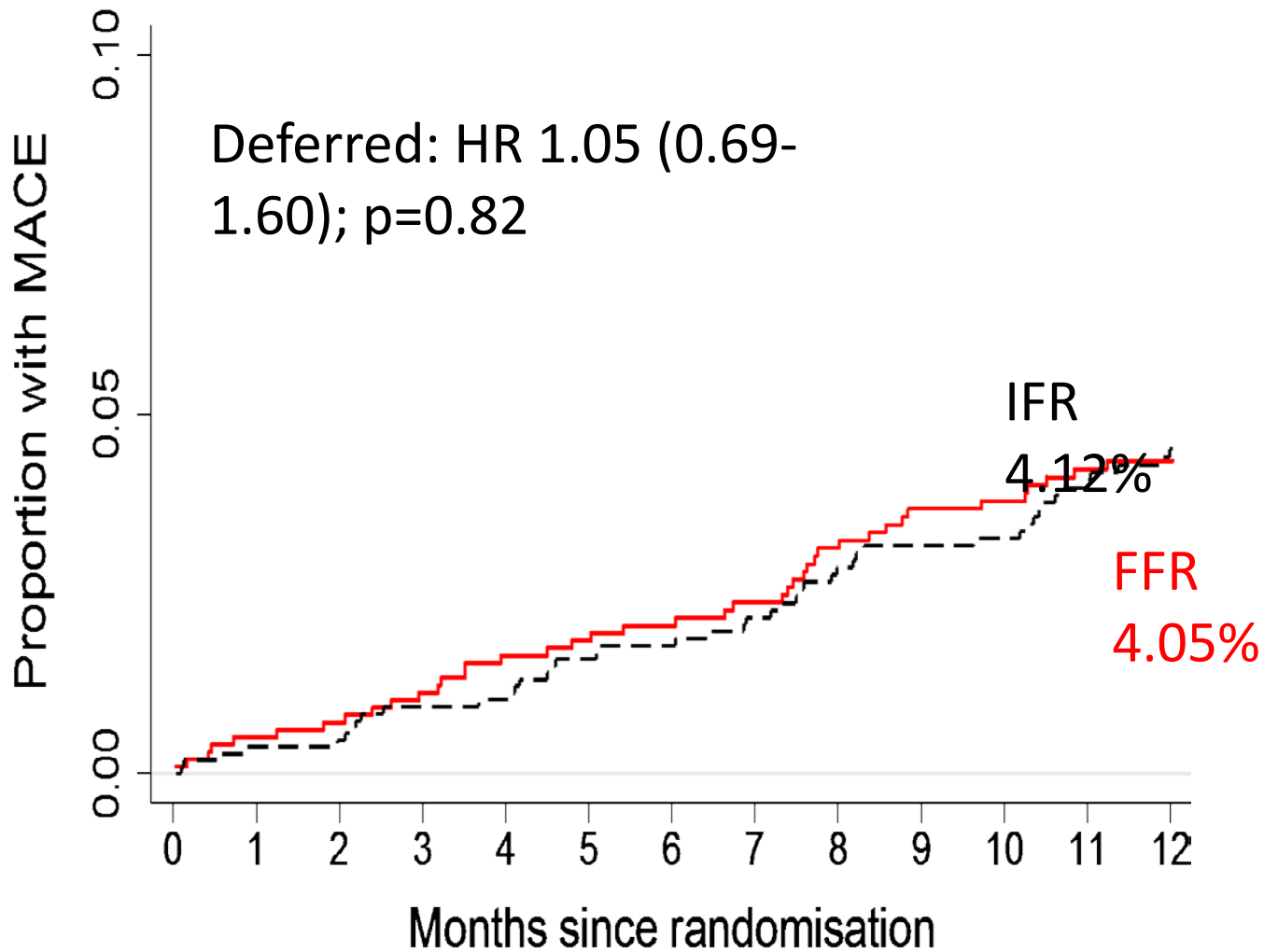
MACE in iFR and FFR guided revascularisation (all patients)



MACE similar and low at 1 year after iFR- and FFR-based revascularisation decision-making



Outcomes in deferred patients

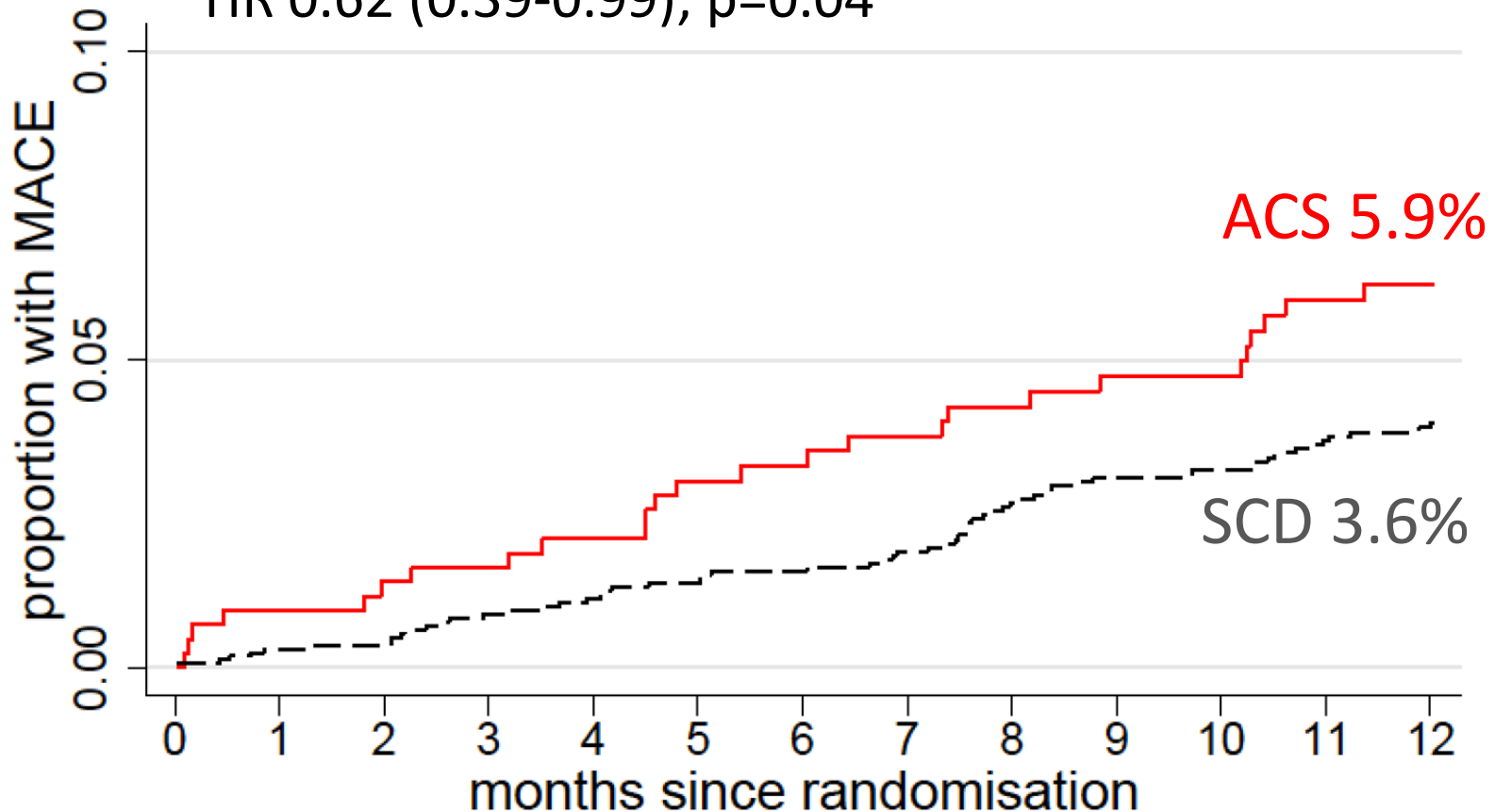


Similar and low MACE rates at 1 year after iFR- and FFR- based deferral



Outcomes in deferred patients according to clinical presentation

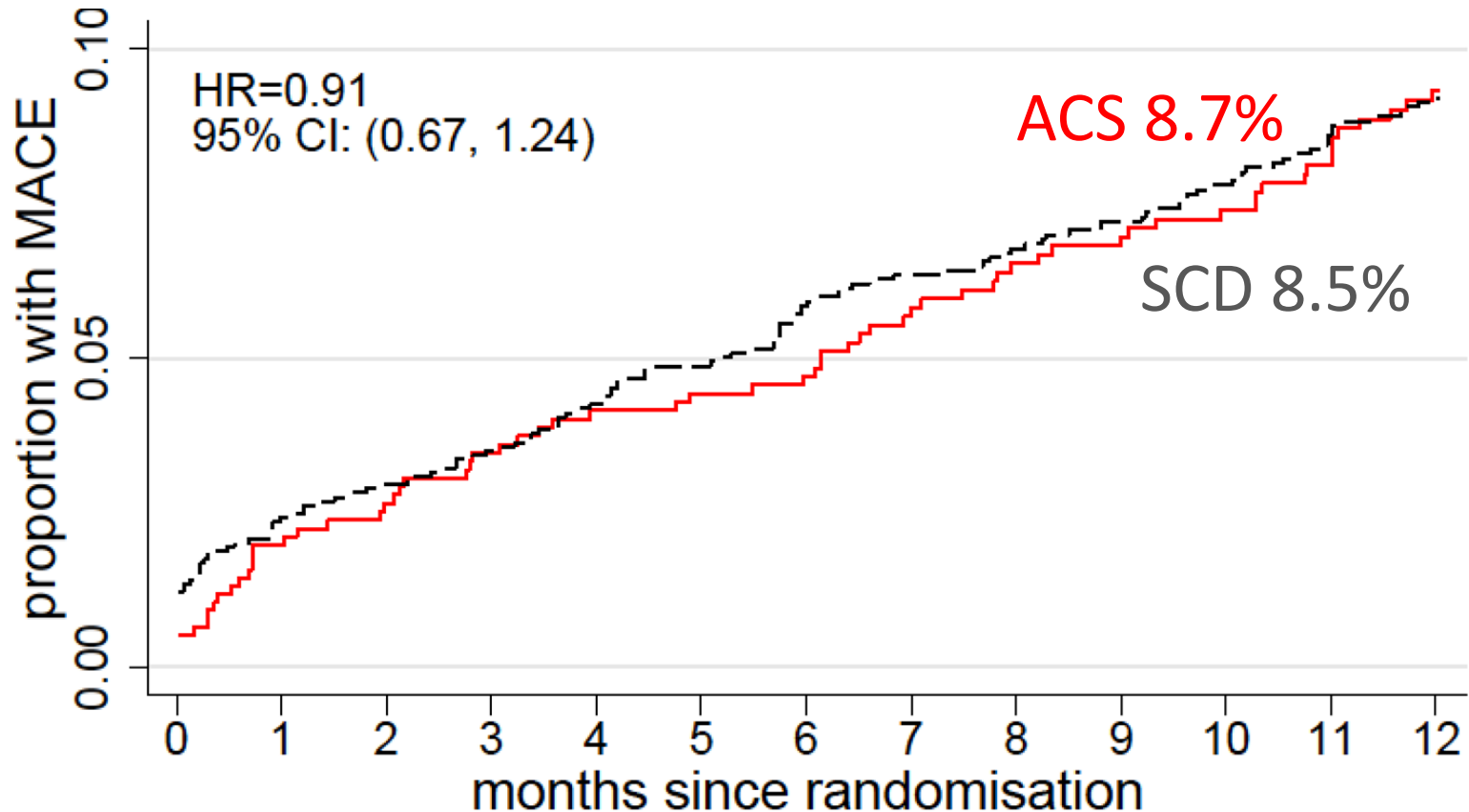
HR 0.62 (0.39-0.99); p=0.04



In deferred patients, clinical presentation did influence MACE rate



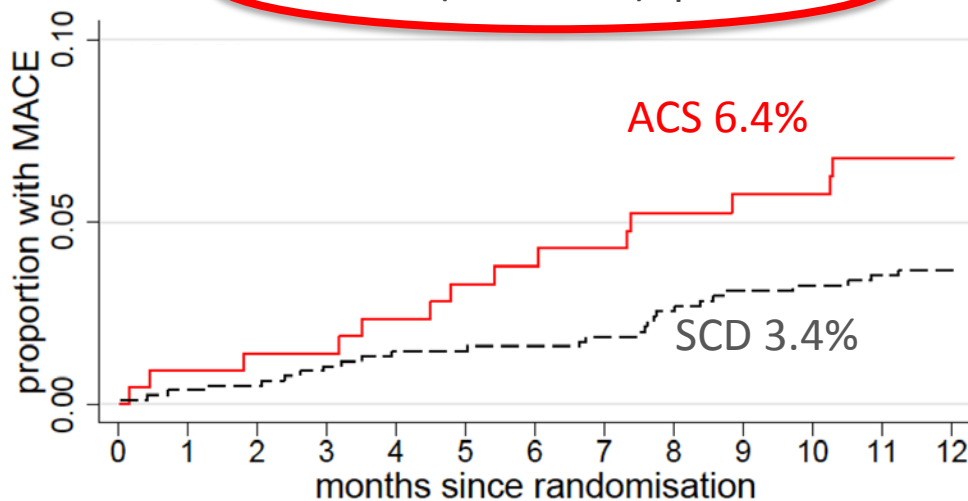
Outcomes in treated patients according to clinical presentation



Unadjusted outcomes after deferral by clinical presentation and iFR or FFR

FFR

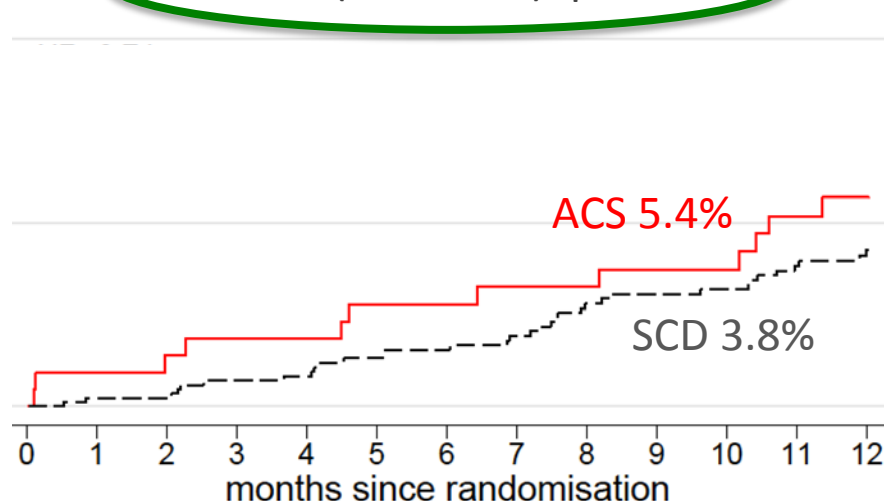
HR 0.52 (0.27-1.00); p<0.05



In FFR-deferred patients, MACE is significantly higher in ACS than SCD

iFR

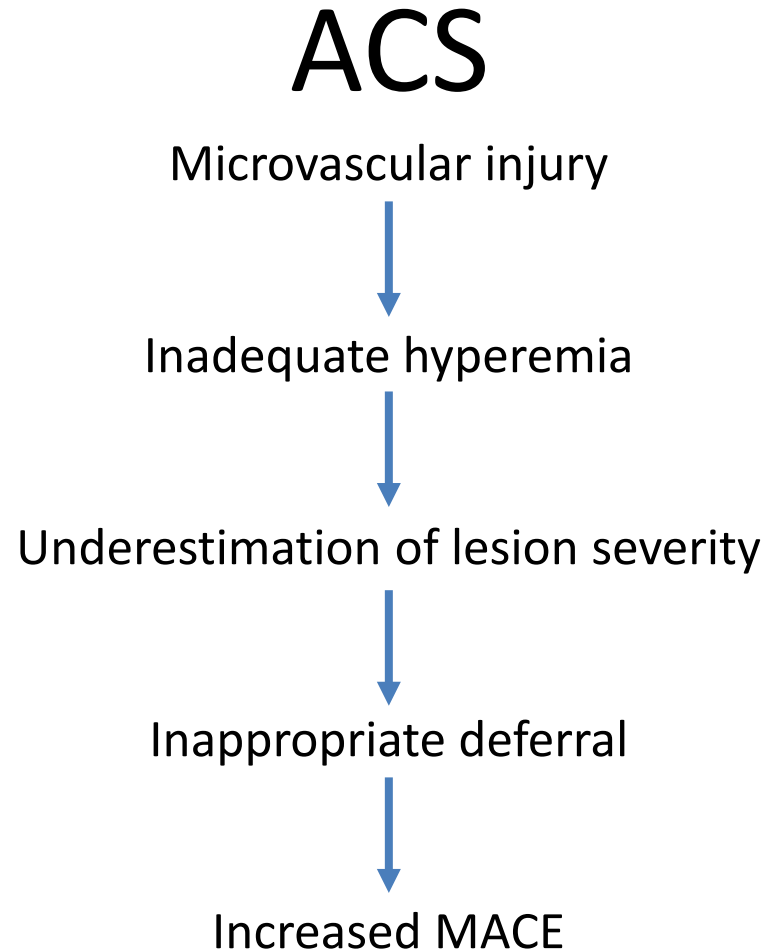
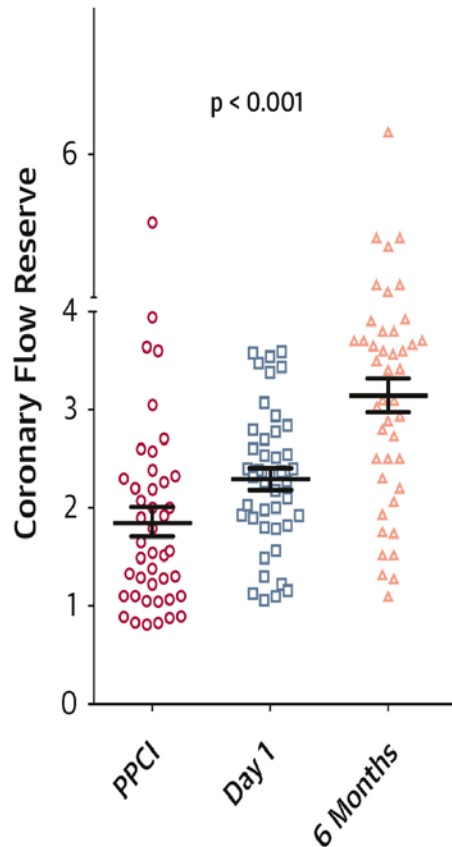
HR 0.74 (0.38-1.43); p=0.37



In iFR-deferred patients, MACE is similar in ACS and SCD



Possible mechanism for increased event rates in ACS patients being guided with FFR



Example of a DEFINE FLAIR PATIENT RANDOMIZED IN VERONA.



54 y.o male

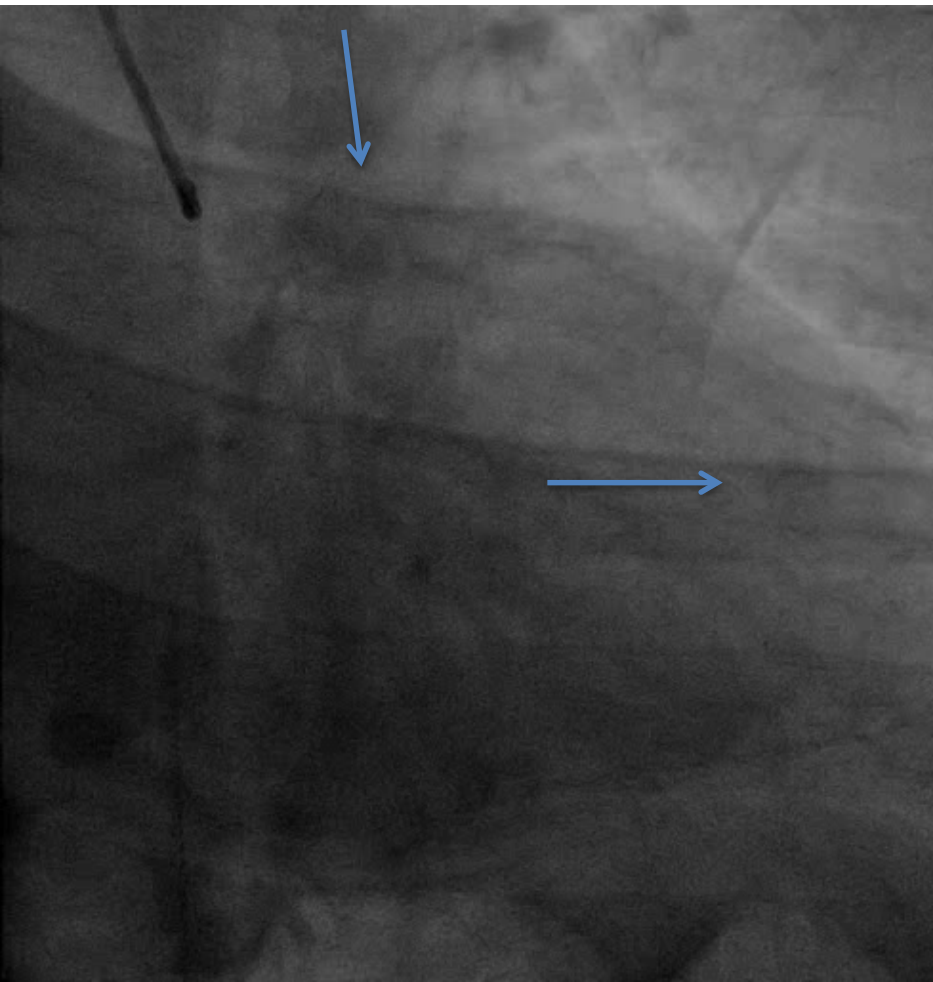
ACS presentation

Proximal LAD culprit

Distal LAD significant

PCI on LAD

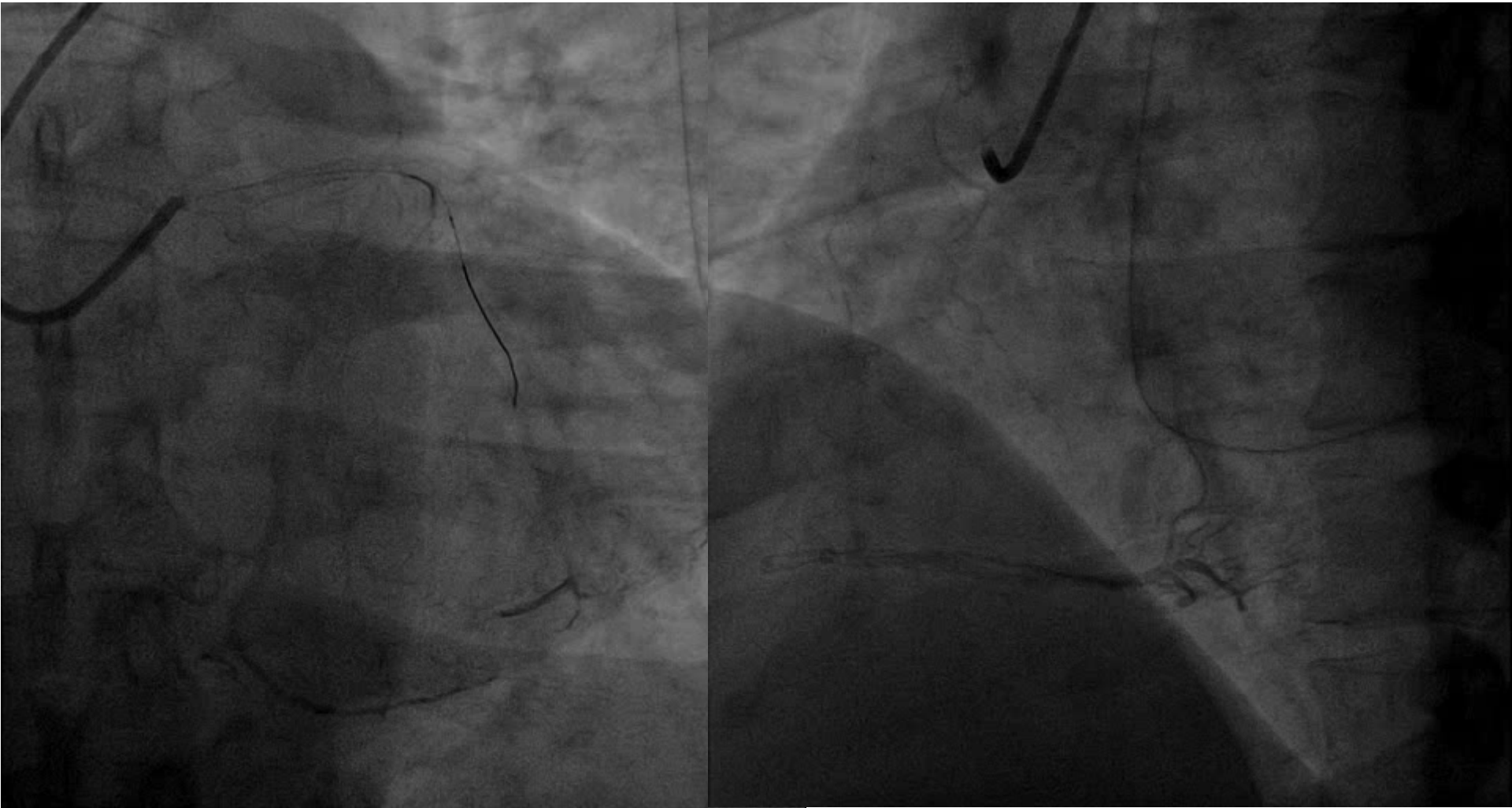
Significant lesions on ostial RI
and LCx



PCI on LAD



Significant lesions on ostial RI and LCx and the RCA



Pre-discharge functional assessment of the RI and Cx

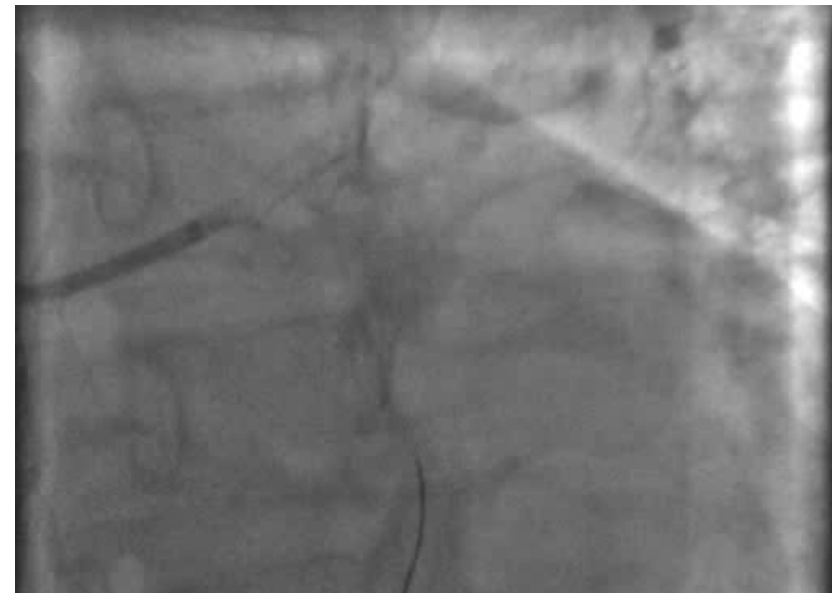
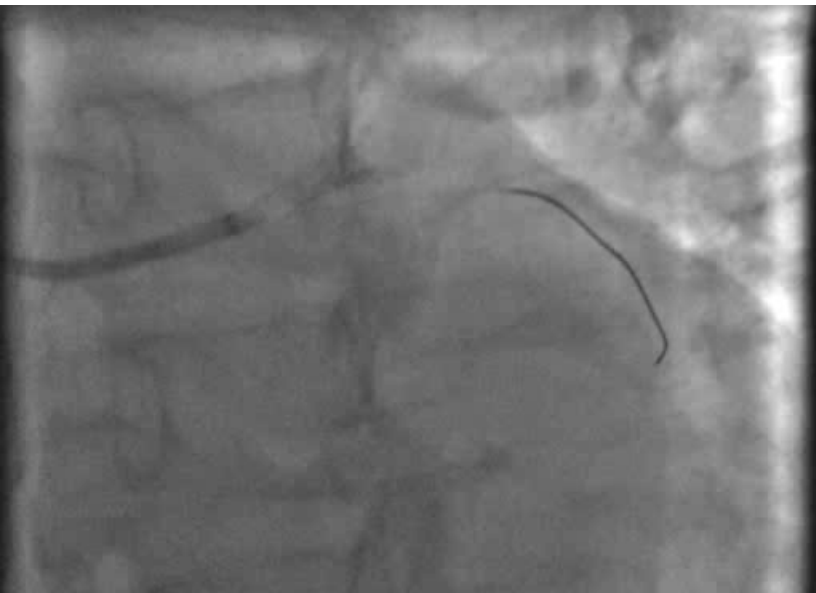


Enrolled
DEFINE
FLAIR
TRIAL

May 4
2014

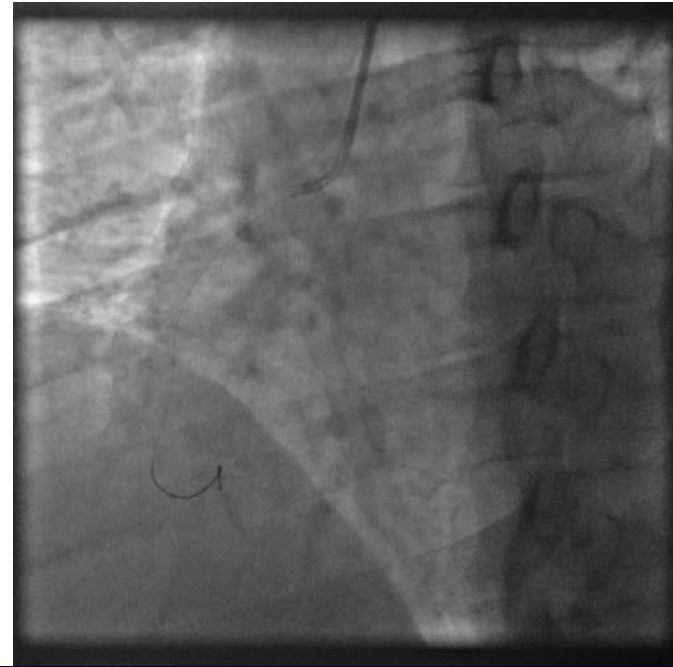
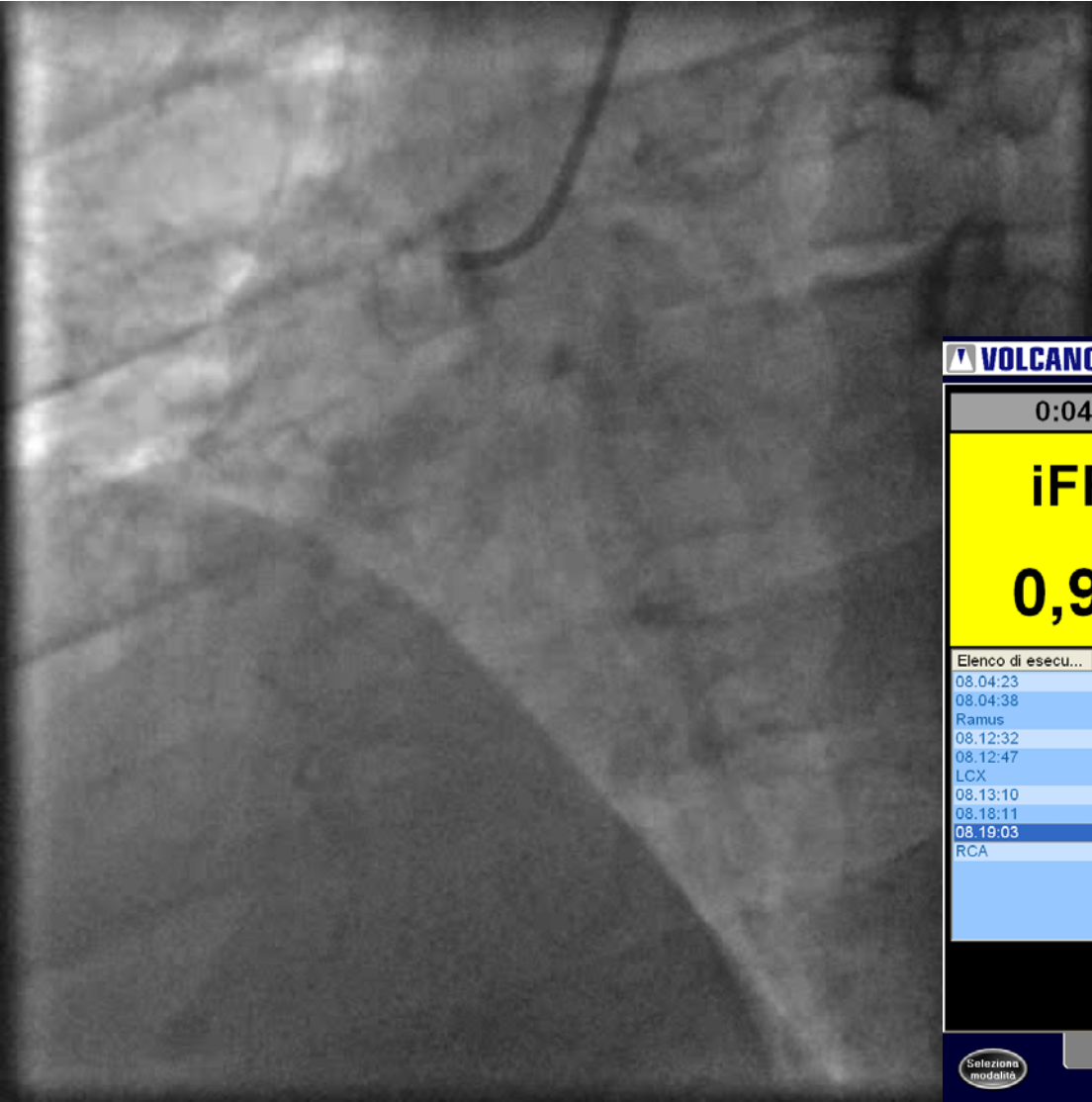


Pre-discharge functional assessment of the RI and Cx



Pre-discharge functional assessment of the RCA

Enrolled DEFINE FLAIR TRIAL May 2014





**AZIENDA OSPEDALIERA UNIVERSITARIA INTEGRATA
VERONA**



(D.Lgs.n.517/1999 - Art. 3 L.R. Veneto n. 18/2009)

DIPARTIMENTO AD ATTIVITA' INTEGRATA CARDIOVASCOLARE E TORACICO

UNITA' OPERATIVA COMPLESSA DI CARDIOLOGIA - Direttore: Prof. Corrado Vassanelli

Sede di Borgo Trento - P.le Stefani, 1 - 37126 Verona - Tel. 045 8122320 - Fax 045 8122311 - 045 80273

e-mail: clinica.cardiologica@ospedaleuniverona.it

Pagina 1 di 2

Paziente :	[REDACTED]		
Nato il :	27/04/1960	Età: 55	Patient ID: 1C7PM
Data Esame :	13/05/2015	Codice Fiscale : MAAPRR60D27Z313K	
Provenienza :	ESTERNI		
Esame :	CICLOERGOMETRO (P00076)		

One year F-up

DATI ESAME

Numero Esame : 14396

Peso : 76 Altezza : 171

BSA : 1.90 BMI : 25.99 Carico teorico massimo (Watt) : 171.00 Carico teorico massimo (METS) : 8.71

INDICAZIONE

Indicazione : Valutazione funzionale in paziente con recente IMA

Test eseguito : IN TERAPIA MEDICA

ECG DI BASE

RITMO SINUSALE

Note : esiti di necrosi inferiore

DETTAGLIO TEST

Test da sforzo eseguito a carichi scalari di [W/min] : 25/2



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e-mail: clinica.cardiologica@ospedaleuniverona.it

Pagina 1 di 3

20 months F-up

Paziente :	██████████		
Nato il :	27/04/1960	Età: 55	Patient ID: 1C7PM
Data Esame :	21/12/2015	Codice Fiscale : MAAPRR60D27Z313K	
Provenienza :	ESTERNI		
Esame :	ECOCOLORDOPPLER CARDIACO A RIPOSO E DOPO PROVA		

INDICAZIONE

Cardiopatìa ischemica post-infartuale (STEMI inferiore con esiti di angioplastica + stent medicato di coronaria discendente anteriore prossimale e POBa Da distale) CD e CX con stenosi non critiche (valutate dopo alcuni giorni con FFR). Ecocardiogramma predimissione non anoamide della cinetica segmentaria
test da sforzo 13-5-2015 : Non evidenza clinico-strumentale di ischemia inducibile.
Ha in ottobre accusato alcuni epsodi di dopore otracico a riposo
Esame condotot in corretto wo del bisoprololo
ecocardiogramma di base : cardiopatìa ipertensiva
ECG : ritmo sinusale bassi voltaggiim QRS

DATI TEST

Quesito clinico : Ricerca di ischemia **Tipo esame :** Ecocardiogramma trans-toracico
Video N : VIVID 7 **Qualità esame :** Buona
Frequenza cardiaca : 73 **Ritmo cardiaco :** Sinusale **Pressione art. [mmHg] :** 115/75 MMHG
Peso (Kg) : 74 **Altezza (cm) :** 174 **BSA :**1.9 **BMI :**24.44
Procedura : Da sforzo
Note : 25 w 2 minuti
Atropina : NO **Carico / Dose Max. :** 125

Paziente : [REDACTED]

Nato il : 27/04/1960

Età: 55

Patient ID: 1C7PM

Data Esame : 21/12/2015

Codice Fiscale : MAAPRR60D27Z313K

Provenienza : ESTERNI

Esame : ECOCOLORDOPPLER CARDIACO A RIPOSO E DOPO PROVA

NON ANGOR
MODERATA DIPSNEA AL MASSIMO DELLO SFORZO
NON VARIAZIONI ST
IPERGINESIA IN TUTTI I SEGMENTI DEL VENTRICOLO SINISTRO

CONCLUSIONI

Non angor.
Non alterazioni elettrocardiografiche.
Non alterazioni di cinetica, nè in condizioni basali, nè durante sforzo(ad una frequenza cardiaca significativa)(89 %)
Ipertensione sistodiastolica da sforzo

Il Medico Specializzando

Il Medico Cardiologo

This patient has completed 3.5 years follow-up

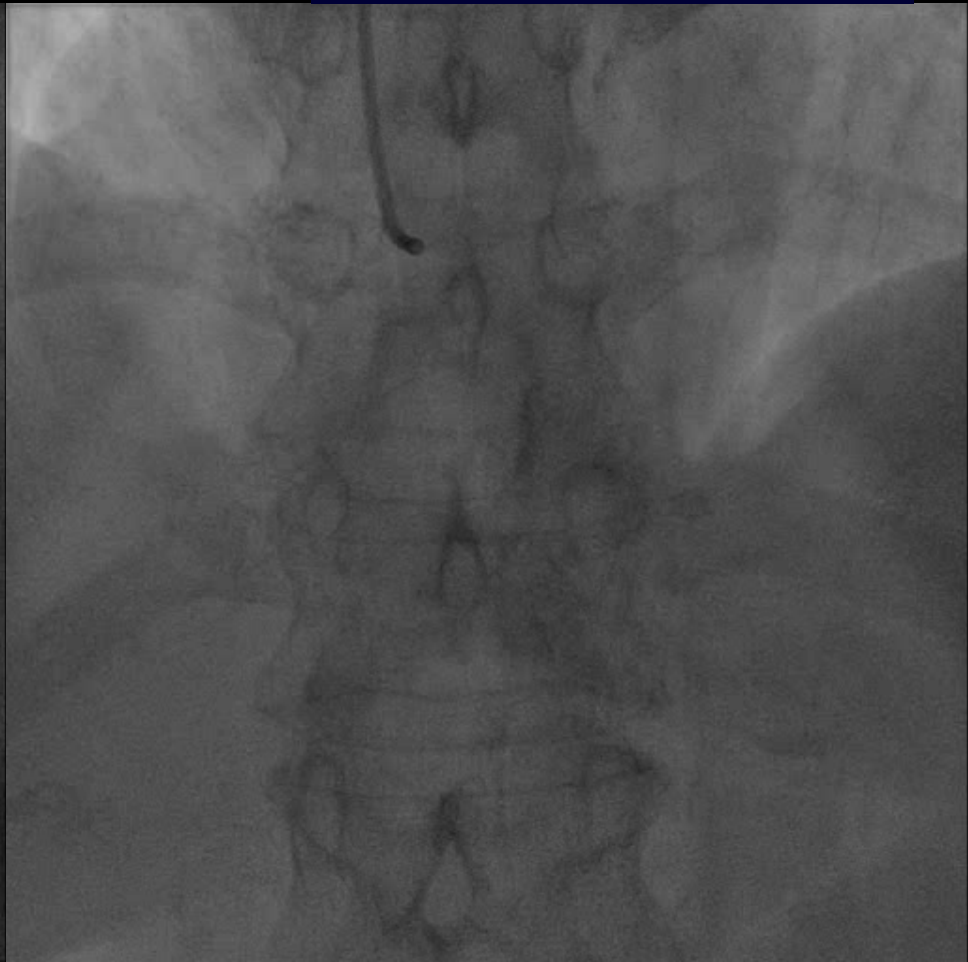
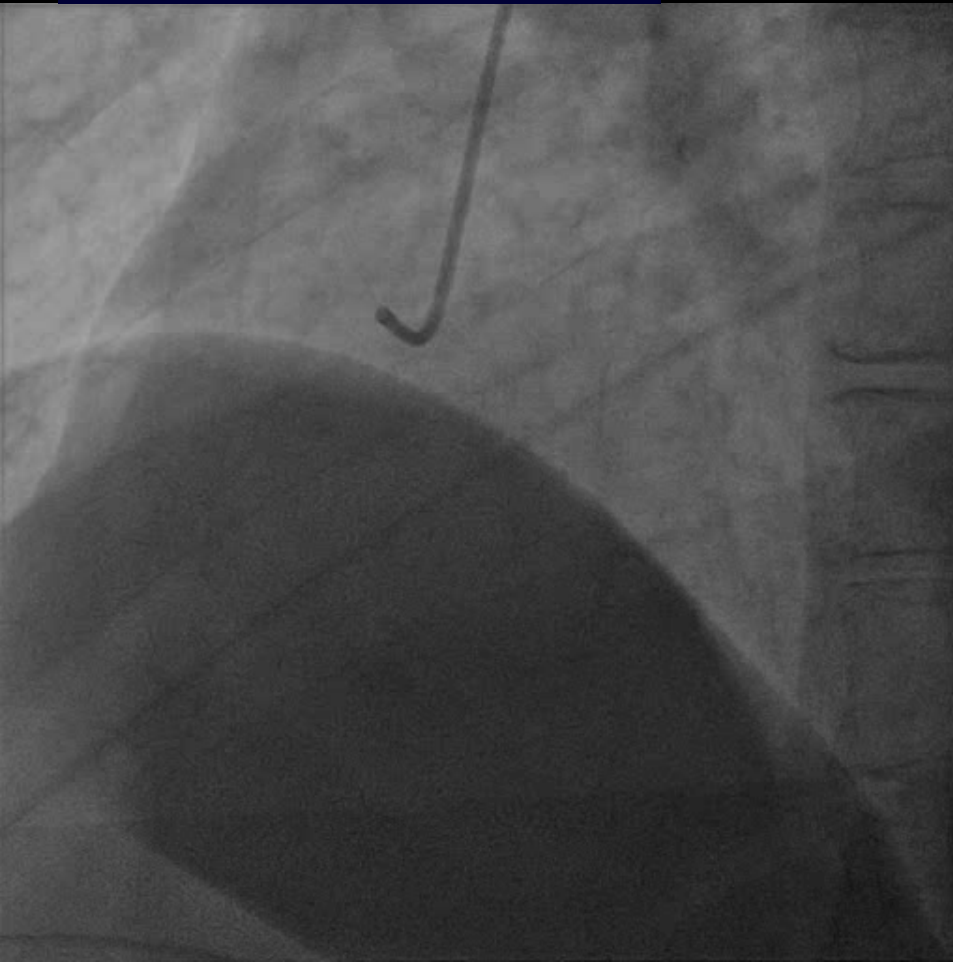
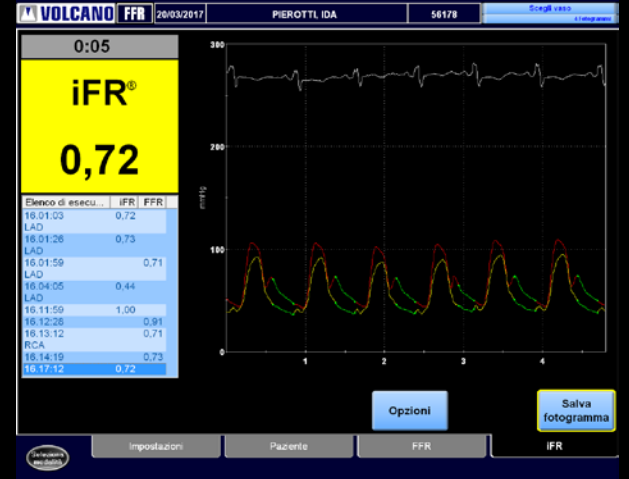
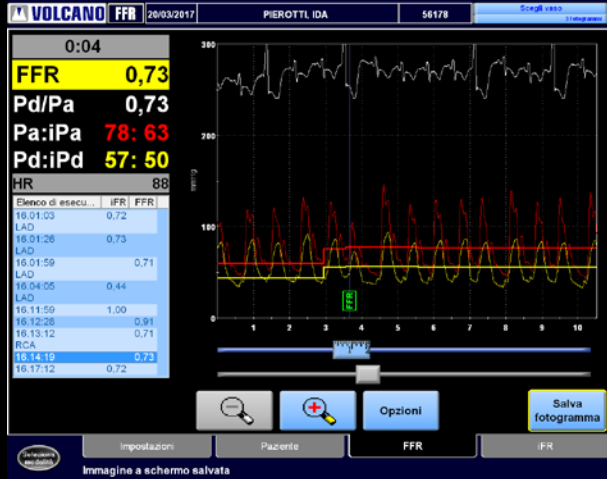
- No clinical events
- No angina

iFR Scout functional assessment and OCT-guided coronary reconstruction with BVS

53 yo female

Obese, diabetic, strong family history of CAD

Admitted for ACS with diffuse ST segment
derpession and mild troponin rise

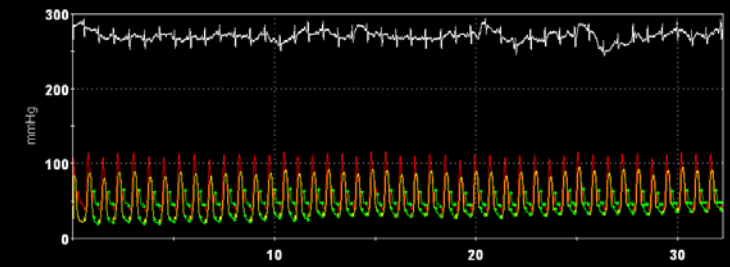
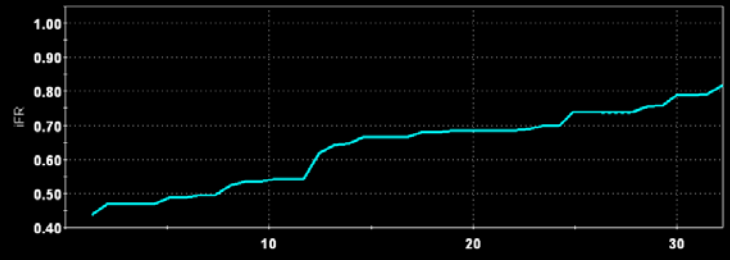




0:49

iFR[®]
Distale
0,44

Elenco di esecu...	iFR	FFR
16.01:03	0,72	
LAD		
16.01:26	0,73	
LAD		
16.01:59	0,71	
LAD		
16.04:05	0,44	
LAD		
16.11:59	1,00	
LAD		
16.12:28	0,91	
LAD		
16.13:12	0,71	
RCA		
16.14:19	0,73	
LAD		
16.17:12	0,72	



[-] [+] Opzioni Salva fotogramma

0:10

FFR 0,71
Pd/Pa 0,71
Pa:iPa 62:109
Pd:iPd 44:67
HR 84

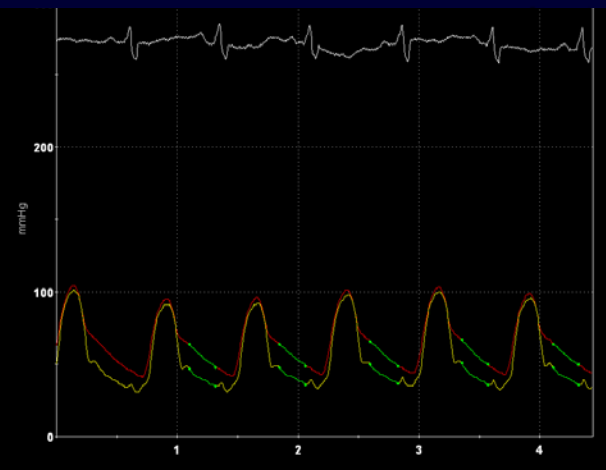
Elenco di esecu...	iFR	FFR
16.01:03	0,72	
LAD		
16.01:26	0,73	
LAD		
16.01:59	0,71	
LAD		
16.04:05	0,44	
LAD		
16.11:59	1,00	
LAD		
16.12:28	0,91	
LAD		
16.13:12	0,71	
RCA		
16.14:19	0,73	
LAD		
16.17:12	0,72	

Seleziona modalità

Impostazioni Paziente FFR iFR

iFR[®]
0,73

Elenco di esecu...	iFR	FFR
16.01:03	0,72	
LAD		
16.01:26	0,73	
LAD		
16.01:59	0,71	
LAD		
16.04:05	0,44	
LAD		
16.11:59	1,00	
LAD		
16.12:28	0,91	
LAD		
16.13:12	0,71	
RCA		
16.14:19	0,73	
LAD		
16.17:12	0,72	



Opzioni Salva fotogramma

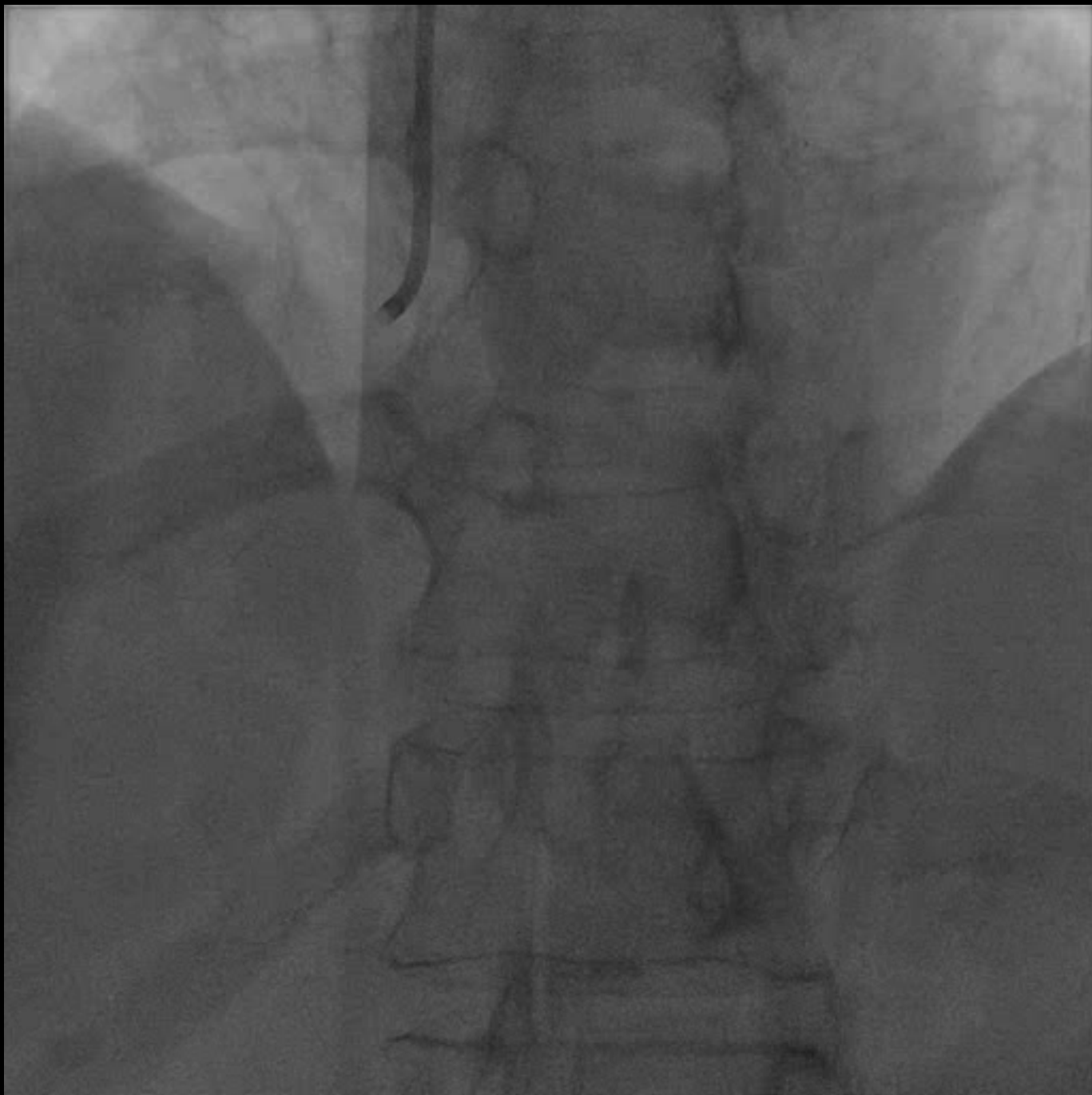
Impostazioni Paziente FFR iFR

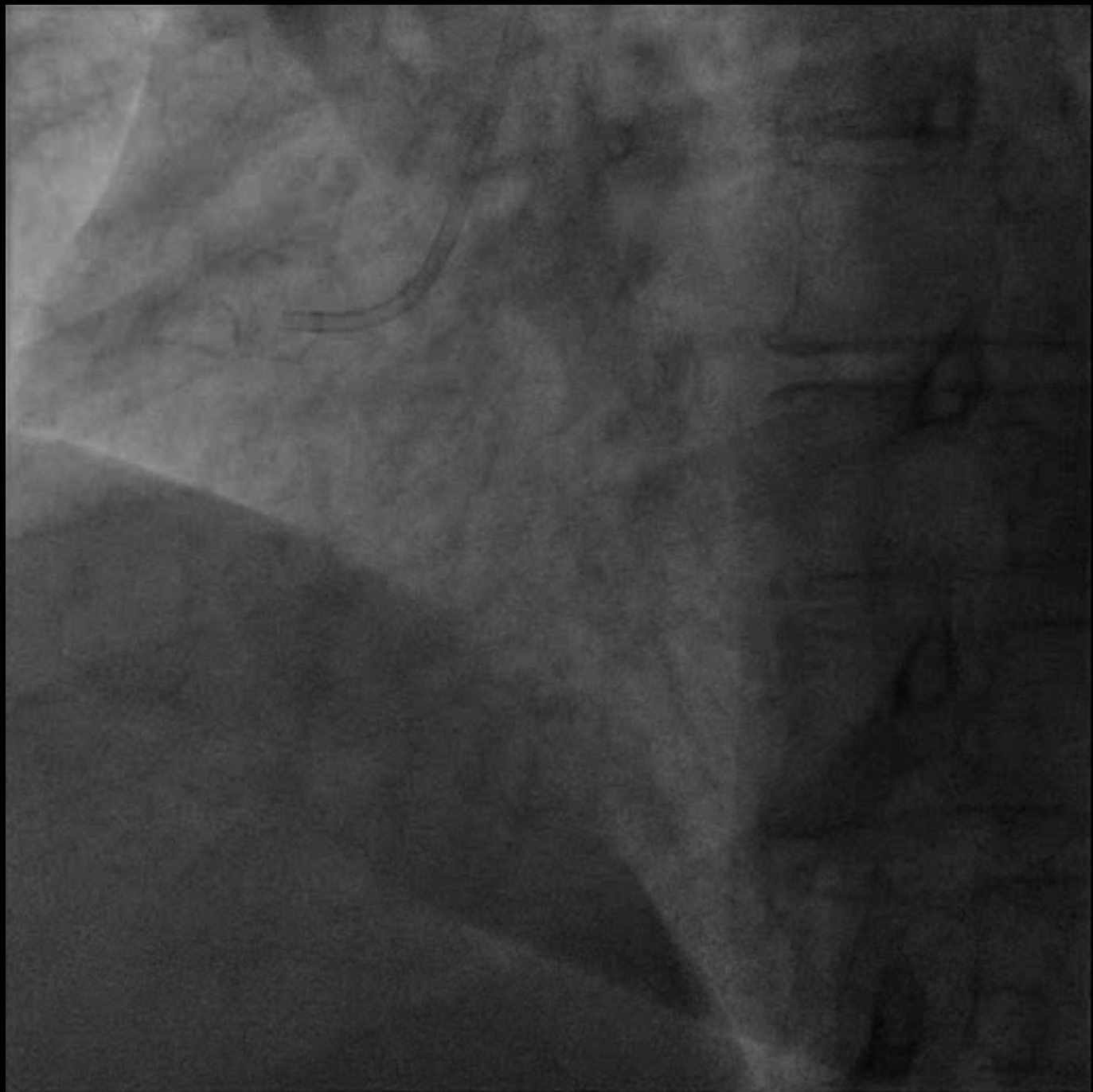
Heart Team Discussion

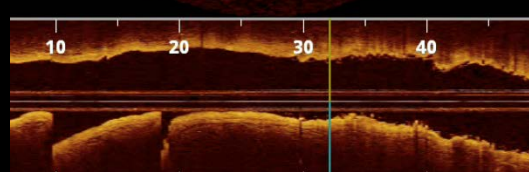
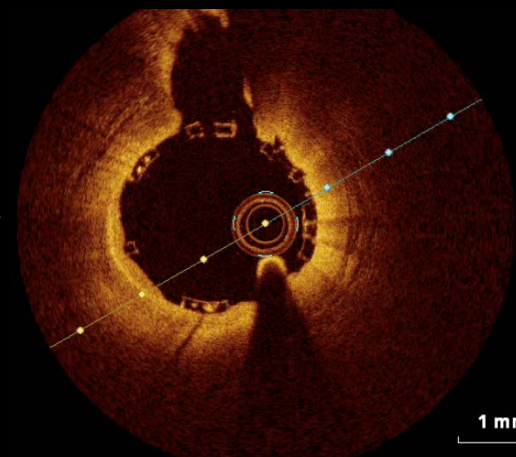
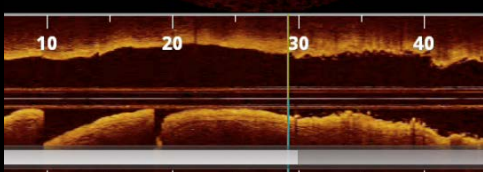
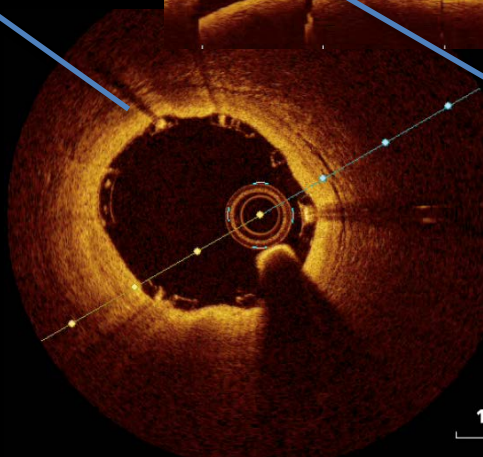
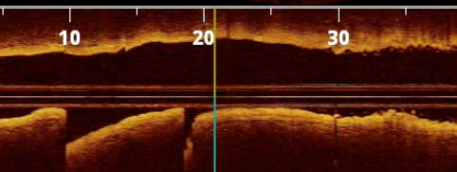
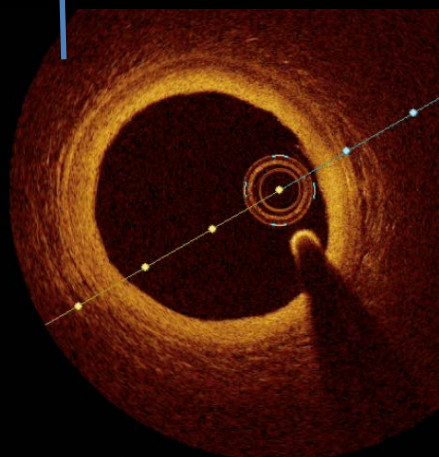
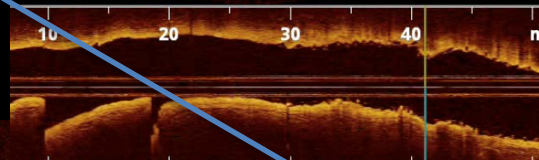
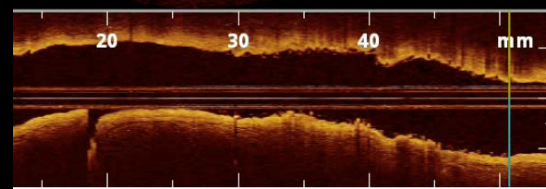
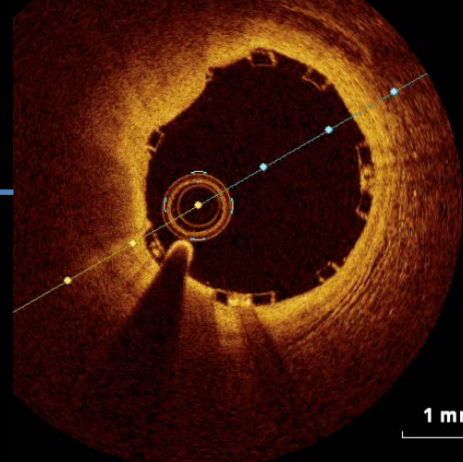
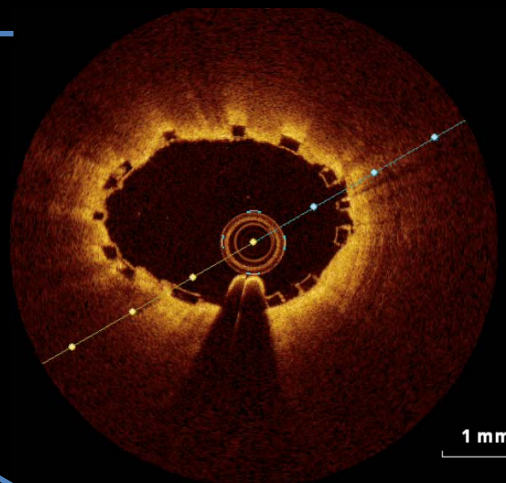
- The patient was strongly advised to undergo CABG.
- She categorically refused surgery because her father died few years before during a by-pass operation. Furthermore, because of her young age She decided to postpone surgery for eventual recurrences.

PCI strategy

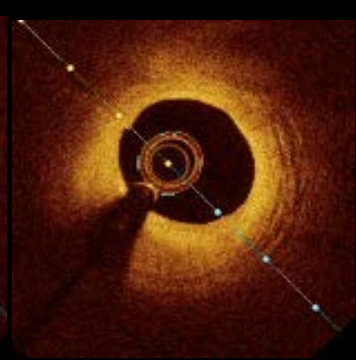
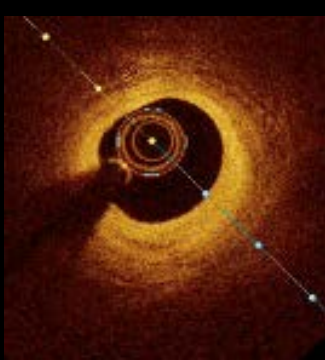
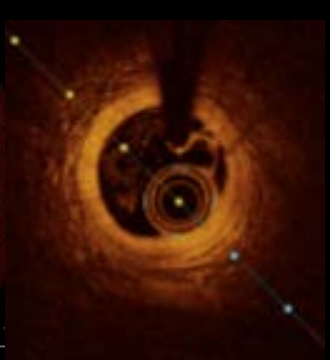
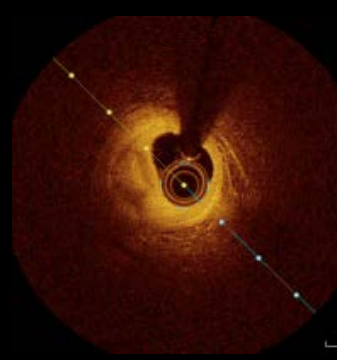
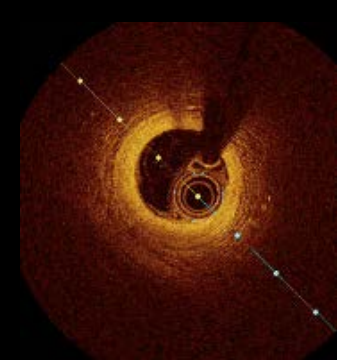
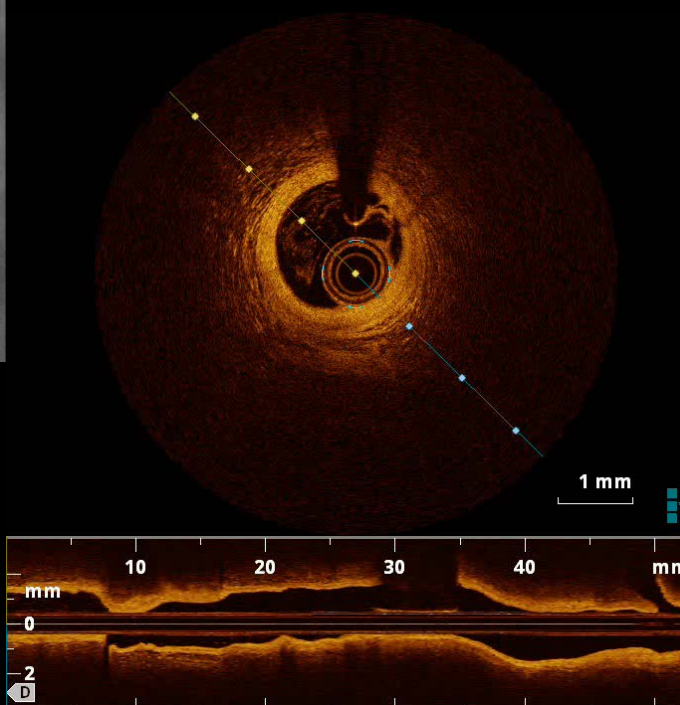
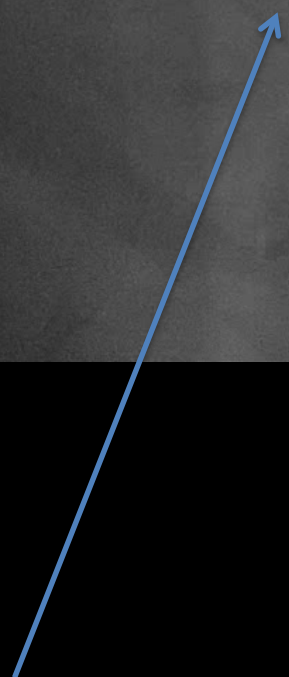
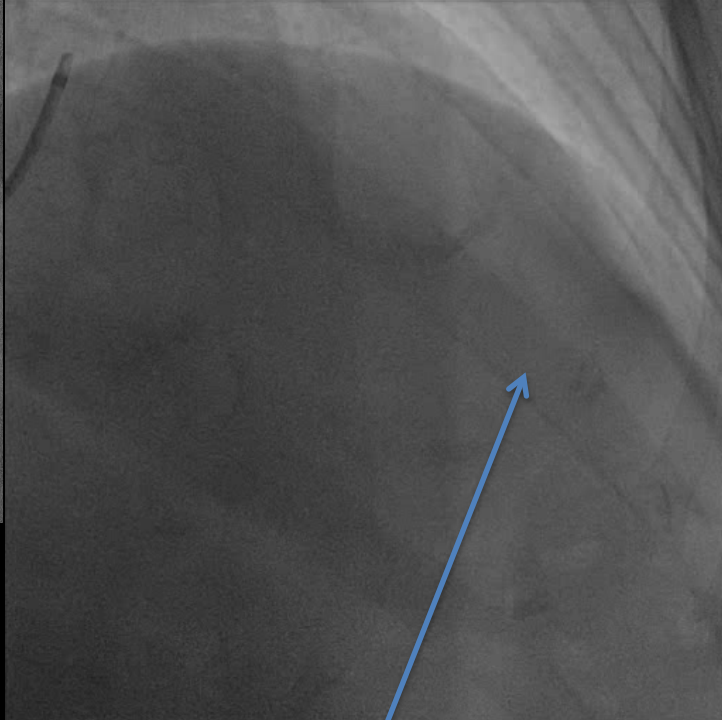
- Determine segments to be treated
- Vessel preparation for BVS reconstruction
- BVS optimization
- Final OCT assessment
- Medical therapy and follow-up strategy

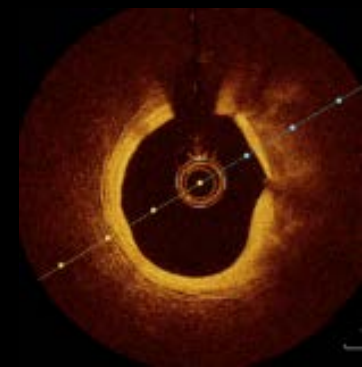
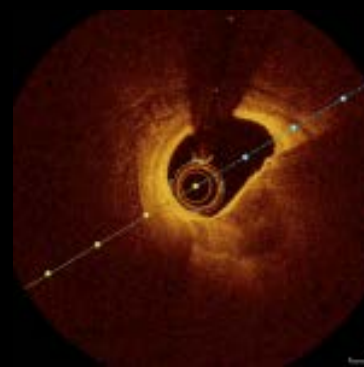
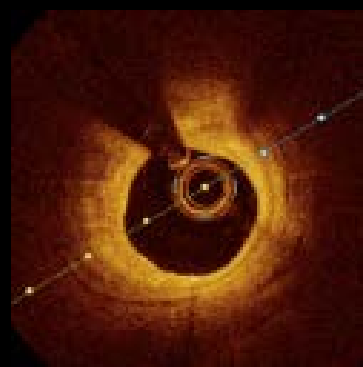
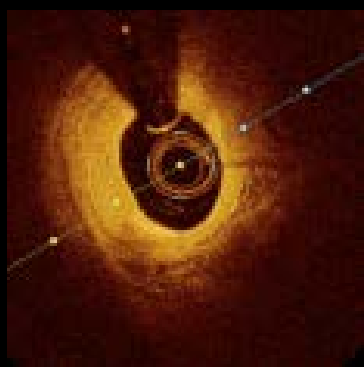
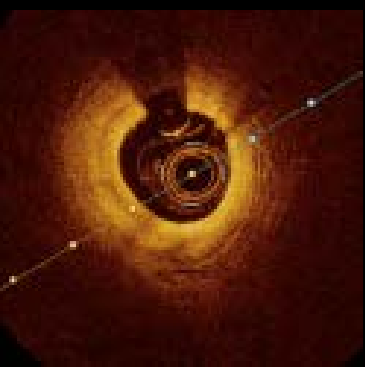
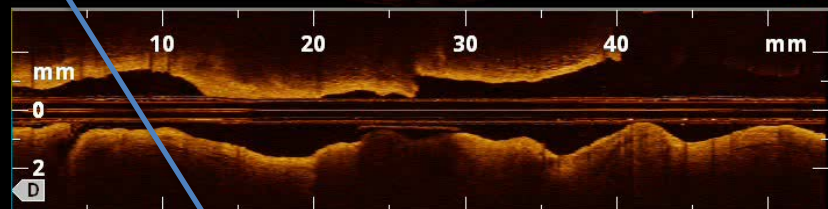
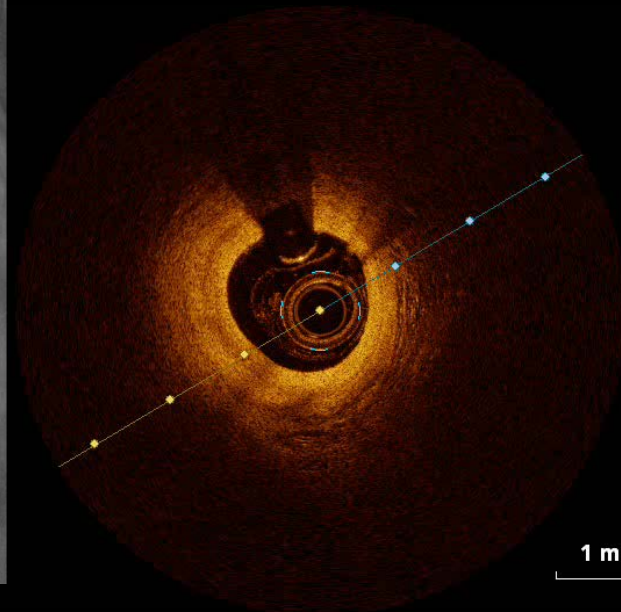
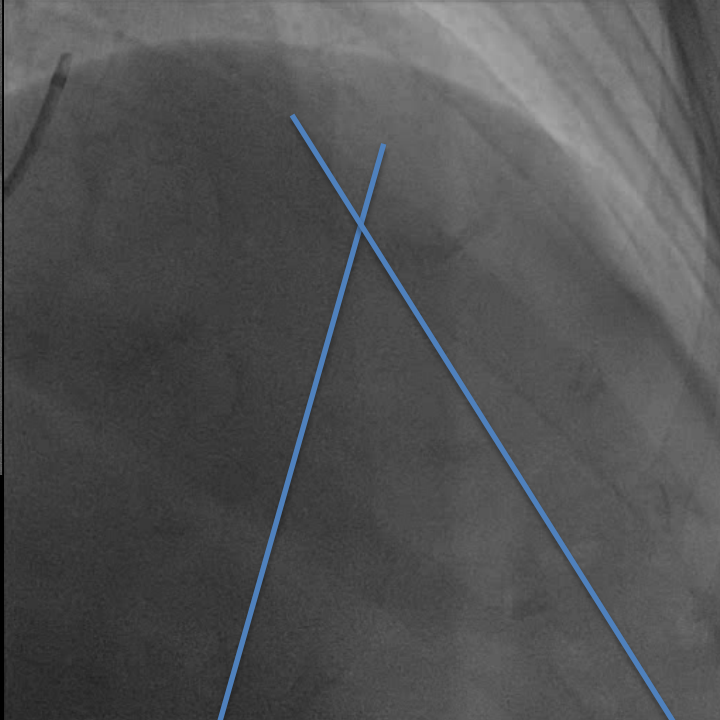




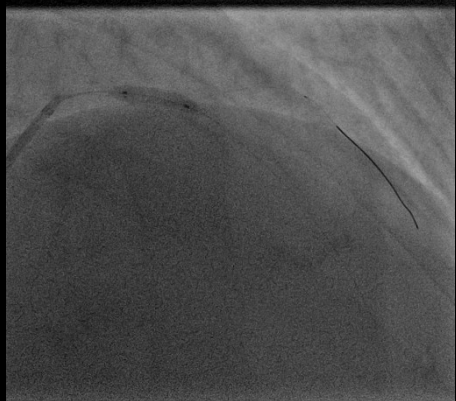
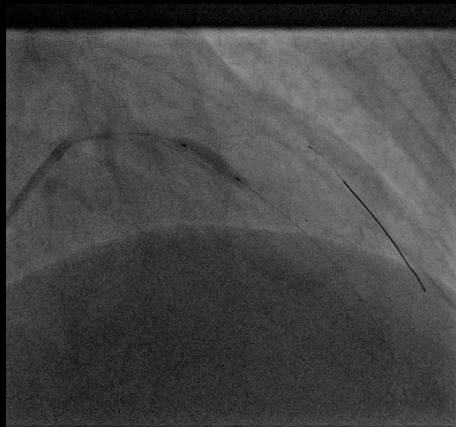
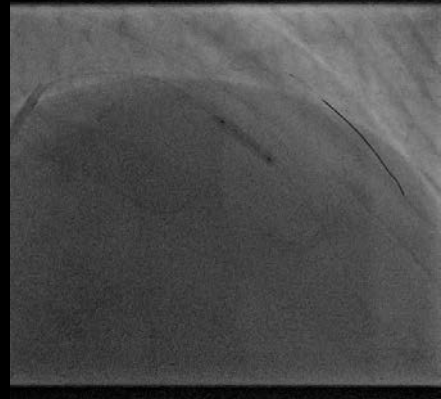
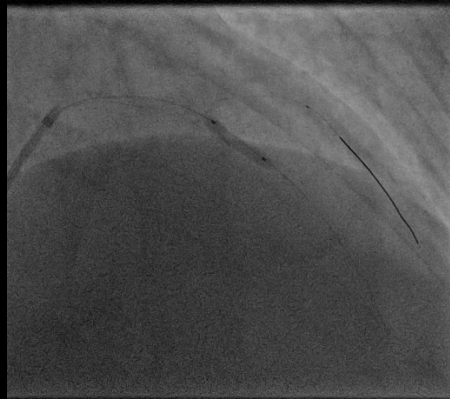
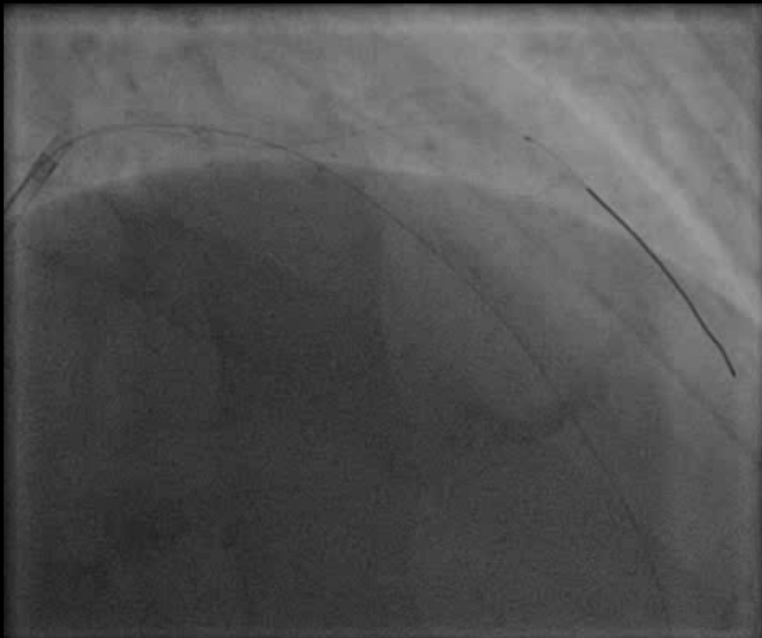


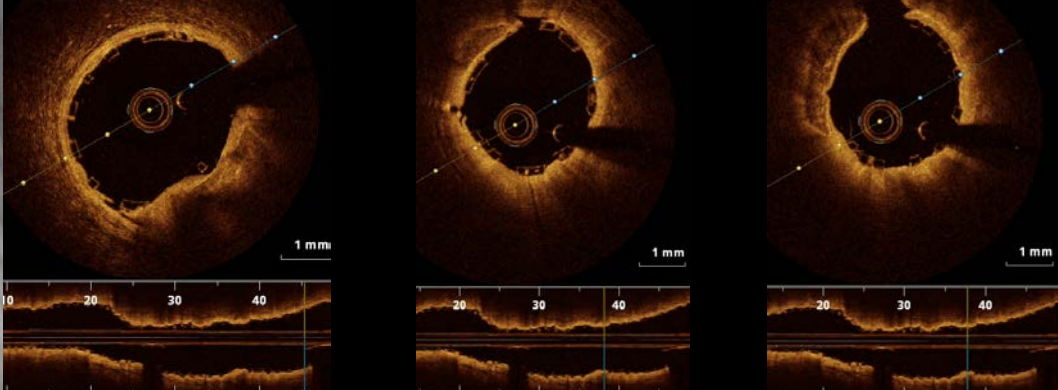




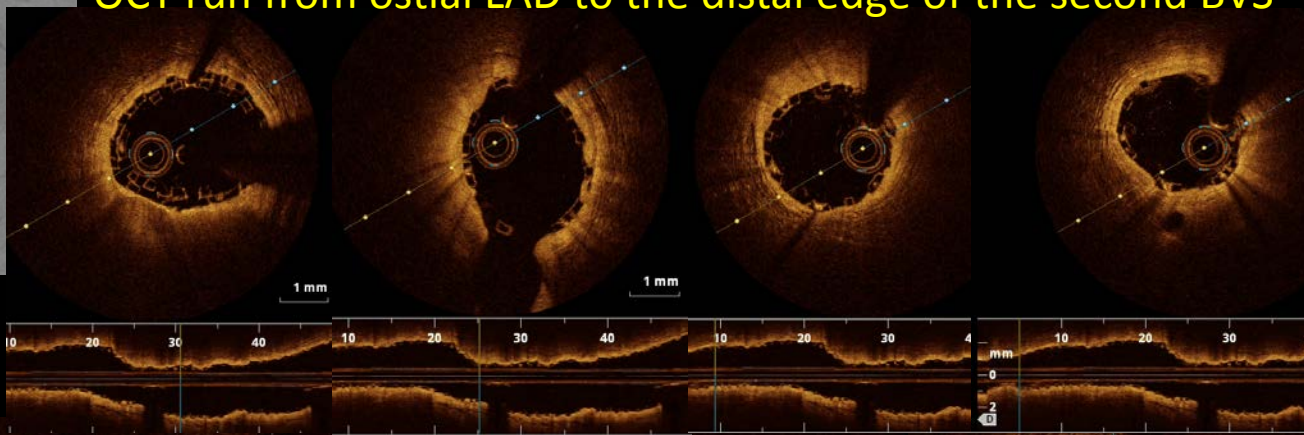




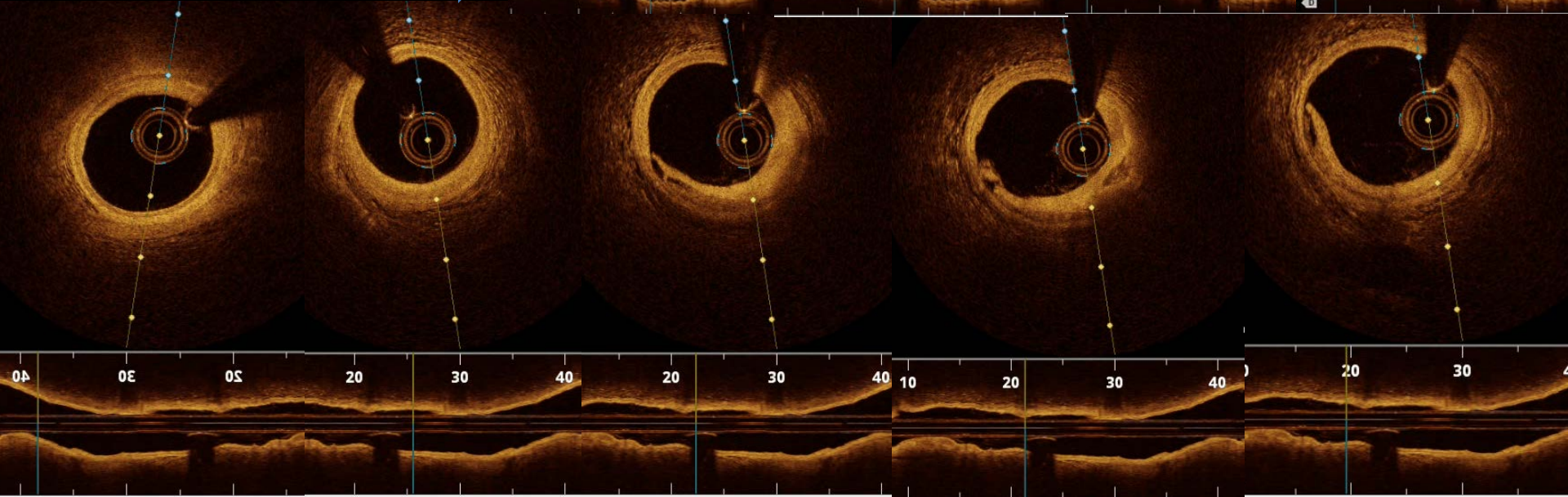




OCT run from ostial LAD to the distal edge of the second BVS



Distal LAD treated with DEB
From prox to dist

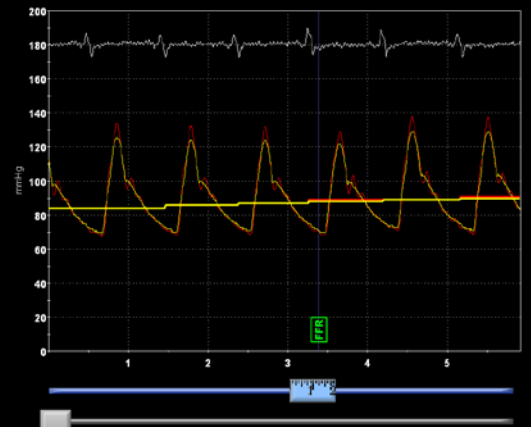


0:03

FFR 0,99
Pd/Pa 0,99
Pa:iPa 89: 70
Pd:iPd 88: 71

HR 66

Elenco di esecu...	IFR	FFR
08.18:56		0,99
08.19:37		0,88
LCX		
08.21:34		0,73
LAD Pre-Stent		
08.23:03		0,00
08.24:22		0,79
LAD Pre-Stent		
08.25:30		0,78
LAD Pre-Stent		
08.40:58		0,90
08.41:44		0,84
LAD Post-Stent		
08.43:02		0,89



[-] [+] Opzioni Salva fotogramma

Conclusions

- 2 large randomized trials comparing iFR vs FFR in a total of ~4500 pts demonstrate *non-inferiority or iFR* with respect to clinical endpoints at 1 year
- iFR is associated with *less procedural discomfort* and shorter procedure time
- DEFINE-FLAIR and iFR SwedeHeart are the largest RCT in physiological guided revascularization
- Largest cohort of ACS patients
- The universal use of iFR will increase the application of physiology in the Cath Lab
- iFR, unlike FFR, lends itself to a more ductile application throughout the procedure to investigate serial lesions and diffuse disease (less “full metal” or “full plastic” stenting)

