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Ελληνικού Κολλεγίου Καρδιολογίας**



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Συνεδριακό Κέντρο Διάσελο

Μέτσοβο

# Latest Data in Physiology Assessment (FFR): *iFR, CT-FFR, Angio-FFR*

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# Fractional Flow Reserve

## The “Gold Standard” for Invasive Functional Assessment

- **FFR** = Pd/Pa during hyperemia
- FFR to detect coronary lesions that would benefit from revascularisation
- **FFR-guided PCI**
  - Improves patient outcomes
  - Reduces stent implantations
  - Is cost-effective

*The* **NEW ENGLAND**  
**JOURNAL** *of* **MEDICINE**

ESTABLISHED IN 1812

JANUARY 15, 2009

VOL. 360 NO. 3

Fractional Flow Reserve versus Angiography  
for Guiding Percutaneous Coronary Intervention

*The* **NEW ENGLAND**  
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SEPTEMBER 13, 2012

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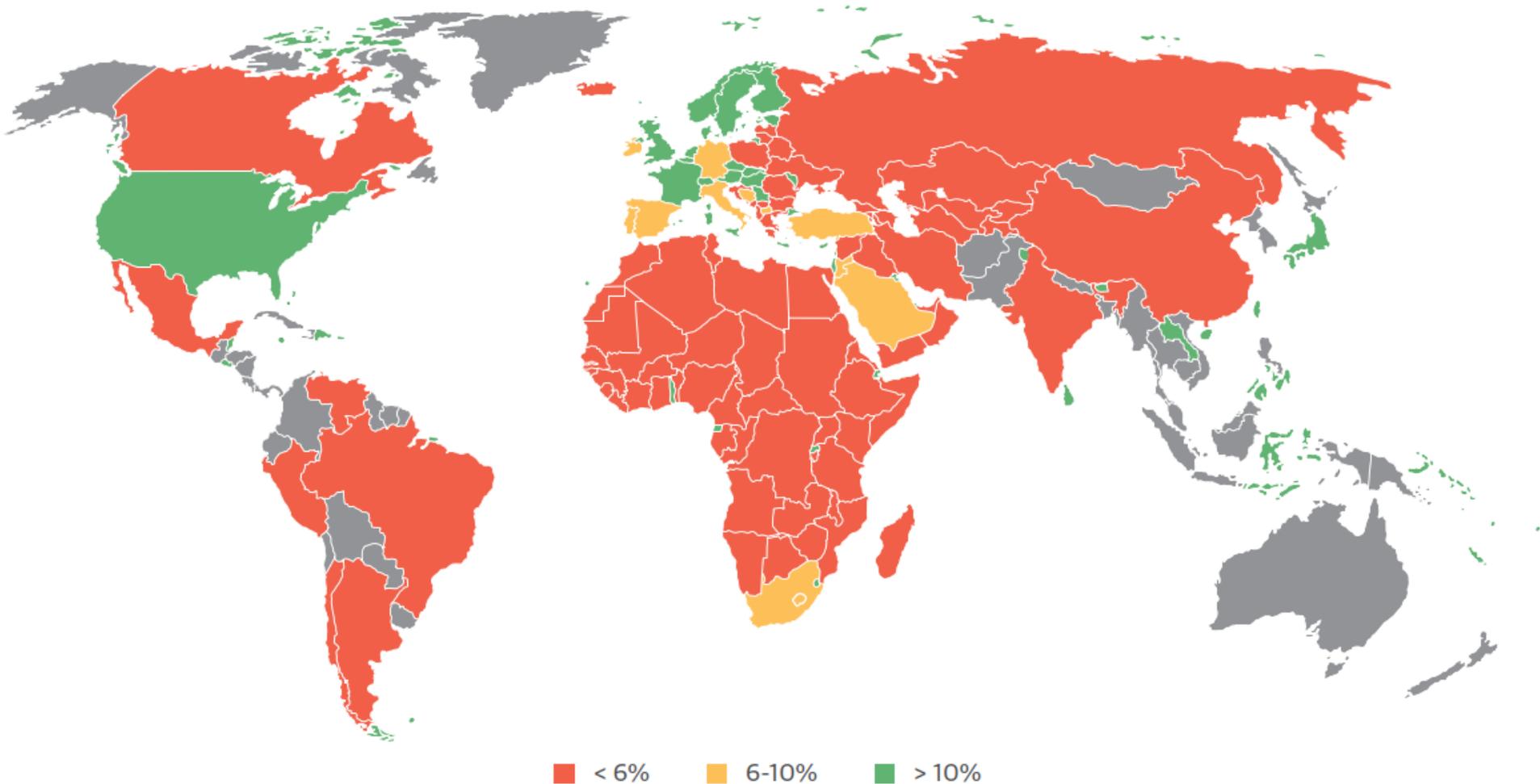
Fractional Flow Reserve–Guided PCI versus Medical Therapy  
in Stable Coronary Disease

Pijls NH, et al. *J Am Coll Cardiol* 2007

Tonino PA, et al. *N Engl J Med* 2009

De Bruyne B, et al. *N Engl J Med* 2012

# Global Adoption of FFR in Catheter Laboratories in 2016



# Low Adoption of FFR in Clinical Practice

- More invasive – More risk
  - Intracoronary manipulation of the pressure wire
  - Administration of vasodilators (adenosine)
- Additional time
- Additional cost
- Operator's choice: confidence in visual assessment



AV block (2-8%)  
Bronchospasm  
Headache, flush

# Resting (non-hyperemic) pressure-derived indices as an alternative for hemodynamic severity of coronary artery disease

Resting Pd/Pa

Contrast FFR

**instantaneous  
wave-Free Ratio (iFR)**

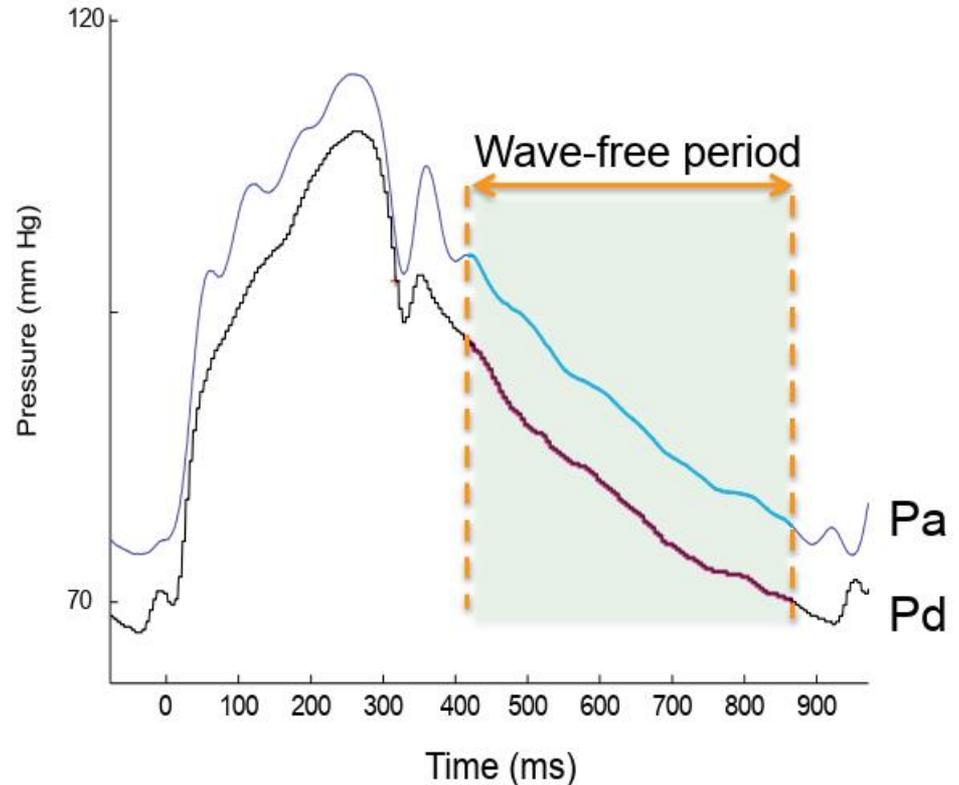
Resting Full-cycle  
Ratio (RFR)

diastolic Pressure  
Ratio (dPR)

**No administration of adenosine**

# iFR (instantaneous wave-Free Ratio)

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

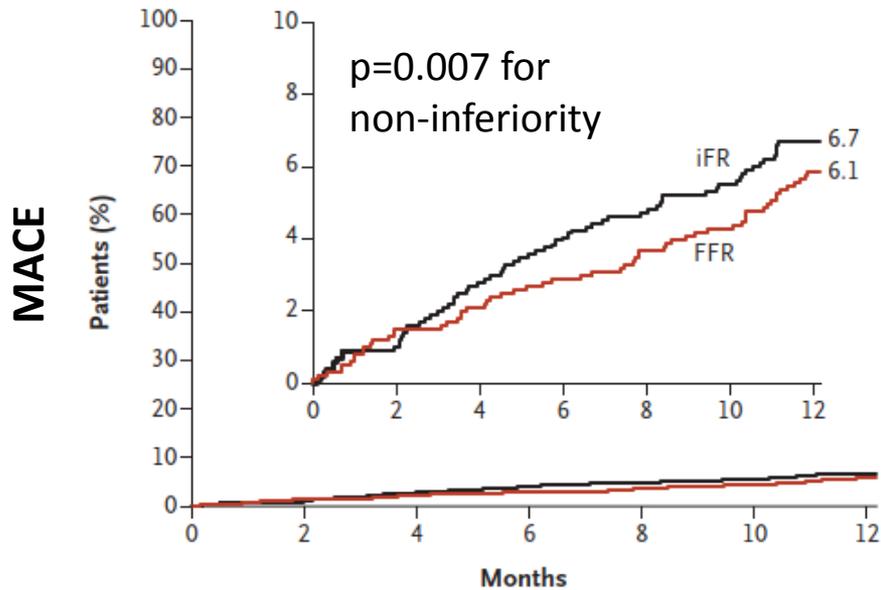


## **wave-free period:**

*25% of the way into diastole and ending 5 ms before the end of diastole*

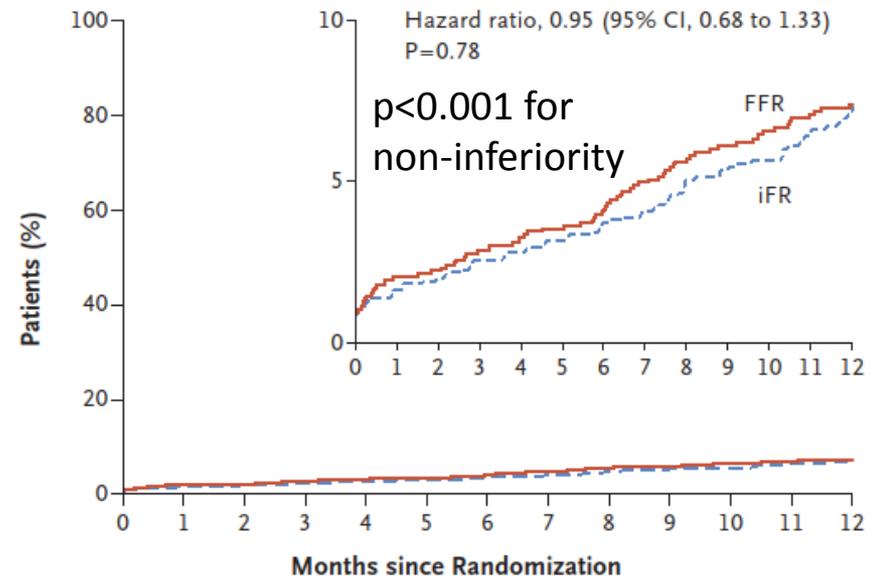
# Non-inferiority of iFR vs FFR for MACE

## iFR-SWEDEHEART RCT



No. at Risk	0	2	4	6	8	10	12
iFR	1012	1002	984	971	963	956	944
FFR	1007	990	984	976	968	961	946

## DEFINE-FLAIR RCT



No. at Risk	0	1	2	3	4	5	6	7	8	9	10	11	12
iFR	1242	1149	1131	1122	1118	1111	1088	1052	1037	1027	1019	995	764
FFR	1250	1169	1156	1149	1144	1141	1119	1081	1066	1055	1046	1017	793

MACE: death from any cause, nonfatal myocardial infarction, or unplanned revascularization

FFR cut-off = 0.80  
iFR cut-off = 0.89

Gotberg M, et al. *N Engl J Med* 2017  
Davies J, et al. *N Engl J Med* 2017

# iFR in ESC Guidelines

## When to perform revascularisation?

### Indications for revascularization in patients with stable angina or silent ischaemia

Extent of CAD (anatomical and/or functional)		Class <sup>a</sup>	Level <sup>b</sup>
For prognosis	Left main disease with stenosis >50% <sup>c 69-71</sup>	I	A
	Proximal LAD stenosis >50% <sup>c 2,68,70,72</sup>	I	A
	Two- or three-vessel disease with stenosis >50% with impaired LV function (LVEF ≤35%) <sup>c 41,62,68,70,73-83</sup>	I	A
	Large area of ischaemia detected by functional testing (>10% LV) or abnormal invasive FFR <sup>d 24,59,84-90</sup>	I	B
	Single remaining patent coronary artery with stenosis >50% <sup>c</sup>	I	C
For symptoms	Haemodynamically significant coronary stenosis <sup>c</sup> in the presence of limiting angina or angina equivalent, with insufficient response to optimized medical therapy. <sup>e 24,63,91-97</sup>	I	A

© ESC 2018

<sup>c</sup> With documented ischaemia or a haemodynamically relevant lesion defined by  $FFR \leq 0.80$  or  $iwFR \leq 0.89$

## When physiology?

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
When evidence of ischaemia is not available, $FFR$ or $iwFR$ are recommended to assess the haemodynamic relevance of <u>intermediate-grade stenosis</u> . <sup>15,17,18,39</sup>	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI. <sup>29,31</sup>	IIa	B

ESC Guidelines on Myocardial Revascularisation. 2018

# iFR in SCAI Position paper

## Focused update of expert consensus statement: Use of invasive assessments of coronary physiology and structure

A position statement of the society of cardiac angiography and interventions

### Recommendations

#### FFR/iFR

##### Definitely beneficial:

In SIHD, when non-invasive stress imaging is uncertain, non-diagnostic or unavailable, FFR/iFR can be used to assess the functional significance of intermediate coronary stenoses.

In SIHD, PCI of lesions found significant by FFR/iFR improves symptom control and decreases the need for hospitalization requiring urgent revascularization when compared to medical therapy alone. Abnormal values should be considered in context of the patient's entire clinical picture.

In SIHD, medical therapy is indicated for an angiographically intermediate non-LMCA stenosis when  $FFR > 0.80$  or  $iFR > 0.89$ .

In SIHD, medical therapy is indicated for an angiographically intermediate LMCA stenosis when  $FFR > 0.80$ .

In SIHD, to assess the severity of stenoses in series and select targets for stenting

In multivessel coronary disease, PCI guided by FFR measurement improves outcomes and saves resources when compared to angiography guided PCI.

##### Probably beneficial

In multivessel coronary disease, measuring FFR/iFR may allow reclassification of number of vessels diseased (Functional SYNTAX score), and consequently guide decisions regarding revascularization by CABG or PCI.

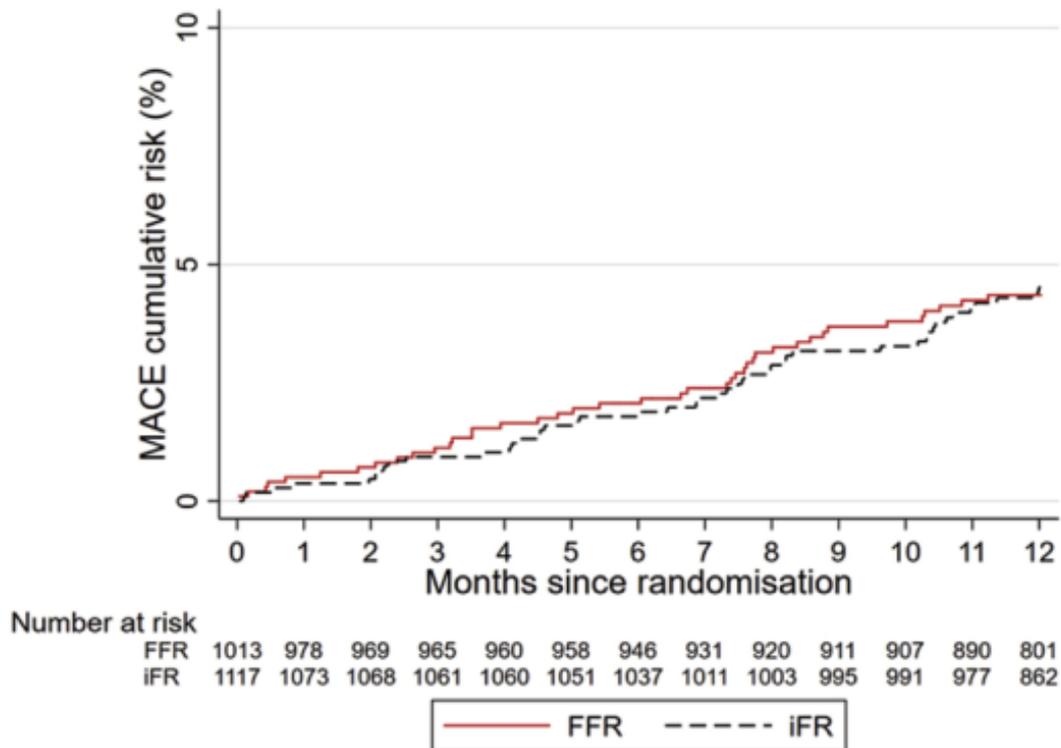
# Meta-analysis of Death and MI in iFR vs FFR RCTs

	iFR n (%)	FFR n (%)	Risk Ratio	95% CI	P Value
Unplanned revascularization					
DEFINE-FLAIR	46 (4.0)	63 (5.3)	0.75	(0.52–1.09)	0.13
iFR-SWEDEHEART	47 (4.6)	46 (4.6)	1.02	(0.68–1.51)	0.94
Overall			0.87	(0.65–1.16)	0.34
Test for heterogeneity: $\chi^2 = 1.18$ df=1 ( $P=0.277$ ), $I^2 = 15.6\%$					
Nonfatal myocardial infarction					
DEFINE-FLAIR	31 (2.7)	28 (2.4)	1.14	(0.69–1.89)	0.61
iFR-SWEDEHEART	22 (2.2)	17 (1.7)	1.29	(0.69–2.41)	0.43
Overall			1.20	(0.81–1.77)	0.37
Test for heterogeneity: $\chi^2 = 0.09$ df=1 ( $P=0.767$ ), $I^2 = 0\%$					
Death					
DEFINE-FLAIR	22 (1.9)	13 (1.1)	1.74	(0.88–3.44)	0.11
iFR-SWEDEHEART	15 (1.5)	12 (1.2)	1.24	(0.59–2.64)	0.57
Overall			1.50	(0.90–2.48)	0.12
Test for heterogeneity: $\chi^2 = 0.42$ df=1 ( $P=0.516$ ), $I^2 = 0\%$					
Death or myocardial infarction					
DEFINE-FLAIR	53 (4.6)	41 (3.5)	1.33	(0.89–1.98)	0.16
iFR-SWEDEHEART	37 (3.7)	29 (2.9)	1.27	(0.79–2.05)	0.33
Overall	<b>90 (~4.2%)</b>	<b>70 (~3.2%)</b>	1.30	(0.96–1.77)	<b>0.09</b>

# Deferral of Revascularisation: FFR vs iFR

**FIGURE 3** Cumulative Risk for Primary Endpoint (Major Adverse Cardiac Events) by Physiological Technique in the Deferred Population

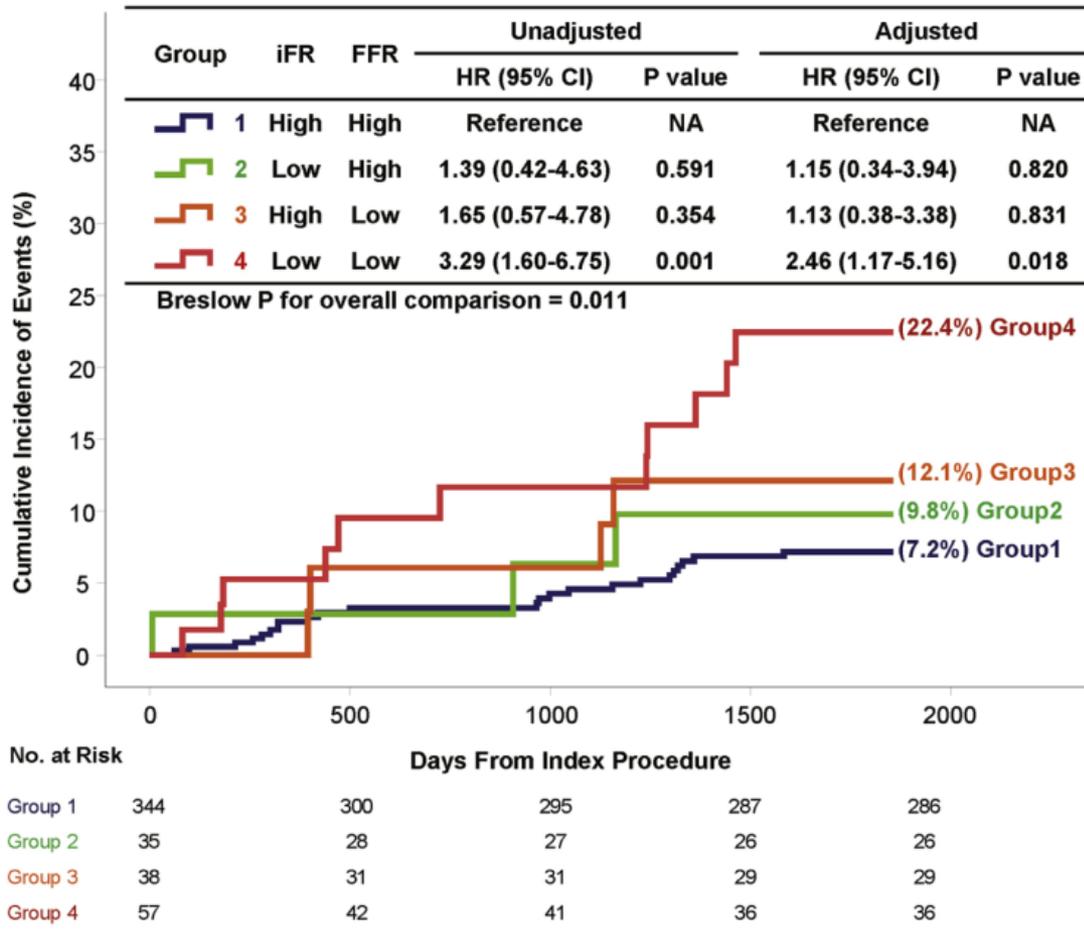
Pooled analysis  
of FFR-iFR RCTs



Shown is the cumulative risk for the composite of death from any cause, nonfatal myocardial infarction, or unplanned revascularization at 1 year. MACE = major adverse cardiac event(s); other abbreviations as in [Figure 1](#).

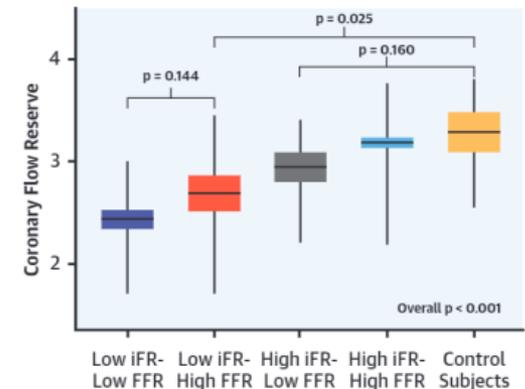
# Discordance between FFR and iFR: Clinical Outcomes of Deferred Patients

**FIGURE 5** Comparison of Patient-Oriented Composite Outcome Among Patients With Deferred Lesions According to Classification by FFR and iFR



840 vessels (596 pts)

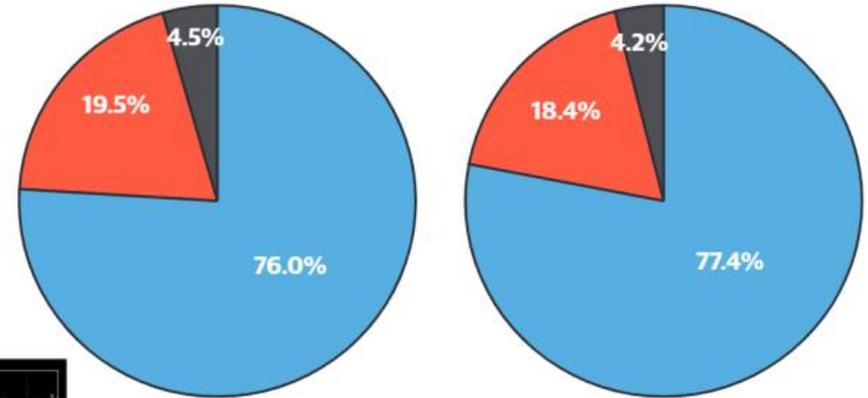
## Differences in vasodilatory capacity



Kaplan-Meier curves are shown for the 5 groups of patients with deferred lesions according to classification by iFR and FFR. Adjusted covariates in multivariable model included age, sex, hypertension, hypercholesterolemia, and diameter stenosis. Abbreviations as in [Figures 1 and 4](#).

# Residual Ischemia After Successful Angiographic PCI: DEFINE-PCI Study

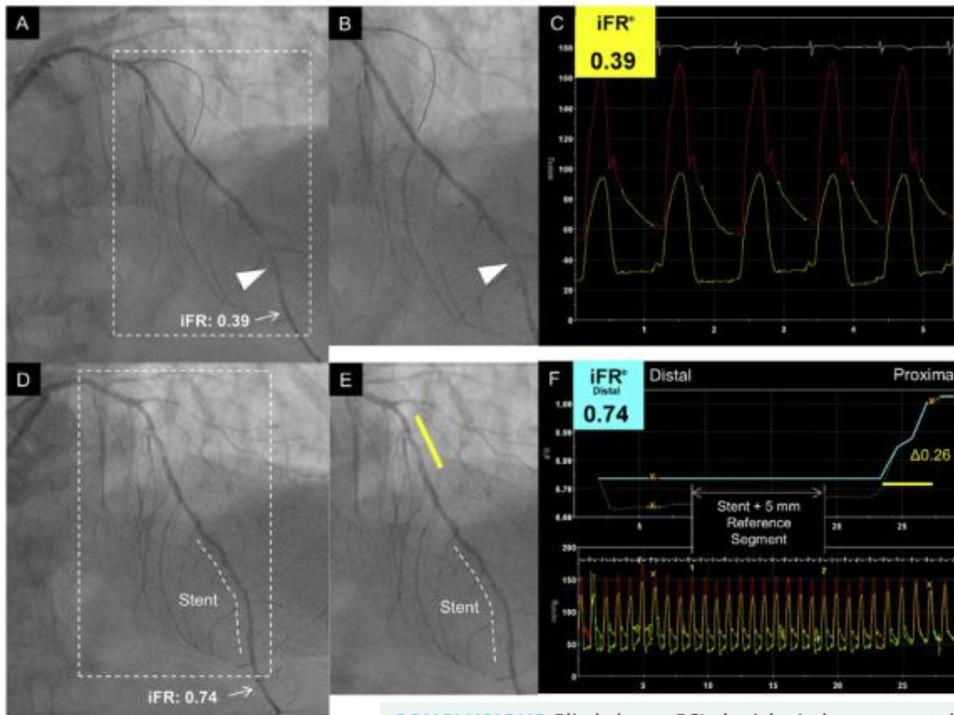
## CENTRAL ILLUSTRATION Post-Percutaneous Coronary Intervention Coronary Physiology



Patient Level

Vessel Level

- Post-iFR  $\geq 0.90$
- Focal Lesion with Post-iFR  $< 0.90$
- Diffuse Lesion with Post-iFR  $< 0.90$



**CONCLUSIONS** Blinded post-PCI physiological assessment detected residual ischemia in nearly 1 in 4 patients after coronary stenting despite an operator-determined angiographically successful result. Most cases of residual ischemia were due to inapparent focal lesions potentially amenable to treatment with additional PCI. (Physiologic Assessment of Coronary Stenosis Following PCI [DEFINE PCI]; [NCT03084367](https://clinicaltrials.gov/ct2/show/study/NCT03084367)) (J Am Coll Cardiol Intv 2019;12:1991-2001) © 2019 by the American College of Cardiology Foundation.

# Adenosine-free Indices

Resting Pd/Pa

Contrast FFR

**instantaneous  
wave-Free Ratio (iFR)**

Resting Full-cycle  
Ratio (RFR)

diastolic Pressure  
Ratio (dPR)

**THEY Negate the use of vasodilators (adenosine) for  
induction of hyperemia**

**BUT  
THEY Require a pressure wire for invasive  
measurements**

# From Lumenogram to “Functional Angiography” and the Evolution of Virtual Fractional Flow Reserve

Has the Time Come for Outcome-Based Trials?

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Michail I. Papafaklis, MD,  
PhD  
Andreas Baumbach, MD

## THE ADVENT OF FUNCTIONAL ANGIOGRAPHY

### *Angiography-based FFR*

- Add a functional component to angiography by using a computer-simulated index
- No need for coronary instrumentation and adenosine infusion
- Obtain an FFR-equivalent color-coded coronary artery map

# Imaging → Functional Assessment

## ≈ *Functional Coronary Imaging*

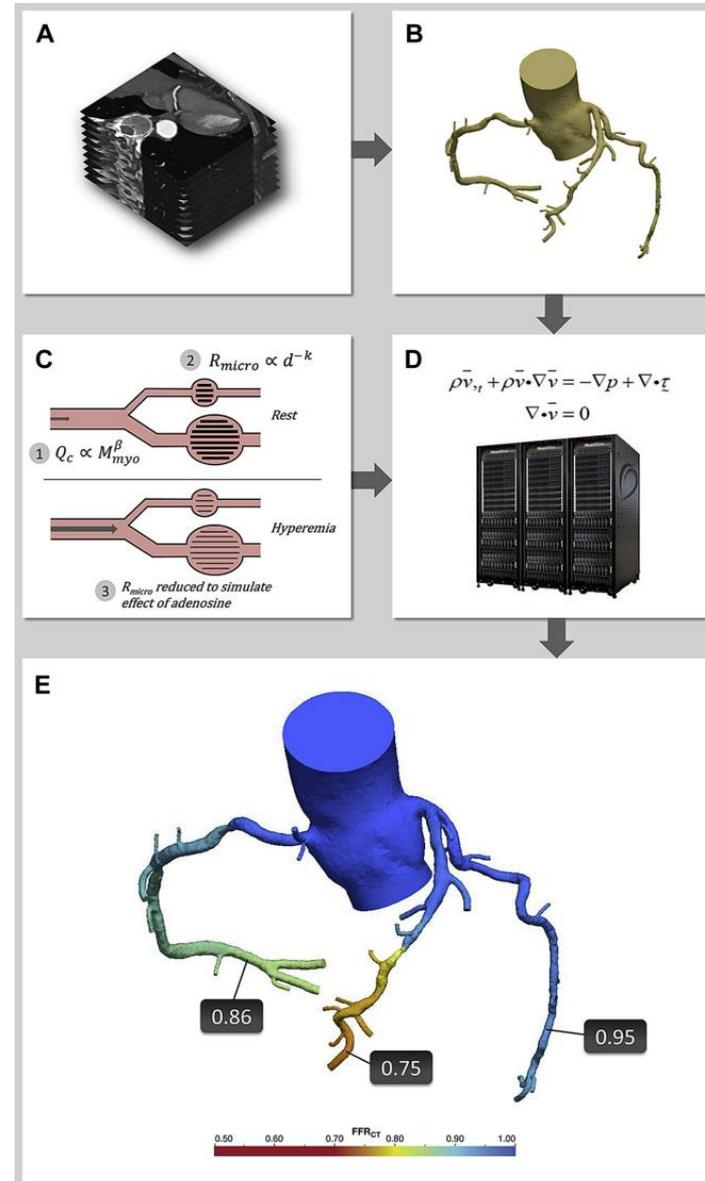
- Methodologies to **compute FFR surrogates** using *principles of fluid dynamics* applied to *vascular geometries* derived either from noninvasive CTCA or from invasive angiography
  - **Step 1: Construct a computer (*in silico*) model of the 3-dimensional geometry**
  - **Step 2: Prescribe inflow and outflow (boundary conditions)**
    - Simplified boundary conditions
    - **OR** Physiologic model of the heart and arterial system as a closed hydraulic circuit (Windkessel parameters of arterial compliance, microvascular resistance)
  - **Step 3: Implement a calculation method (principles of fluid dynamics)**
    - Computational Fluid Dynamics (CFD) techniques = Finite elements and Numerical solution of 3-D Navier-Stokes equations (differential equations of fluid motion)
    - **OR** Approximate algebraic method using simple equations

# Computed Tomography Coronary Angiography

## FFR-CT

- CT coronary angiographic dataset
- Sophisticated 3-dimensional mathematical modelling of coronary flow, pressure and resistance (CFD and Windkessel model)
- 1-4 hrs of processing time
- **Validated in prospective multicentre trials against invasive FFR in stable patients with suspected CAD**
- Improved diagnostic accuracy over CTCA alone
- FDA-approved class II Coronary Physiological Simulation Software

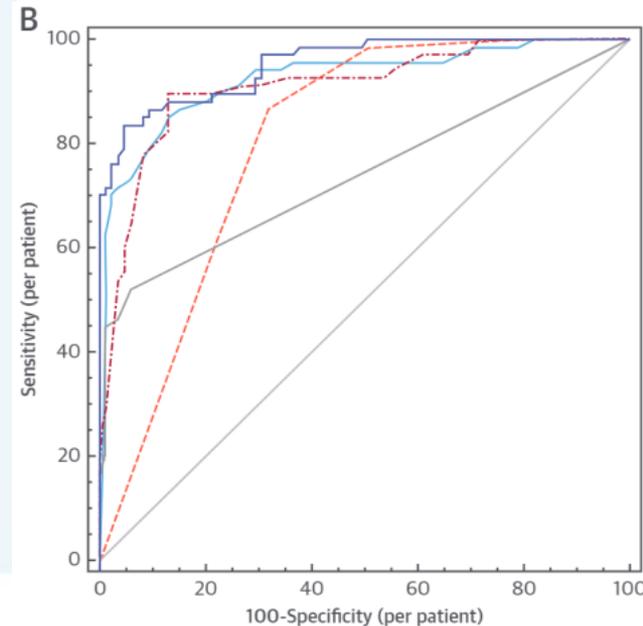
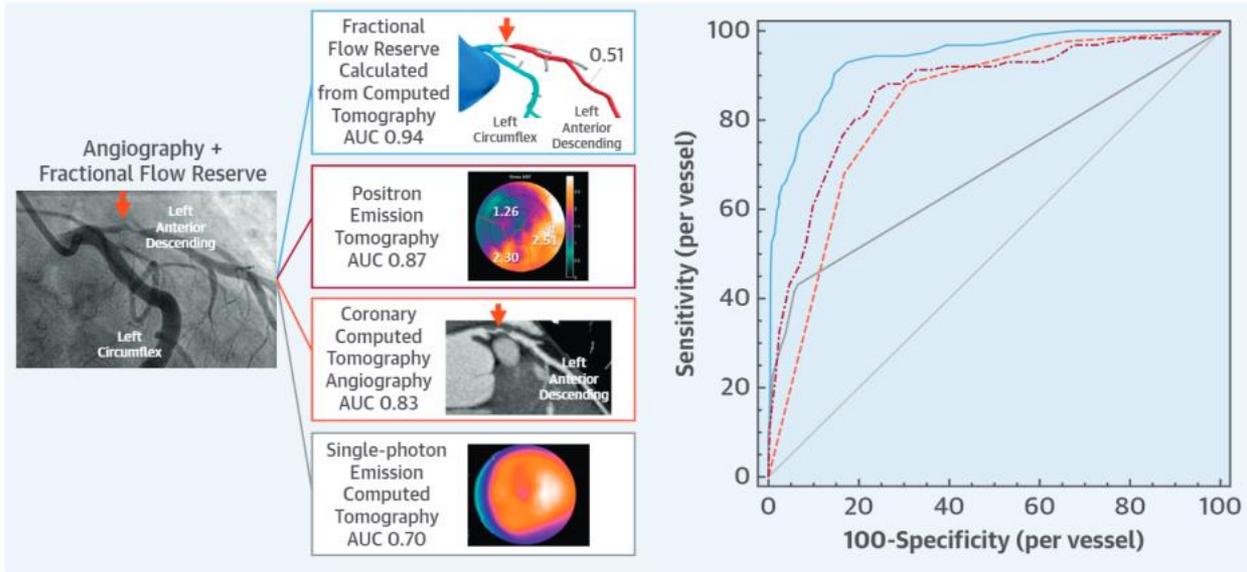
Taylor CA et al. *J Am Coll Cardiol* 2013  
Norgaard BL et al. *J Am Coll Cardiol* 2014



# FFR-CT vs Perfusion Imaging: PACIFIC Trial substudy

157 patients: FFR, SPECT, PET, and CTA with evaluable FFR-CT  
(51 patients were not fully [3-vessel]evaluable by FFR-CT)

## CENTRAL ILLUSTRATION Discriminative Ability of Imaging Modalities for the Detection of Per-Vessel Fractional Flow Reserve-Defined Ischemia



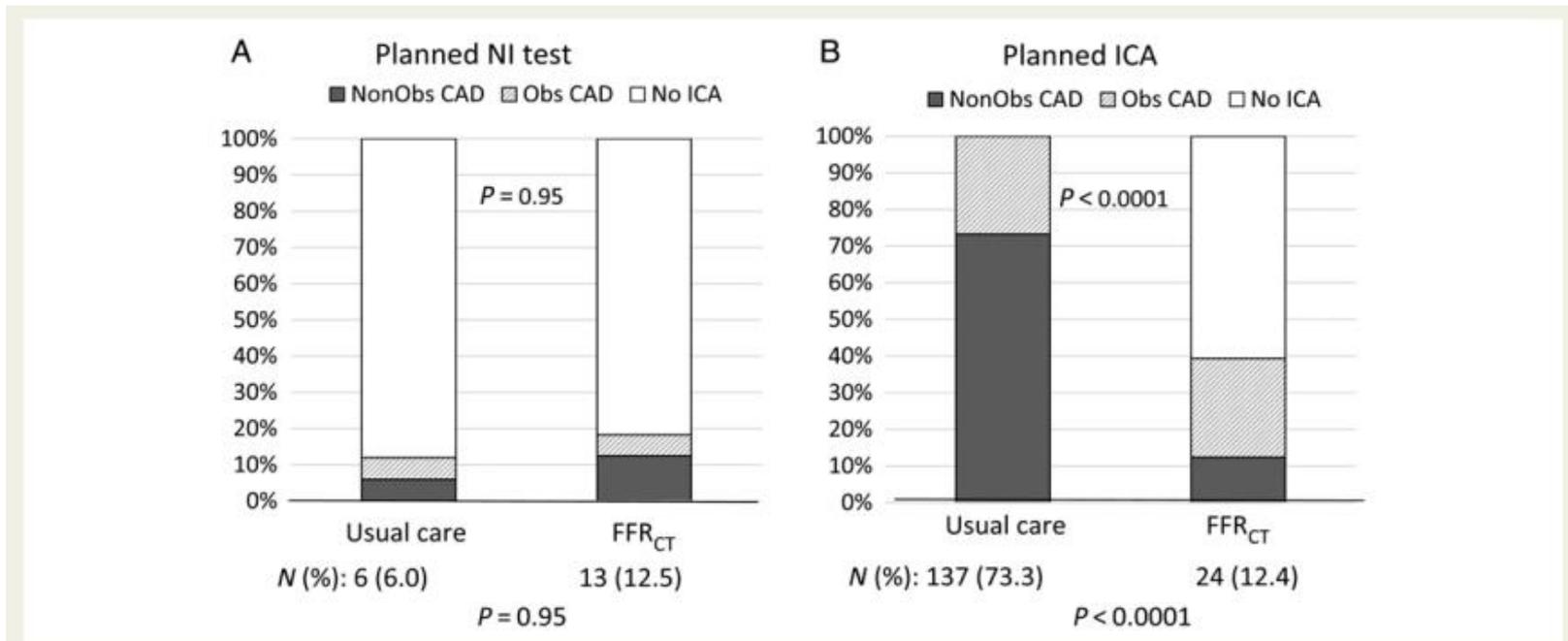
FFR <sub>CT</sub>	AUC 0.92 (0.87-0.96)
CTA	AUC 0.81 (0.74-0.87)
SPECT	AUC 0.75 (0.67-0.81)
PET	AUC 0.91 (0.85-0.95)
CTA + FFR <sub>CT</sub>	AUC 0.95 (0.91-0.98)

Driessen, R.S. et al. *J Am Coll Cardiol.* 2019;73(2):161-73.

Significance of stable coronary artery disease, as defined by invasive FFR, was prospectively tested with several noninvasive imaging modalities. Each patient underwent FFR<sub>CT</sub>, PET, coronary CTA, SPECT, and ICA with FFR, regardless of imaging results as illustrated by the typical imaging findings of a severe left anterior descending artery stenosis in the colored boxes. Curves with corresponding colors indicate that FFR<sub>CT</sub> demonstrated the greatest AUC for the detection of per-vessel ischemia. CTA = coronary computed tomography angiography; FFR = fractional flow reserve; FFR<sub>CT</sub> = fractional flow reserve calculated from computed tomography; ICA = invasive coronary angiography; PET = positron emission tomography; SPECT = single-photon emission computed tomography.

# FFR-CT Diagnostic Strategy vs Usual Care in Suspected CAD: PLATFORM study

Rate of invasive catheterisation without obstructive coronary artery disease



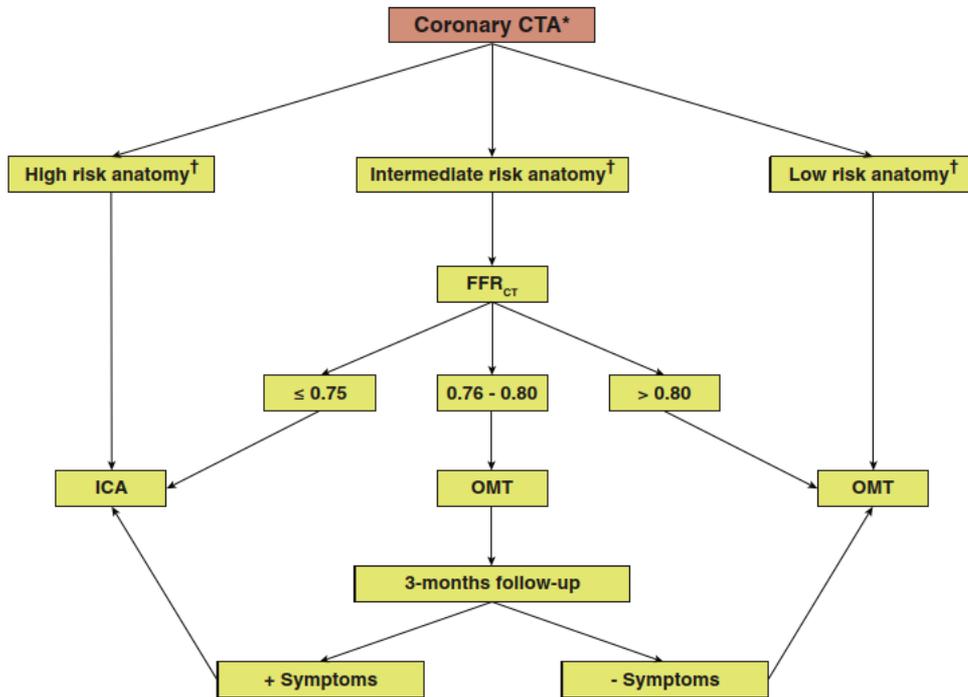
**Figure 2** Determination of the rate of invasive catheterization without obstructive coronary artery disease. NI, non-invasive; ICA, invasive coronary angiography; Obs CAD, obstructive coronary artery disease; FFR<sub>CT</sub>, computation of fractional flow reserve from coronary computed tomographic angiography data.

## Conclusions

Computed tomographic angiography/fractional flow reserve by CTA was a feasible and safe alternative to ICA and was associated with a significantly lower rate of invasive angiography showing no obstructive CAD.

# Decision-Rule Algorithm based on CTCA

FIGURE 6 The "Aarhus" FFR<sub>CT</sub> Decision-Rule Algorithm



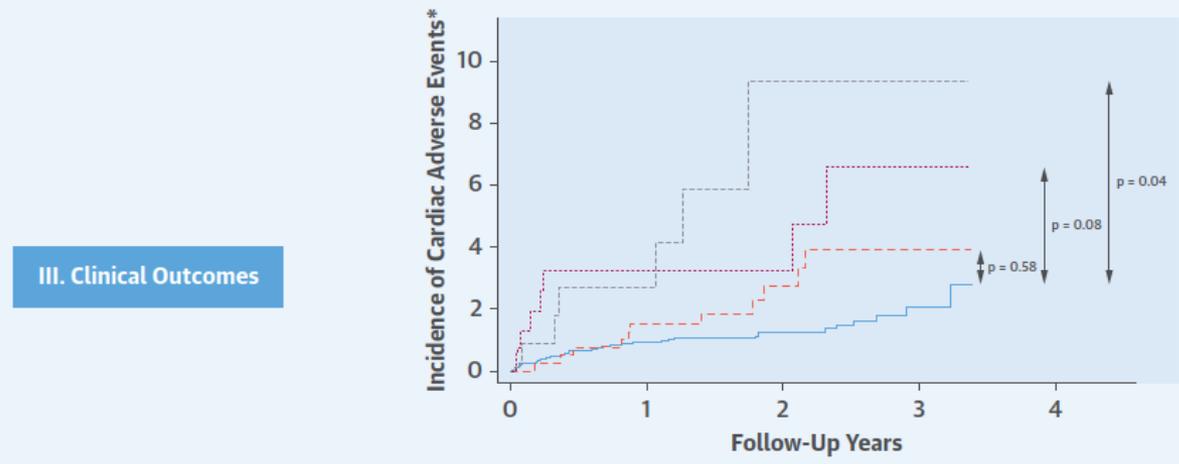
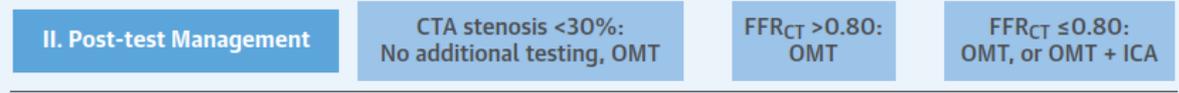
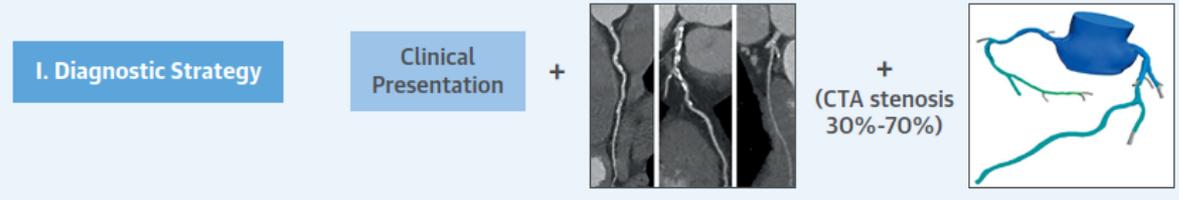
Noorgard BL et al. *J Am Coll Cardiol Img* 2016

\*Patients with new-onset chest pain without known coronary artery disease, low to intermediate pre-test probability of disease, and in whom a diagnostic coronary CTA result can be expected. †"High risk anatomy" is defined as the presence of left main, 3-vessel and/or high-grade left anterior descending artery stenosis; "intermediate risk anatomy" as 1 or 2 intermediate stenoses (30% to 70%); and "low risk anatomy" as normal or stenosis <30%. Abbreviations as in Figures 2 and 4.

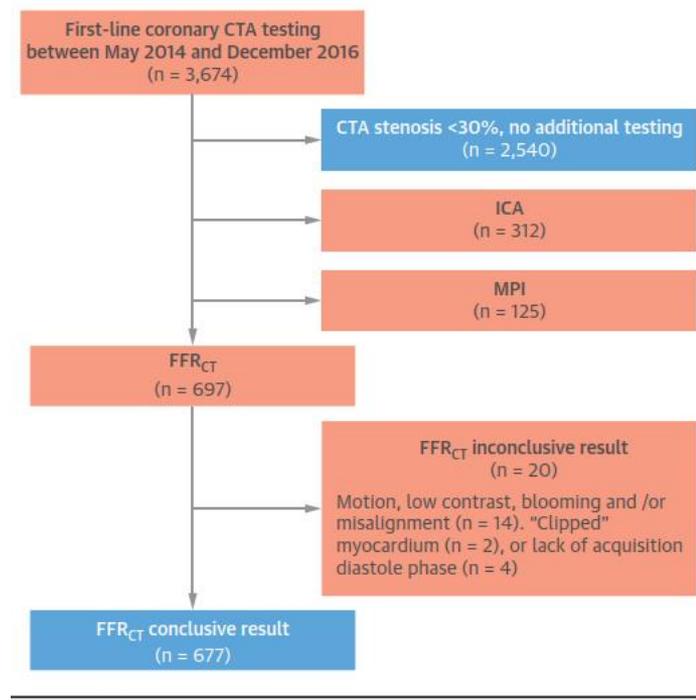
**CONCLUSIONS** FFR<sub>CT</sub> testing is feasible in real-world symptomatic patients with intermediate-range stenosis determined by coronary computed tomography angiography. Implementation of FFR<sub>CT</sub> for clinical decision-making may influence the downstream diagnostic workflow of patients. Patients with an FFR<sub>CT</sub> value >0.80 being deferred from invasive coronary angiography have a favorable short-term prognosis. (*J Am Coll Cardiol Img* 2016; ■:■-■) © 2016 by the American College of Cardiology Foundation.

# Diagnostic and Management Strategy for Suspected CAD: Selective FFR<sub>CT</sub> Testing

**CENTRAL ILLUSTRATION** Diagnostic and Management Strategy With Clinical Outcomes in Patients Undergoing First-Line Coronary Computed Tomography Angiography With Selective FFR<sub>CT</sub> Testing



**FIGURE 2** Flow Chart of Study Patients

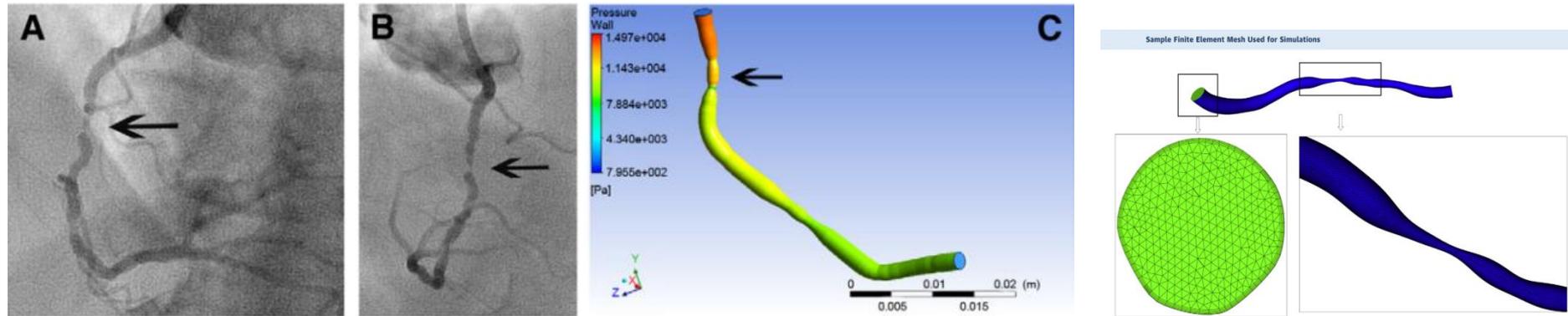


Main study cohorts are presented in **blue boxes**. ICA = invasive coronary angiography; MPI = myocardial perfusion imaging; other abbreviations as in **Figure 1**.

**CONCLUSIONS** In patients with intermediate-range coronary stenosis, FFR<sub>CT</sub> is effective in differentiating patients who do not require further diagnostic testing or intervention (FFR<sub>CT</sub> >0.80) from higher-risk patients (FFR<sub>CT</sub> ≤0.80) in whom further testing with invasive coronary angiography and possibly intervention may be needed. Further studies assessing the risk and optimal management strategy in patients undergoing first-line CTA with selective FFR<sub>CT</sub> testing are needed. (J Am Coll Cardiol 2018;72:2123-34) © 2018 The Authors. Published by Elsevier on behalf of

# Virtual FFR Surrogates From Invasive Angiography

## vFFR



### vFFR (VIRTU-1 and VIRTU-Fast studies)

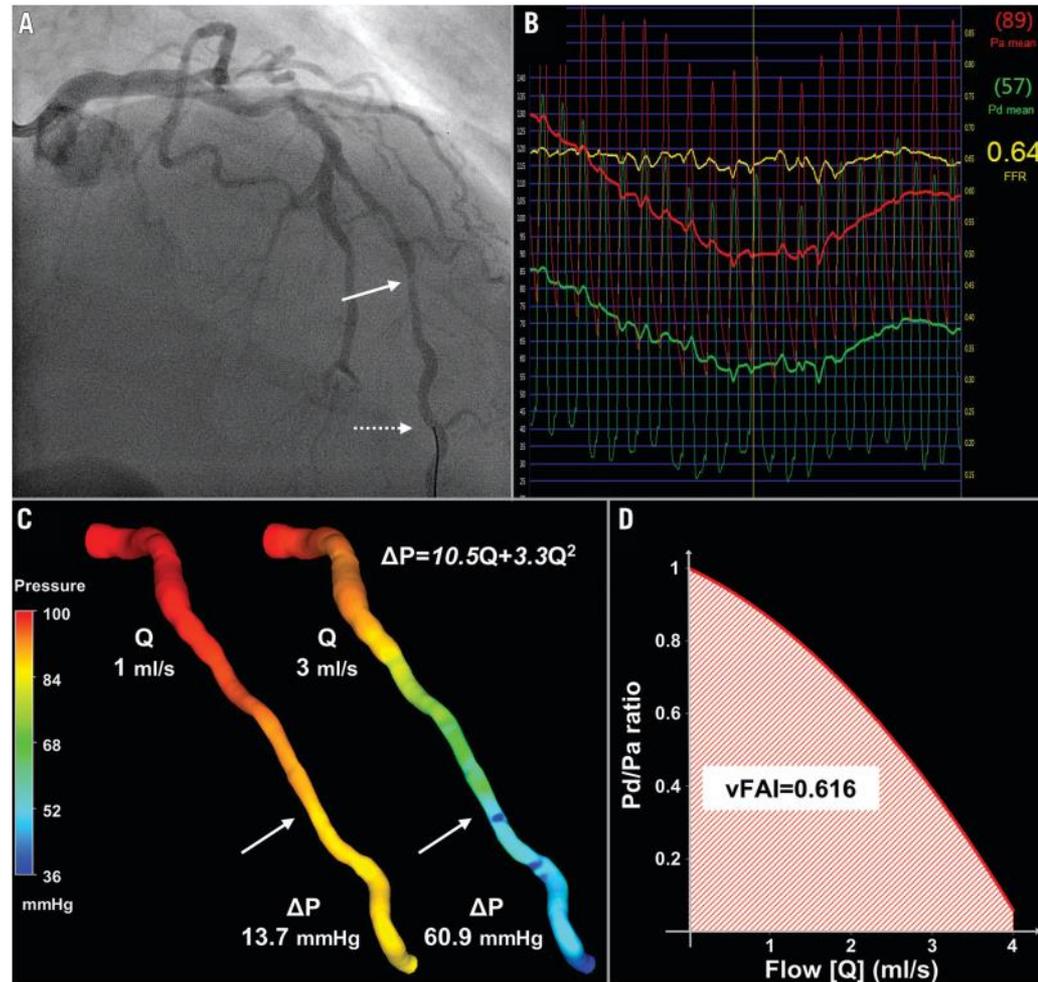
- Early experience in 19 patients
- *Rotational* angiography (3-D geometry)
- Computational fluid dynamics (Navier-Stokes equations of fluid motion)
- Patient-specific Model of microvascular resistance (parameters inferred from invasive measurements)
- >24 hrs can be reduced to <4 min by simplification in the flow simulation

# Virtual FFR Surrogates From Invasive Angiography

## vFAI

### Virtual functional assessment index (vFAI)

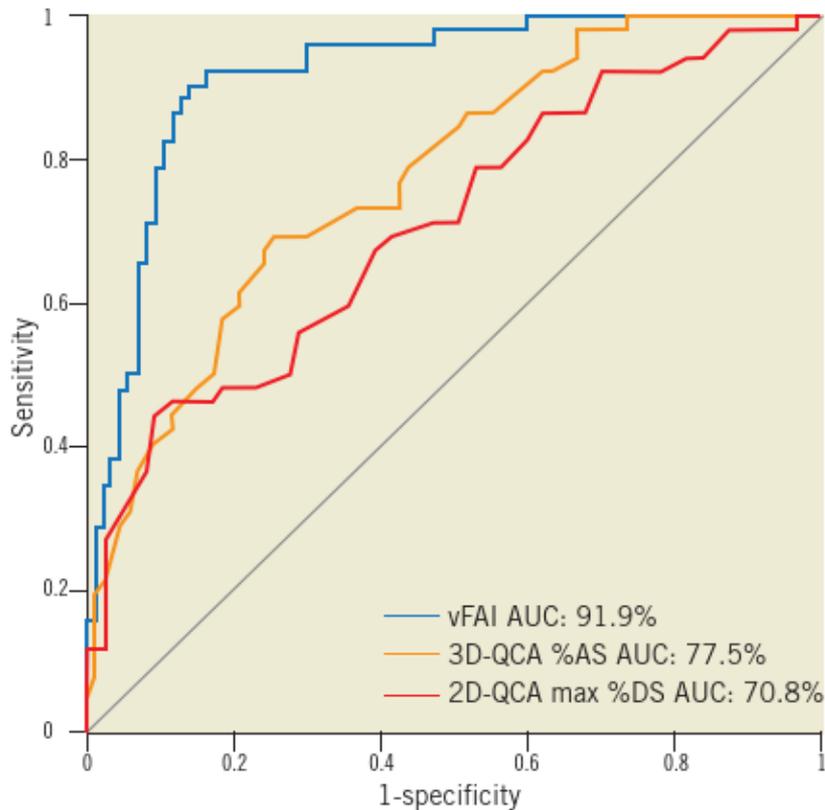
- Validation in 120 patients
- 3-D QCA geometry (routine angiography)
- Navier-Stokes equations of fluid motion
- Generic/universal boundary conditions
  - Quadratic equation for pressure drop across a range of coronary flow values
- Computational time: 7 min



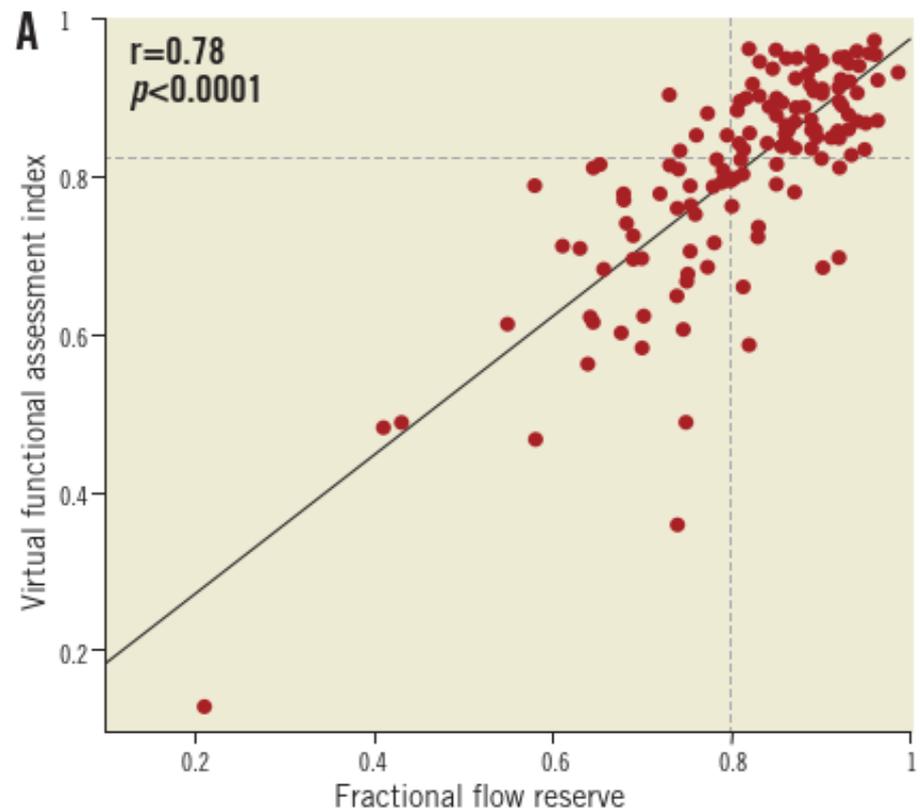
# Virtual FFR Surrogates From Invasive Angiography

## vFAI vs FFR

- High diagnostic performance
- Incremental value to angiography %stenosis (QCA)



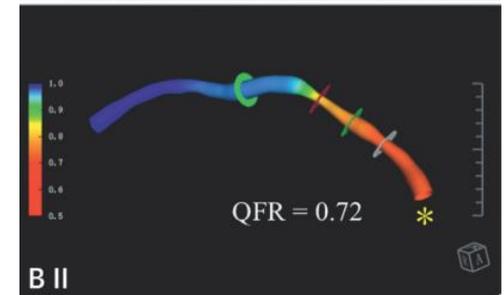
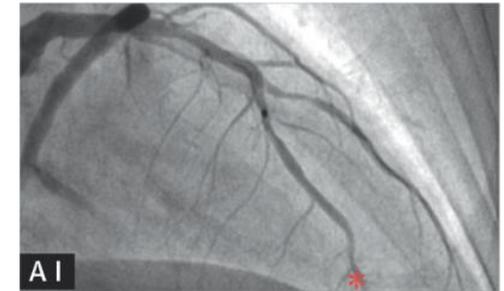
Good correlation to FFR



# QFR From Invasive Angiography

## Quantitative Flow Ratio (QFR)

- 3-D QCA geometry (routine angiography)
- Approximate algebraic method of fluid dynamics: quadratic equation with empirically derived coefficients for pressure drop
- Contrast-flow (cQFR): a hyperaemic flow determined from baseline (resting) conditions (simple frame counting of contrast)
- Time for QFR results: 5 min in online QFR application (FAVOR II Europe-Japan study)



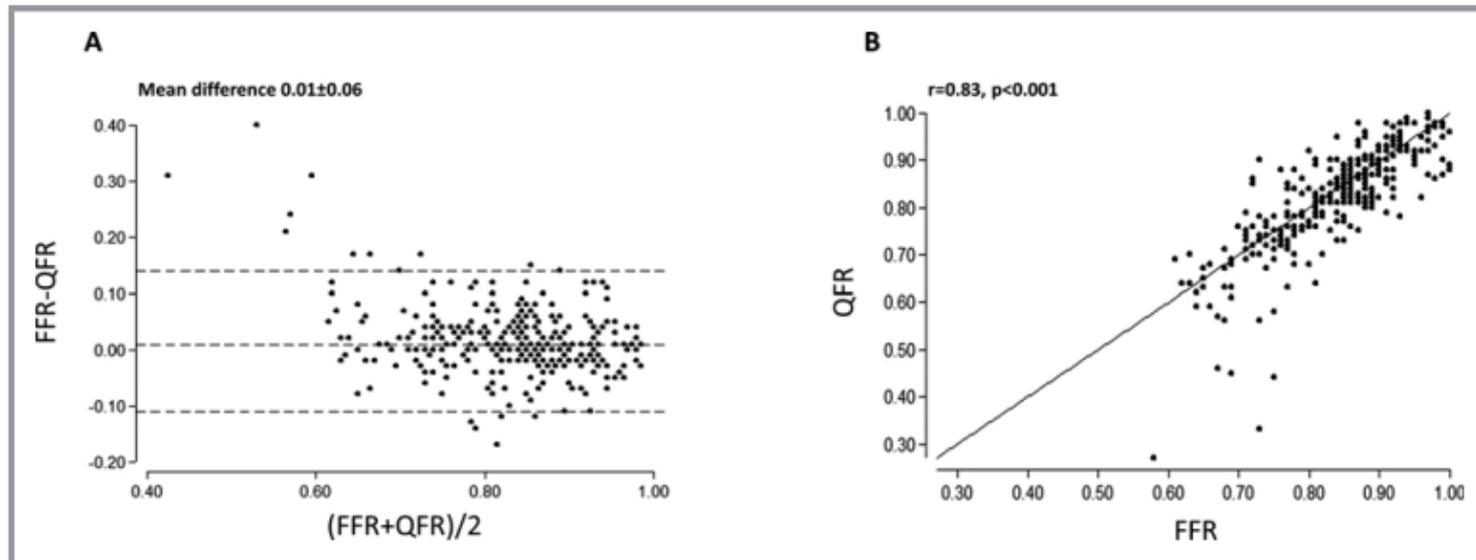
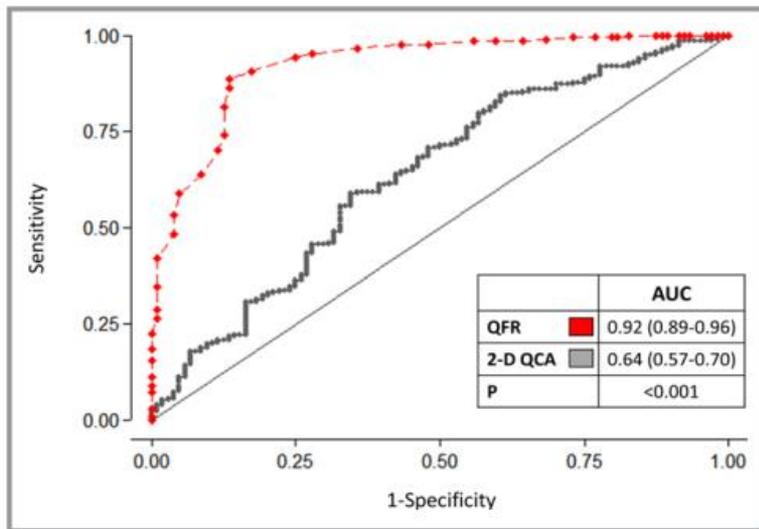
Tu S et al. *JACC Intv* 2016

Xu B et al. *J Am Coll Cardiol* 2017

Westra J et al. *J Am Heart Assoc* 2018

# QFR vs FFR

FAVOR II Europe-Japan study  
329 patients



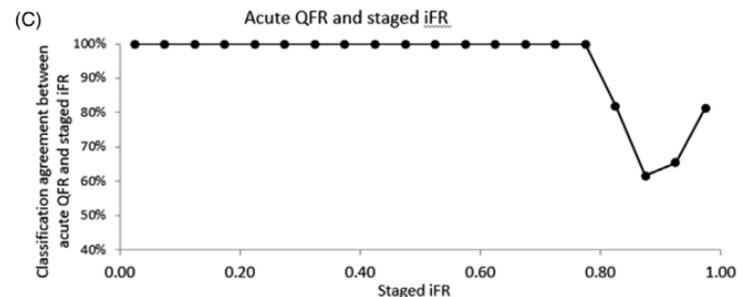
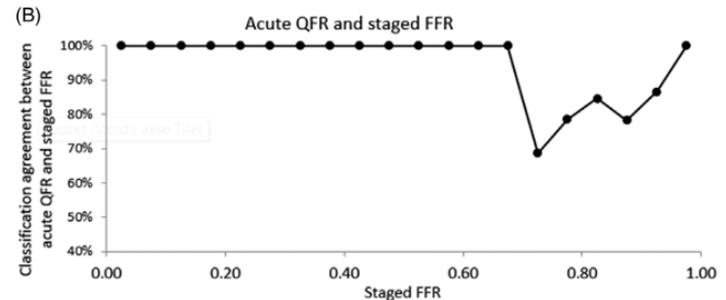
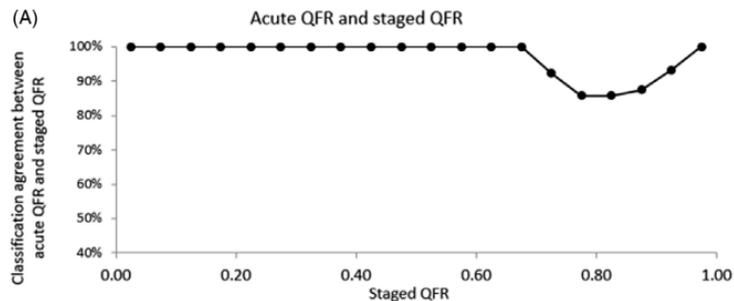
# QFR: Immediate Assessment of NonCulprit Lesions in STEMI

iSTEMI substudy 112 patients (146 lesions)

**TABLE 2** Diagnostic performance of acute phase QFR

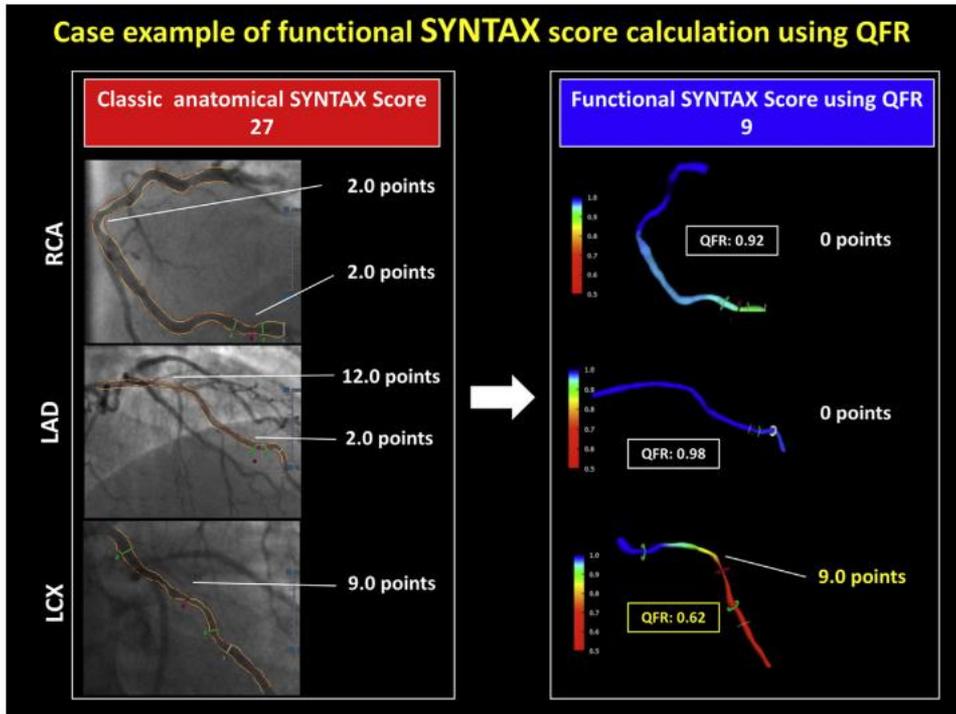
Diagnostic modality	Reference	Classification agreement	Sensitivity	Specificity	PPV	NPV
Acute QFR	Staged QFR	93% (87–99)	92% (78–98)	94% (80–99)	94% (81–99)	91% (76–98)
Acute QFR	Staged FFR	84% (76–90)	83% (69–93)	84% (72–92)	81% (57–92)	86% (76–95)
Acute QFR	Staged iFR	74% (65–83)	73% (58–85)	74% (62–85)	69% (54–81)	78% (66–88)

Diagnostic performance of acute QFR presented as percentage (95% confidence interval) with staged QFR, staged FFR, and staged iFR as references. FFR: fractional flow reserve; iFR: instantaneous wave-free ratio; NPV: negative predictive value; PPV: positive predictive value; QFR: quantitative flow ratio.



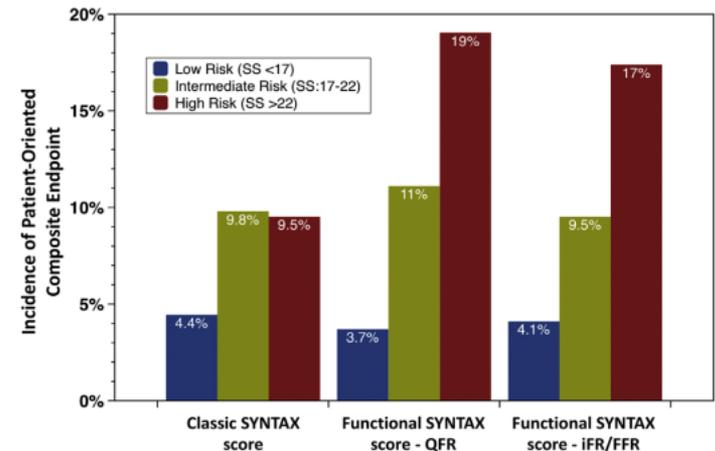
# Functional SYNTAX score using QFR ( $fSS_{QFR}$ )

**FIGURE 4** Representative Case of Functional SYNTAX Score Calculation Derived From Quantitative Flow Ratio



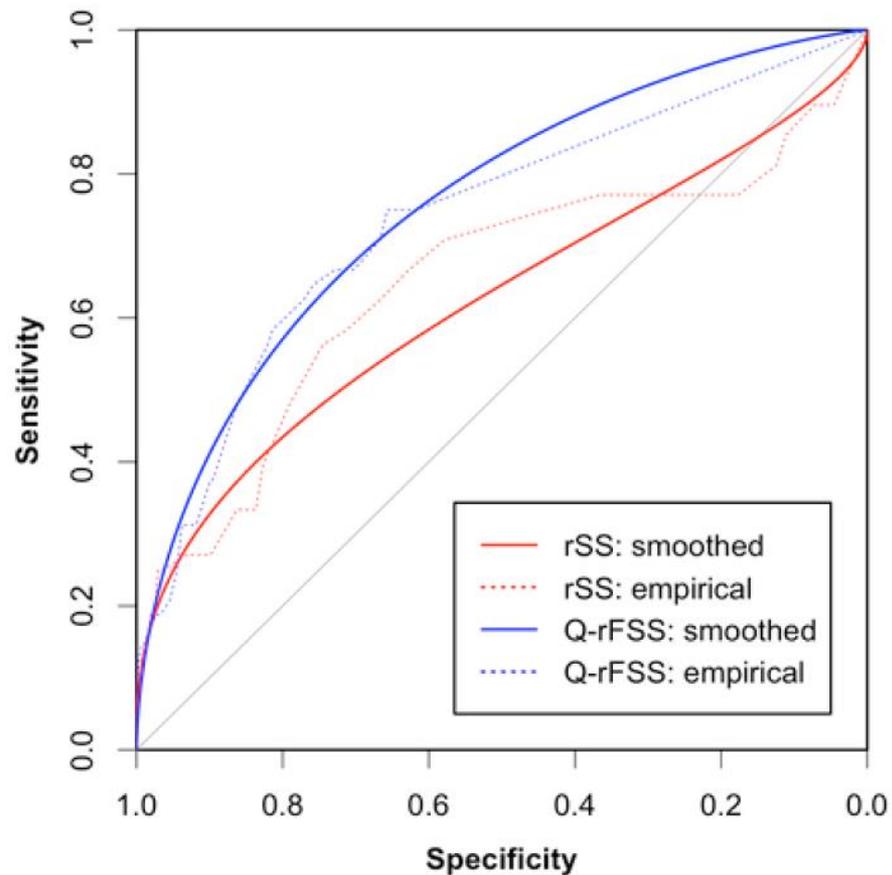
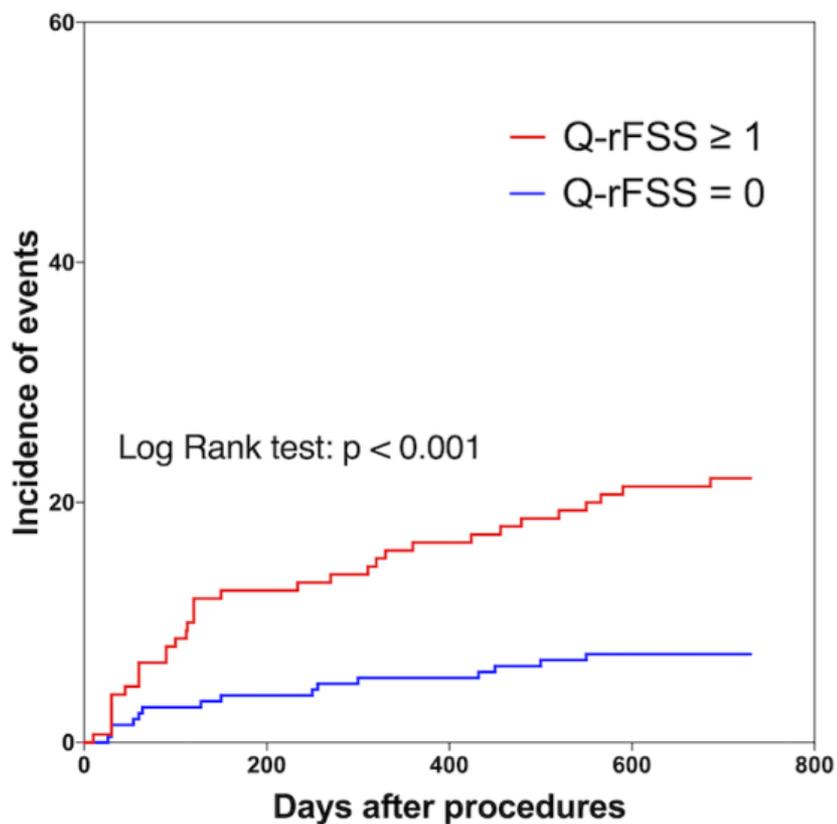
A patient with 3-vessel disease yielded a classic anatomical SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score of 27, which was classified in the high-risk group. In the patient, the functional SYNTAX score derived from quantitative flow ratio (QFR) was as low as 9 (low-risk group) because the functional assessment using QFR revealed that the lesions in the right coronary artery (RCA) and left anterior descending coronary artery (LAD) were not significant.

**FIGURE 6** Incidence of Patient-Oriented Composite Endpoint Stratified According to Classic Anatomic SYNTAX Score, Functional SYNTAX Score Derived From Quantitative Flow Ratio, and Functional SYNTAX Score Derived From Instantaneous Wave-Free Ratio/Fractional Flow Reserve



FFR = fractional flow reserve; iFR = instantaneous wave-free ratio; QFR = quantitative flow ratio, SS = SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score.

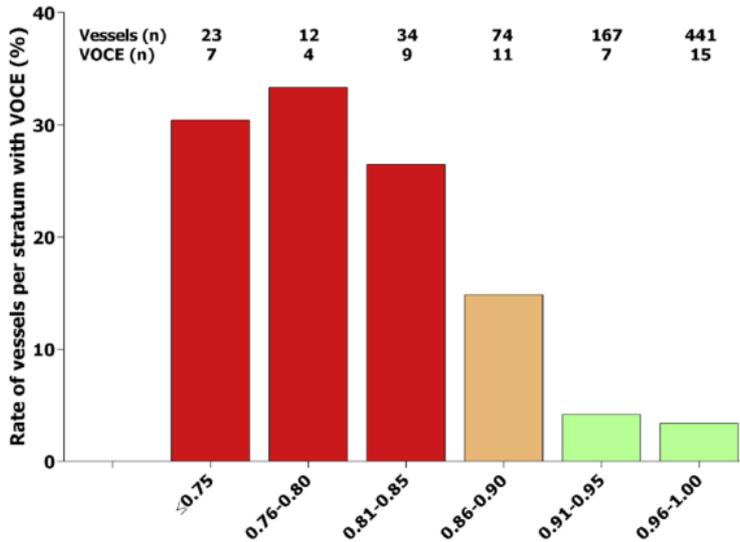
# Residual Functional SYNTAX Score Using QFR (Q-rFSS) After STEMI



# Prognostic value of QFR after Successful PCI

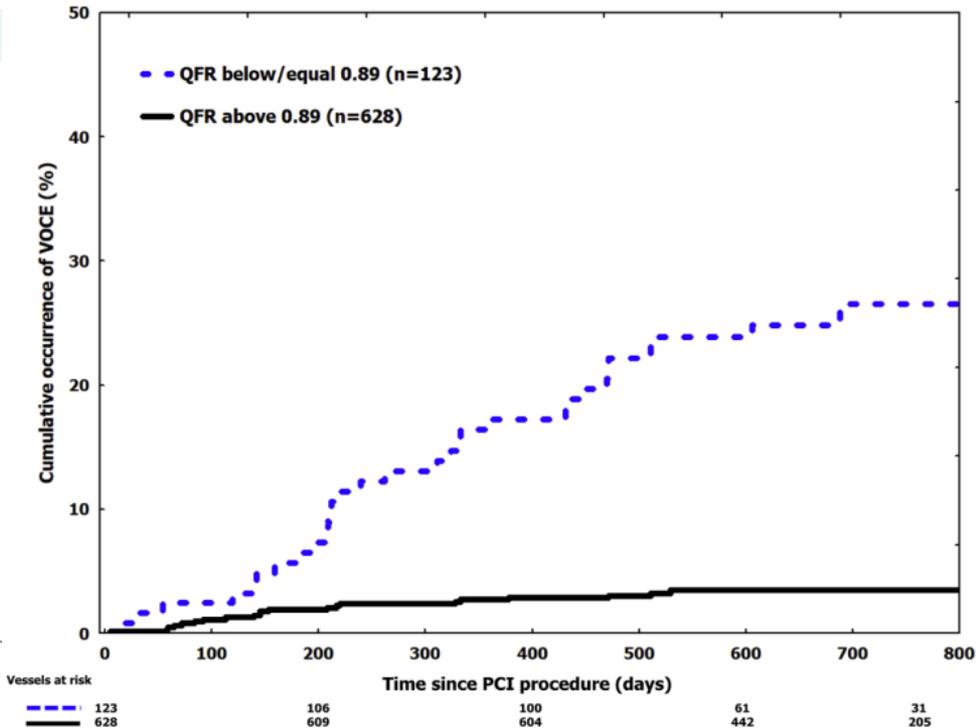
Multicenter HAWKEYE study (602 pts, 751 lesions)

**FIGURE 2** Rate of Vessels With the Vessel-Oriented Composite Endpoint in the Different Post-Percutaneous Coronary Intervention Quantitative Flow Ratio Strata



Colors indicate the distribution according to the best cutoff ( $\leq 0.89$ ) for the prediction of the vessel-oriented composite endpoint (VOCE): **green** for values higher than the cutoff, **orange** for values near the cutoff, and **red** for values less than the cutoff.

**FIGURE 3** Cumulative Occurrence of the Vessel-Oriented Composite Endpoint in Vessels Stratified According to the Best Cutoff



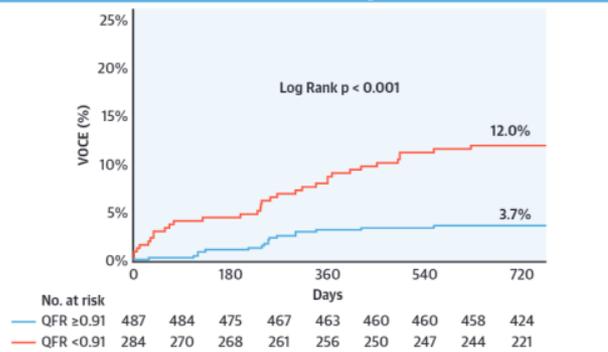
**Black continuous line** = vessels with values of post-percutaneous coronary intervention (PCI) quantitative flow ratio (QFR)  $\leq 0.89$ . **Blue dotted line** = vessels with values  $> 0.89$ . The cutoff of 0.89 was obtained by receiver-operating characteristic curve analysis for the best prediction of the vessel-oriented cardiac endpoint (VOCE).

# Prognostic value of QFR after Successful PCI

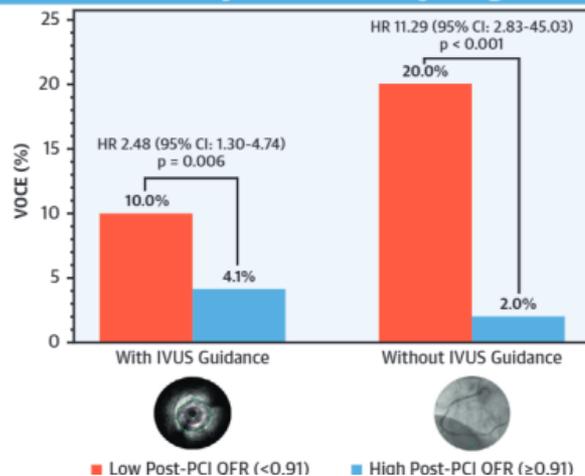
SYNTAX II substudy (all vessels treated with PCI)

**CENTRAL ILLUSTRATION** Relationship Between a Low Post-PCI QFR (<0.91) and 2-Year Composite Clinical Endpoints at the Vessel and Patient Level

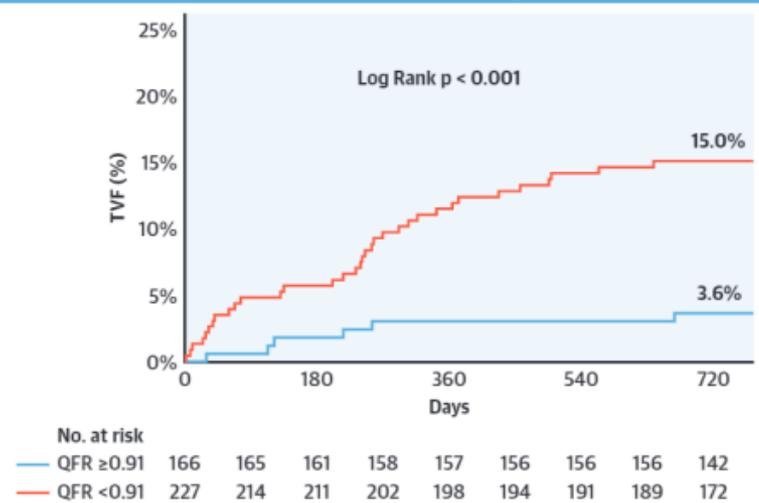
## A Vessel Level Analysis



## B Vessel Level Analysis Stratified by Usage of IVUS



## C Patient Level Analysis

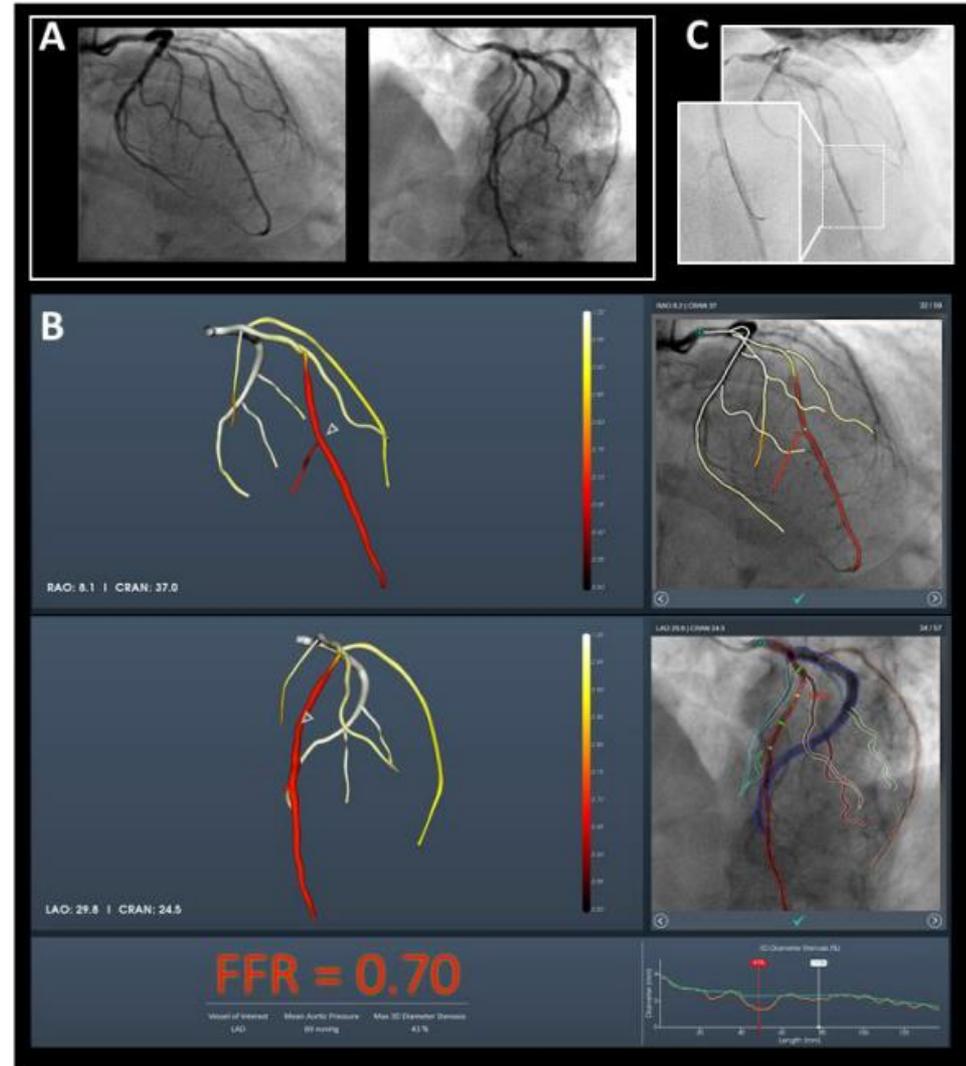


# Virtual FFR Surrogates From Invasive Angiography

FFR<sub>angio</sub>

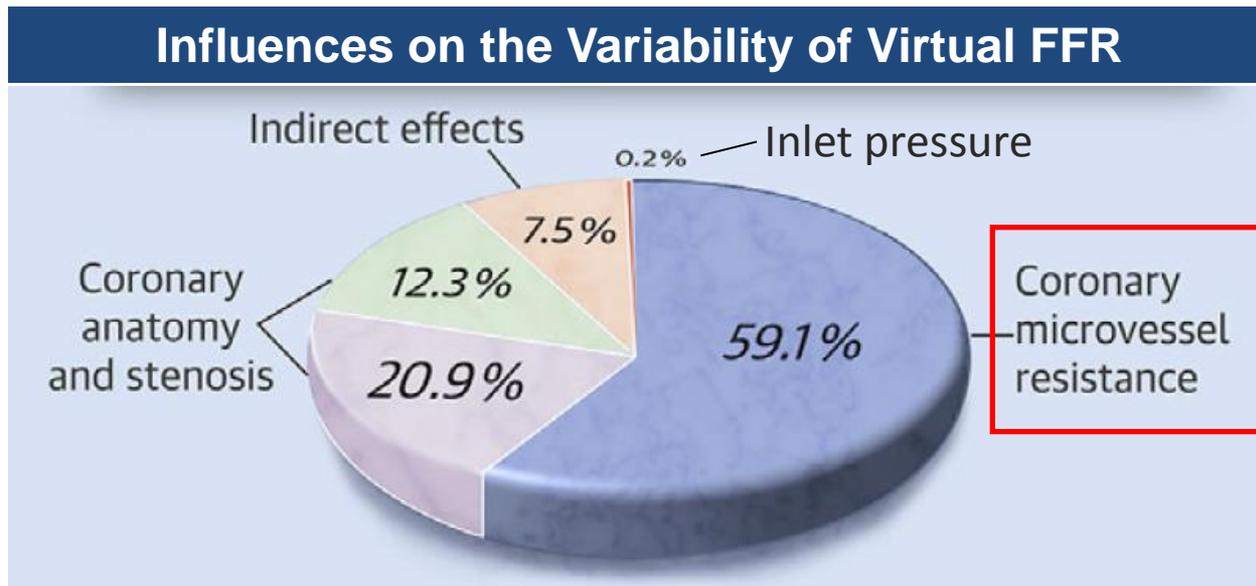
## FFR<sub>angio</sub> tool

- Accuracy studied in 301 patients
- Allows the simulation of FFR in the entire coronary tree including side branches
- Diagnostic accuracy 92%



# Functional Angiography: Challenges

- Time required for the analysis
- Ability of techniques to realistically simulate the *in vivo* conditions
  - Anatomic accuracy of the 3-D coronary and lesion geometry
  - “Physiologic” accuracy of the model computing the virtual index: use of physiological parameters – application of boundary conditions



# Take-home Messages

- Fractional Flow Reserve
  - Gold standard for invasive functional assessment
  - BUT the adoption of FFR in catheter laboratories remains low
- Instantaneous Wave-Free Ratio (iFR)
  - Large body of clinical studies and available randomized data showing non-inferiority in MACE – Adoption in Current Guidelines
- Functional Angiography
  - Can provide an *option without using pressure wires and adenosine*
  - **Opportunity to increase coronary physiology assessment in patients**
  - **FFR-CT** could play an important role as gate-keeper for coronary catheterisation
  - **FFR based on Invasive Angiography** is feasible and provides an *approximation* to wire-FFR with good diagnostic performance
  - ***Need for randomised clinical trials of angio-based FFR and patient outcomes***



Επιστημονική Εκδήλωση

# Σεμινάριο Επιστημονικών Ενώσεων Ελληνικού Κολλεγίου Καρδιολογίας



ΕΛΛΗΝΙΚΟ ΚΟΛΛΕΓΙΟ  
ΚΑΡΔΙΟΛΟΓΙΑΣ

22-23

Νοεμβρίου 2019

Συνεδριακό Κέντρο Διάσελο

Μέτσοβο

