Now *iFR* could be first pick for physiologic decision in *LAD* stenosis

- Pros -

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What is so special of *physiologic decision for the LAD*

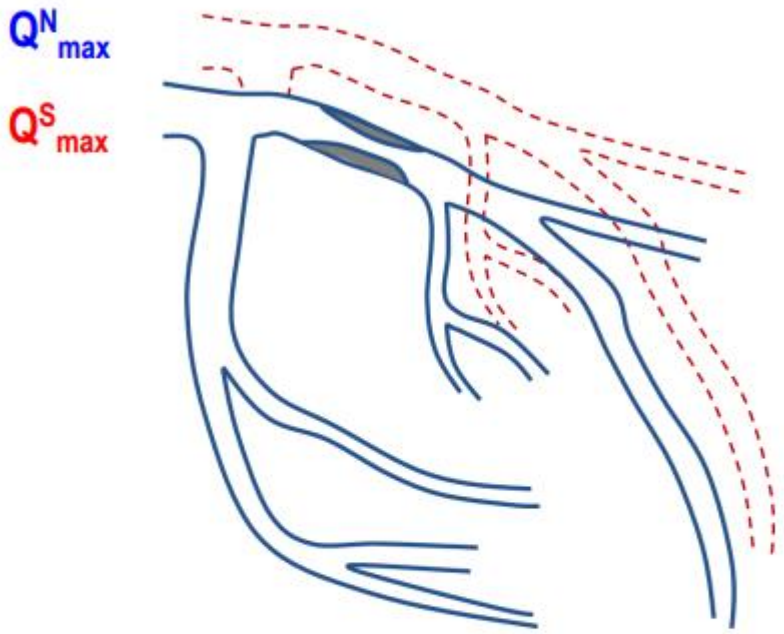
- ✓ The principle of physiologic guidance of revascularization is to identify which deferral is ***safe***.
  - ✓ Safety is more important in intervention

- ✓ The ***LAD*** supplies the most-largest territory of the myocardium
  - ✓ Leaving substantial results and cost-effectiveness of ***intervention or not***
  - ✓ More accurate measurement is needed for the LAD

- ✓ The LAD flow is more dependent on the diastolic phase (wave free period)

FFR vs. iFR

Fractional Flow Reserve (FFR)

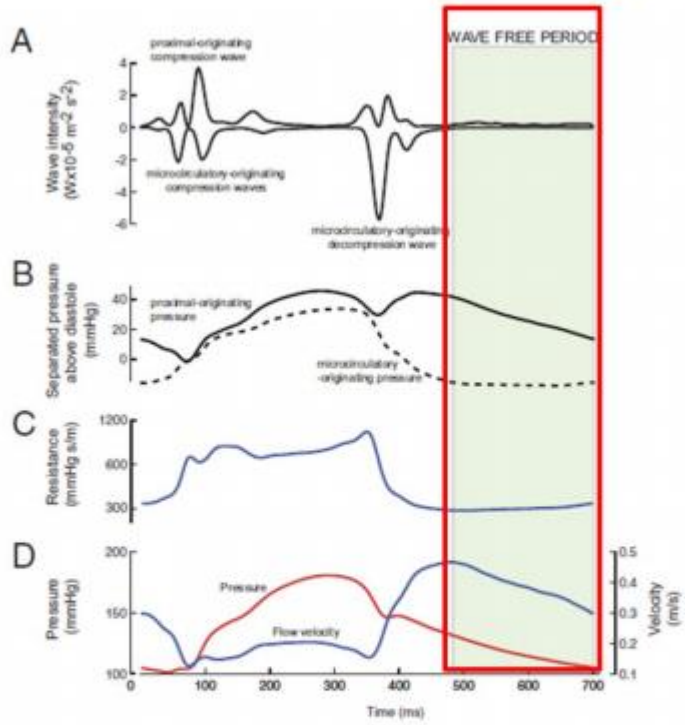


$$FFR = \frac{\text{Maximum flow in presence of stenosis}}{\text{Normal maximum flow}} = \frac{Q^S_{max}}{Q^N_{max}}$$

$$= \frac{(Pd-Pv)/R}{(Pa-Pv)/R} = \frac{\text{Distal Pr } (P_d)}{\text{Proximal Pr } (P_a)}$$

Under Maximal Hyperemia

Instantaneous Wave-Free Ratio (iFR)



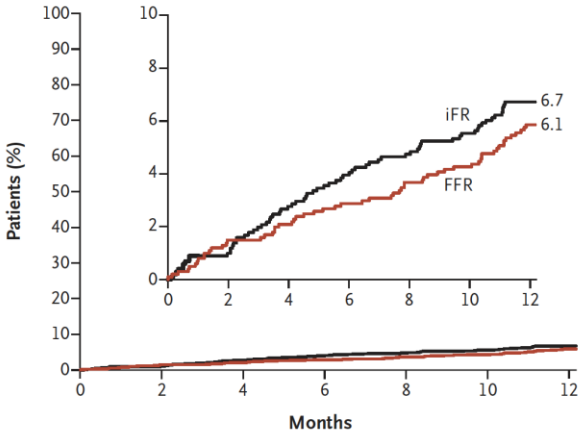
$$iFR = \frac{\text{Distal Pr } (P_d) \text{ under wave free period}}{\text{Proximal Pr } (P_a) \text{ under wave free period}}$$

Under Resting Status

Courtesy of JM Lee

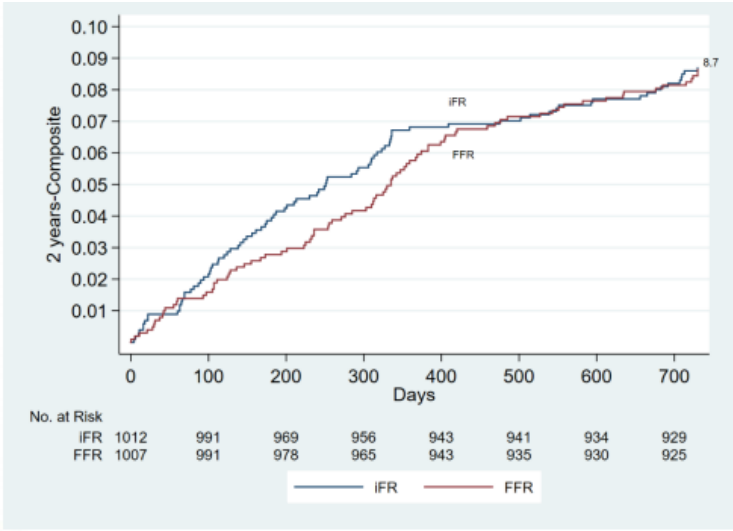
Outcome Data From the DEFINE-FLAIR and Swedeheart

iFR Swedeheart

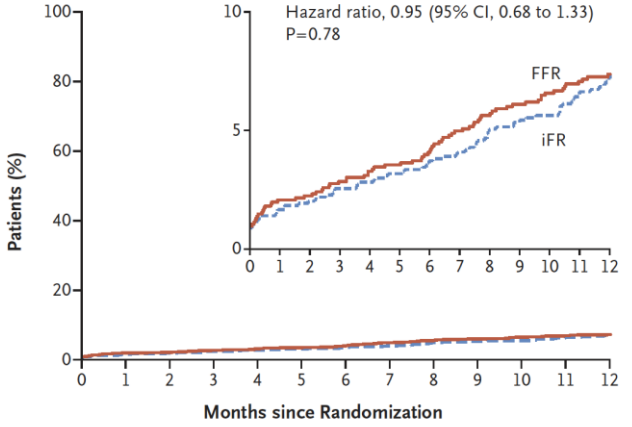


No. at Risk

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

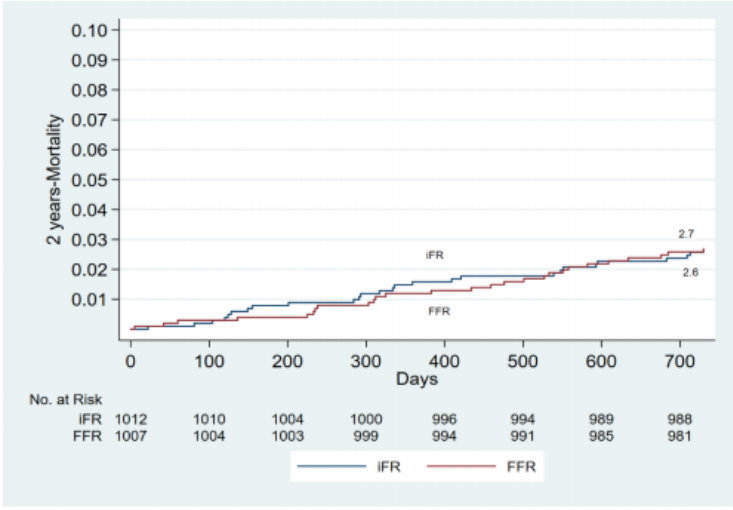


DEFINE FLAIR



No. at Risk

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



Gotberg et al., NEJM 2017, Davis et al., NEJM 2017, Götberg, et al, TCT 2018

FFR vs. iFR

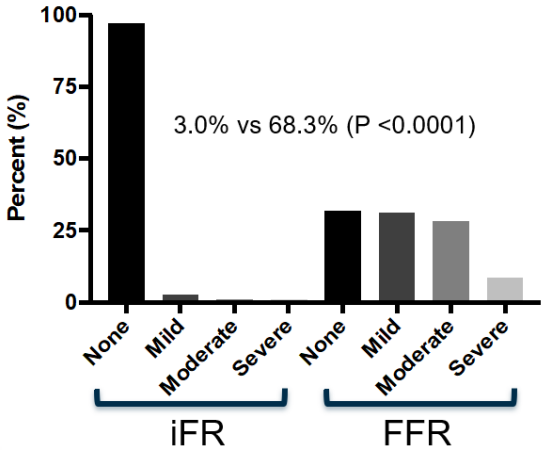
Recommendations	Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.[15,17,18,39]	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI.[29,31]	IIa	B

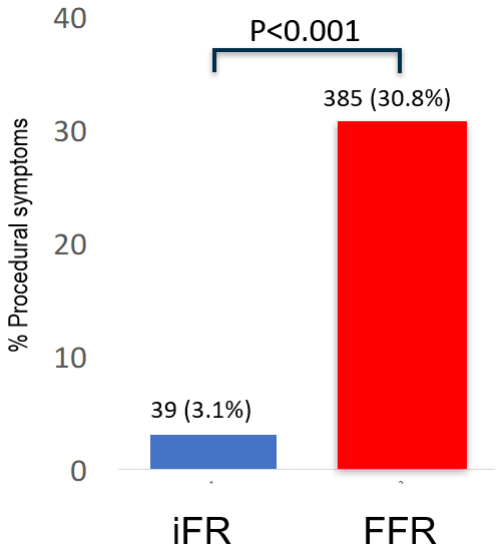
2018 ESC/EACTS Guidelines on myocardial revascularization

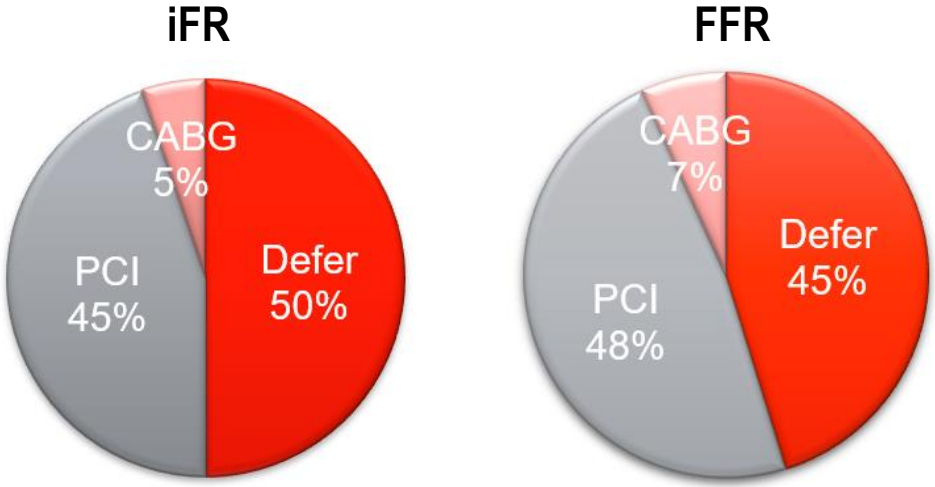
iFR could be first pick for physiologic decision in *LAD* stenosis because….

1) iFR is more sensitive to select those who may not need intervention, in the vulnerable LAD

Outcome Data From the DEFINE-FLAIR and Swedeheart







- ✓ Less chest discomfort by iFR measurement.
- ✓ More deferral by iFR measurement
- ✓ With…..Similar outcomes

Gotberg et al., NEJM 2017, Davis et al., NEJM 2017

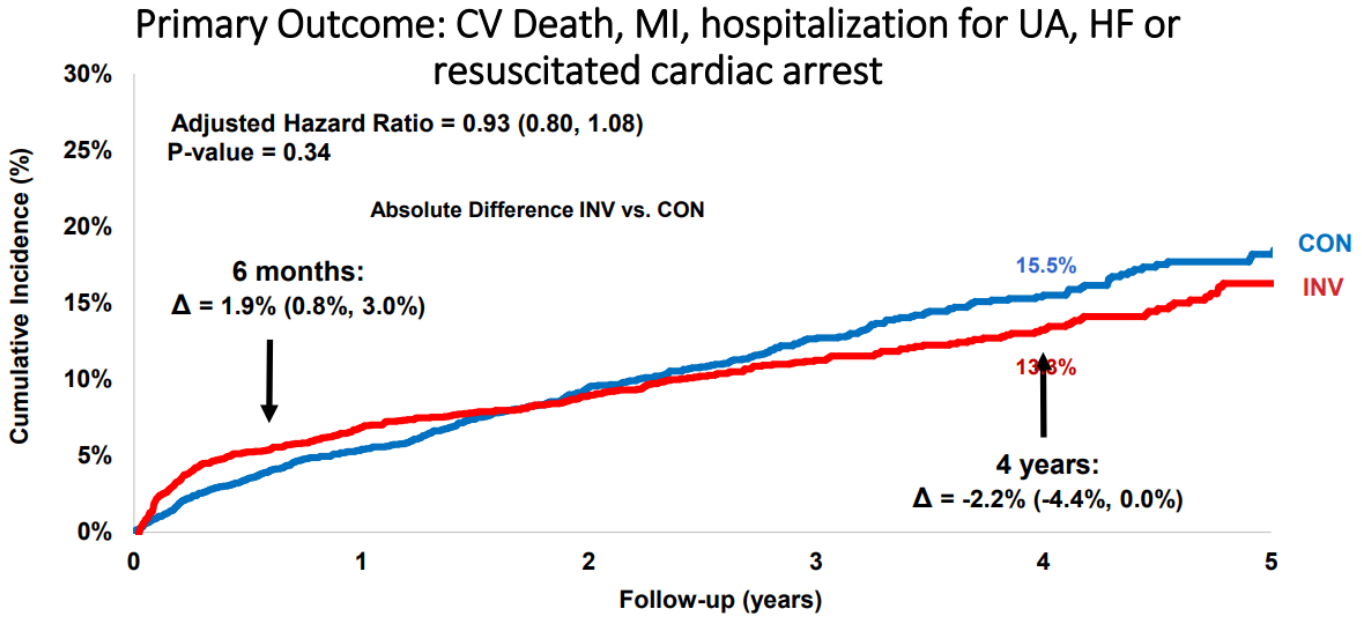
Less intervention = Medical treatment only

ISCHEMIA

International Study Of Comparative Health Effectiveness With Medical And Invasive Approaches (ISCHEMIA):

Inclusion Criteria

- Age ≥21 years
- Moderate or severe ischemia*
  - Nuclear ≥10% LV ischemia (summed difference score ≥7)
  - Echo ≥3 segments stress-induced moderate or severe hypokinesis, or akinesis
  - CMR
    - Perfusion: ≥12% myocardium ischemic, and/or
    - Wall motion: ≥3/16 segments with stress-induced severe hypokinesis or akinesis
  - Exercise Tolerance Testing (ETT) ≥1.5mm ST depression in ≥2 leads or ≥2mm ST depression in single lead at <7 METS, with angina



ISCHEMIA

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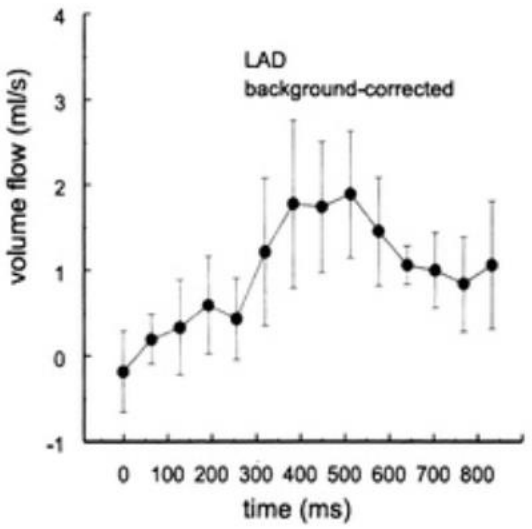
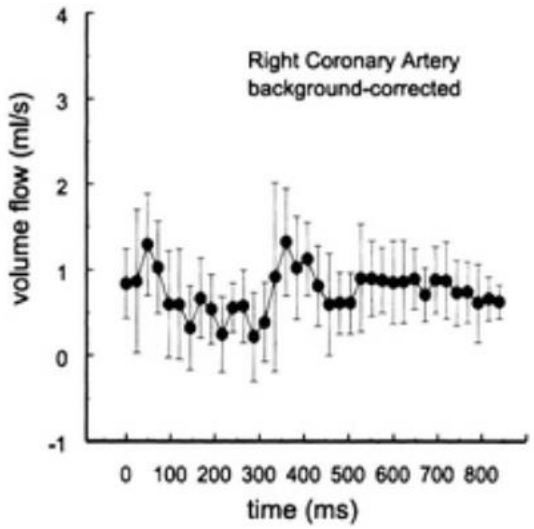
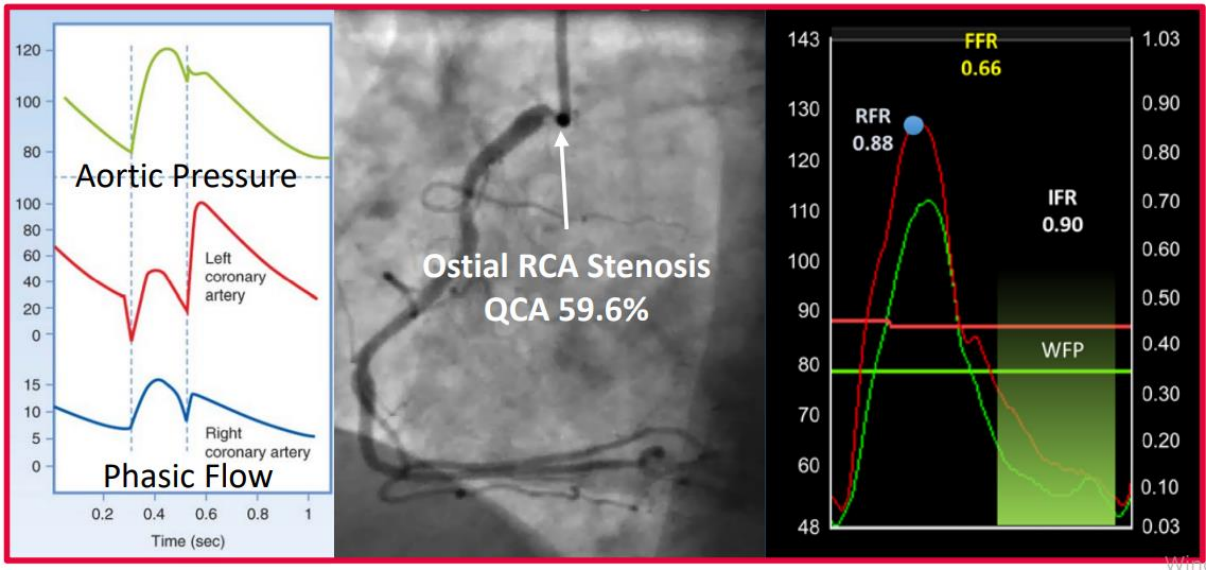
1) iFR is more sensitive to select those who may not need intervention, in the vulnerable LAD

2) The concept of iFR is more logic in assessment of the LAD

Coronary flow of the LAD

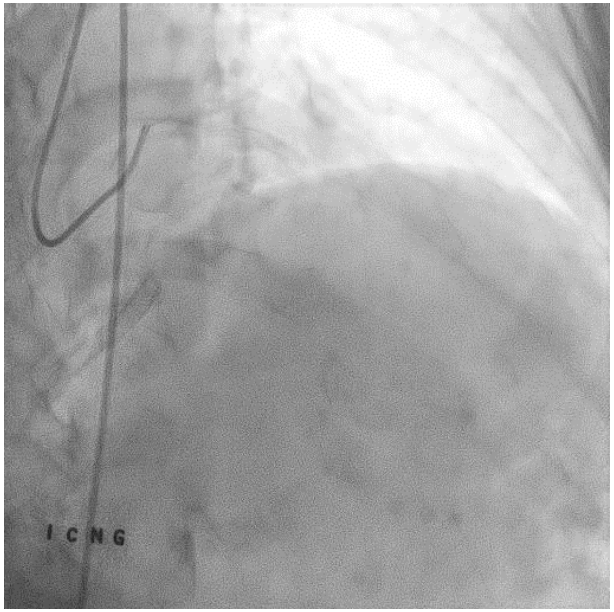


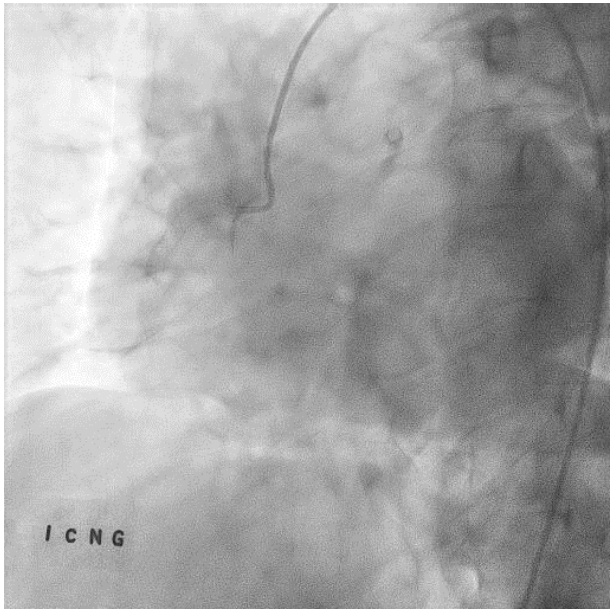


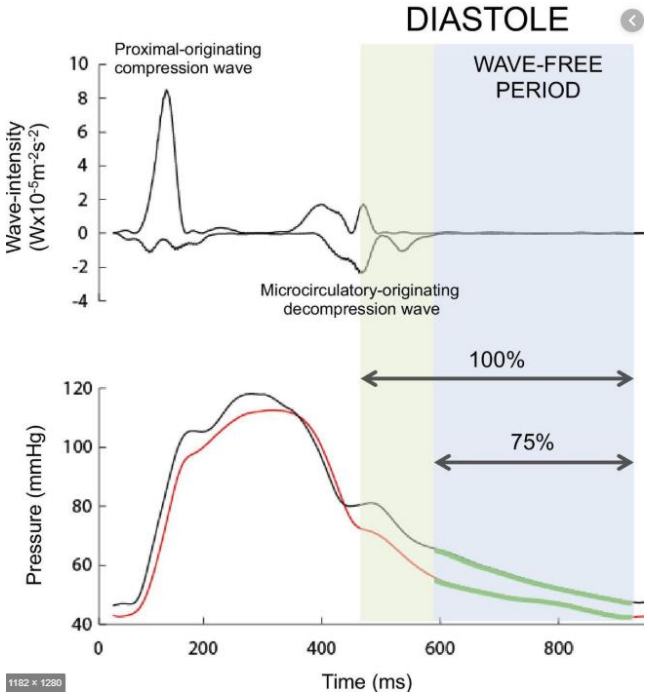


Marcus JT et al., J Comput Assist Tomogr. 1999

Coronary flow of the LAD







- ✓ The diastolic dependent flow in the LAD
- ✓ Technically, more simple to measure, with no worry of overestimation (vs. FFR)

Marcus JT et al., J Comput Assist Tomogr. 1999

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for physiologic decision in _LAD_ stenosis because….

1) iFR is more sensitive to select those who may not need intervention, in the vulnerable LAD

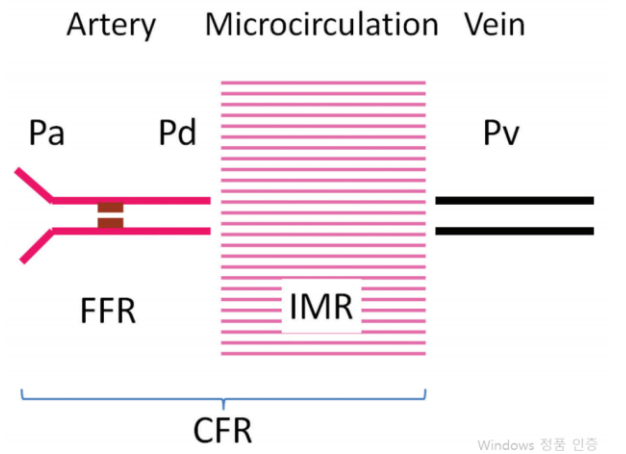
2) The concept of iFR is more logic in assessment of the LAD

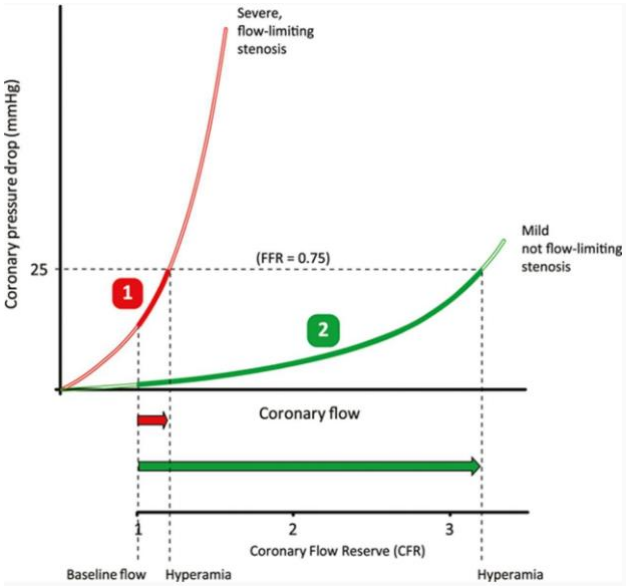
3) iFR is more correlated to the “ULTIMATE” CFR.

Coronary flow reserve

- ✓ Coronary flow reserve (CFR) can identify patients with myocardial blood flow impairment, predict prognosis, and stratify which lesions may benefit from revascularization.
  - ✓ CFR has been largely replaced by FFR
  - ✓ Both indexes need hyperemic blood flow, which may lead to mis-interpretation

- ✓ Upto 30% of cases FFR conflicts with direct measurement of CFR.
  - ✓ Hyperemia in significant epicardial stenosis
  - ✓ Hyperemia in microvascular disease





Johnson NP et al. JACC Cardiovasc Imaging. 2012 Petraco R et al., Circ Cardiovasc Interv. 2014

Coronary flow reserve

Physiological Basis and Long-Term Clinical Outcome of Discordance Between Fractional Flow Reserve and Coronary Flow Velocity Reserve in Coronary Stenoses of Intermediate Severity

Tim P. van de Hoef, MD; Martijn A. van Lavieren, MSc; Peter Damman, MD, PhD; Ronak Delewi, MD; Martijn A. Piek; Steven A.J. Chamuleau, MD, PhD; Michiel Voskuil, MD, PhD; José P.S. Henriques, MD, PhD; Karel T. Koch, MD, PhD; Robbert J. de Winter, MD, PhD; Jos A.E. Spaan, PhD; Maria Siebes, PhD; Jan G.P. Tijssen, PhD; Martijn Meuwissen, MD, PhD; Jan J. Piek, MD, PhD

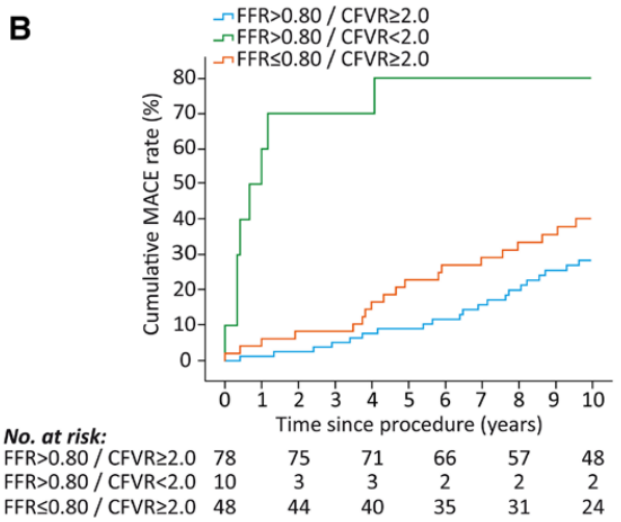


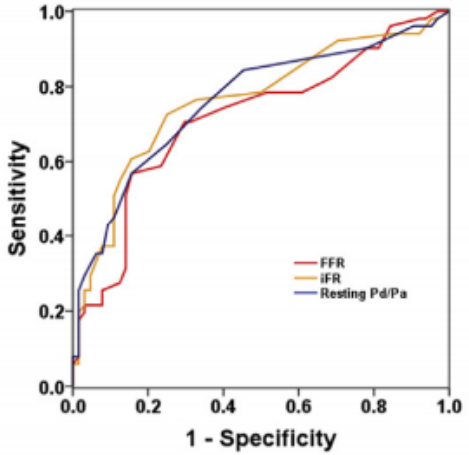
Table 5. Cumulative Major Adverse Cardiac Event Rate at 1, 3, 5, and 10 Years of Follow-Up Stratified by the Specific Accordance and Discordance Groups According to the 0.80 FFR Cut-Off Value

				Concordant Normal vs FFR >0.80 CFVR <2.0		Concordant Normal vs FFR ≤0.80 CFVR ≥2.0		FFR >0.80 CFVR <2.0 vs FFR ≤0.80 CFVR ≥2.0	
FFR 0.80 Cut-Off*	FFR >0.80 CFVR ≥2.0	FFR >0.80 CFVR <2.0	FFR ≤0.80 CFVR ≥2.0	Relative Risk†	*P* Value‡	Relative Risk†	*P* Value‡	Relative Risk†	*P* Value‡
1-year follow-up MACE	1%	60%	6%	46.2 (6.1–349.4)	<0.001	4.9 (0.5–45.6)	0.124	9.5 (2.9–31.7)	<0.001
3-year follow-up MACE	5%	70%	8%	13.5 (4.8–37.6)	<0.001	1.6 (0.4–6.1)	0.465	8.4 (3.0–23.6)	<0.001
5-year follow-up MACE	9%	80%	23%	8.8 (4.1–19.1)	<0.001	2.5 (1.0–6.1)	0.035	3.5 (1.9–6.4)	<0.001
10-year follow-up MACE	28%	80%	40%	2.8 (1.8–4.6)	<0.001	1.4 (0.9–2.4)	0.130	2.0 (1.3–3.2)	<0.001

van de Hoef et al., Circ Cardiovasc Interv. 2014

Coronary flow reserve

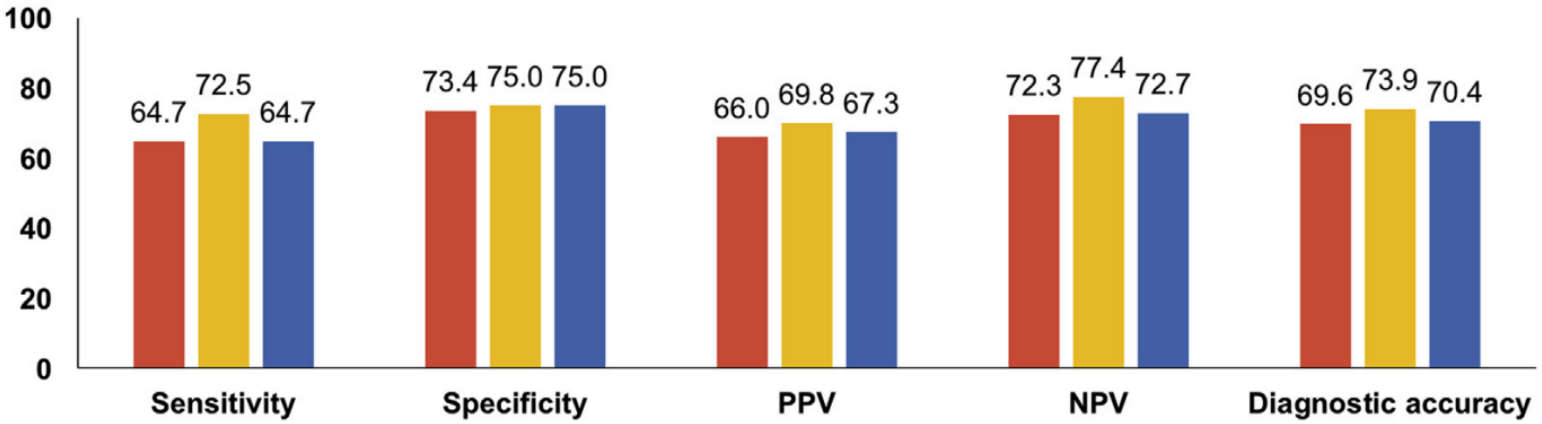
PET-derived CFR<2.0 as a reference standard



	AUC	95% CI	p value
FFR	0.716	0.619-0.813	<0.001
iFR	0.762	0.671-0.854	<0.001
Resting Pd/Pa	0.761	0.670-0.852	<0.001

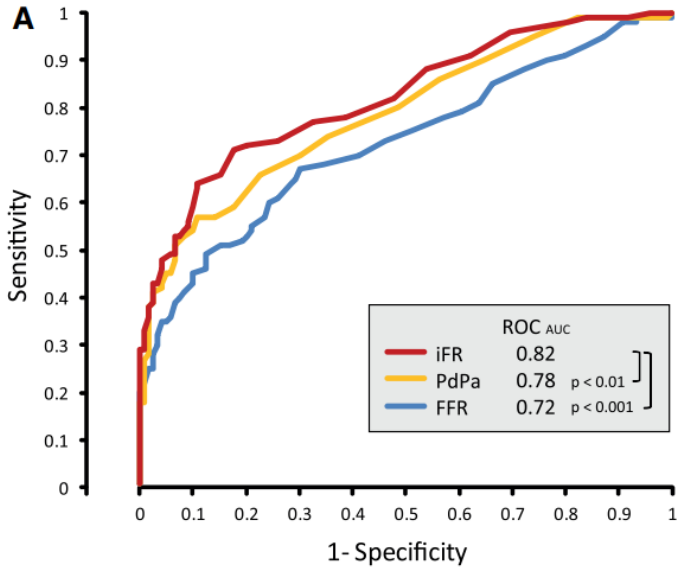
Reference	Testing	Difference between areas	p value
iFR	FFR	0.046	0.133
Resting Pd/Pa		0.045	0.183
iFR	Resting Pd/Pa	0.001	0.932

PET-derived CFR<2.0 as a reference standard



D Hwang et al., J Am Coll Cardiol Intv 2017

Coronary flow reserve



Diagnostic performance of FFR and iFR	FFR	iFR
Cut-off*	0.8	0.89
Diagnostic accuracy	67%	74%
Sensitivity	68%	73%
Specificity	66%	74%
PPV	62%	70%
NPV	72%	77%

* Cut-off: Highest sum of sensitivity and specificity to match a CFVR of 2.0

Table 2. Diagnostic Agreement Between Pressure-Only Indices and Different Cutoffs of Coronary Flow Velocity Reserve

	Whole Sample (186 Patients; 216 Observations)			0.6–0.9 FFR Range (113 Patients; 129 Observations)		
CFR Cutoff	iFR AUC	FFR AUC	*P* Value	iFR AUC	FFR AUC	*P* Value
1.7	0.89 (0.84–0.93)	0.80 (0.73–0.87)	<0.001	0.86 (0.79–0.93)	0.67 (0.56–0.77)	<0.001
2.0	0.82 (0.76–0.88)	0.72 (0.65–0.79)	<0.001	0.78 (0.69–0.86)	0.59 (0.48–0.69)	<0.001
2.5	0.79 (0.74–0.85)	0.71 (0.64–0.78)	0.002	0.74 (0.65,0.83)	0.55 (0.45–0.66)	<0.001
3.0	0.77 (0.70–0.84)	0.69 (0.59–0.79)	0.057	0.76 (0.67–0.86)	0.54 (0.42–0.67)	<0.001

Petraco R et al., Circ Cardiovasc Interv. 2014

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1) iFR is more sensitive to select those who may not need intervention, in the vulnerable LAD

2) The concept of iFR is more logic in the vulnerable LAD

3) More correlated to the ULTIMATE CFR.

AND..the following report

A recent report

✓ iFR vs. FFR for the ***LAD***

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 73, NO. 4, 2019

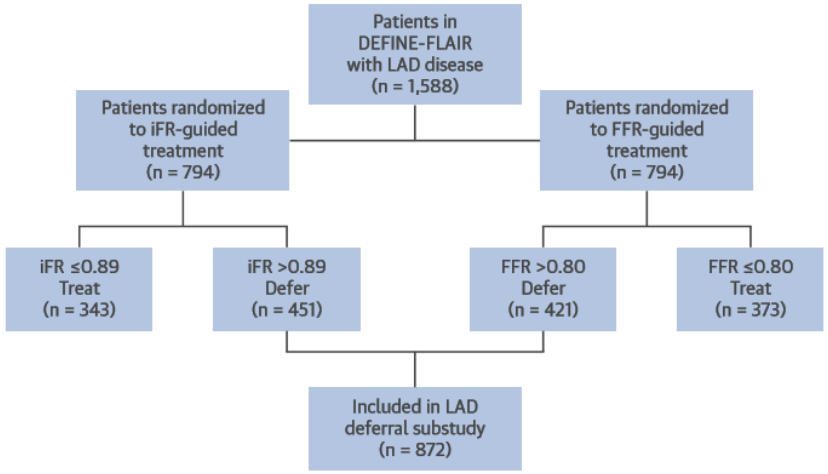
Clinical Events After Deferral of LAD Revascularization Following Physiological Coronary Assessment

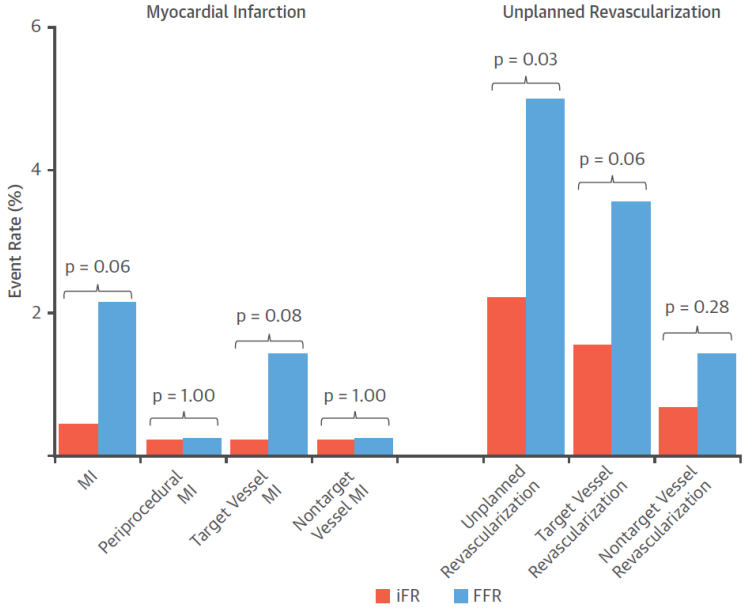
Sayan Sen, PhD,[a] Yousif Ahmad, MD,[a] Hakim-Moulay Dehbi, PhD,[b] James P. Howard, MD,[a] Juan F. Iglesias, MD,[c] Rasha Al-Lamee, MD,[a] Ricardo Petraco, PhD,[a] Sukhjinder Nijjer, PhD,[a] Ravinay Bhindi, PhD,[d] Sam Lehman, PhD,[e] Darren Walters, MD,[f] James Sapontis, MD,[g] Luc Janssens, MD,[h] Christiaan J. Vrints, PhD,[i] Ahmed Khashaba, MD,[j] Mika Laine, PhD,[k] Eric Van Belle, PhD,[l] Florian Krackhardt, MD,[m] Waldemar Bojara, MD,[n] Olaf Going, MD,[o] Tobias Härle, MD,[p] Ciro Indolfi, MD,[q] Giampaolo Niccoli, PhD,[r] Flavio Ribichini, MD,[s] Nobuhiro Tanaka, PhD,[t] Hiroyoshi Yokoi, MD,[u] Hiroaki Takashima, PhD,[v] Yuetsu Kikuta, MD,[w] Andrejs Erglis, PhD,[x] Hugo Vinhas, MD,[y] Pedro Canas Silva, MD,[z] Sérgio B. Baptista, MD,[aa] Ali Alghamdi, MD,[bb] Farrel Hellig, MD,[cc] Bon-Kwon Koo, PhD,[dd] Chang-Wook Nam, PhD,[ee] Eun-Seok Shin, MD,[ff] Joon-Hyung Doh, PhD,[gg] Salvatore Brugaletta, PhD,[hh] Eduardo Alegria-Barrero, PhD,[ii] Martijin Meuwissen, PhD,[jj] Jan J. Piek, PhD,[kk] Niels van Royen, PhD,[ll] Murat Sezer, MD,[mm] Carlo Di Mario, PhD,[nn] Robert T. Gerber, PhD,[oo] Iqbal S. Malik, PhD,[a] Andrew S.P. Sharp, MD,[pp] Suneel Talwar, MD,[qq] Kare Tang, MD,[rr] Habib Samady, MD,[ss] John Altman, MD,[tt] Arnold H. Seto, MD,[uu] Jasvindar Singh, MD,[vv] Allen Jeremias, MD,[ww] Hitoshi Matsuo, PhD,[xx] Rajesh K. Kharbanda, PhD,[yy] Manesh R. Patel, MD,[zz] Patrick Serruys, PhD,[a] Javier Escaned, PhD,[a] Justin E. Davies, PhD[aaa]

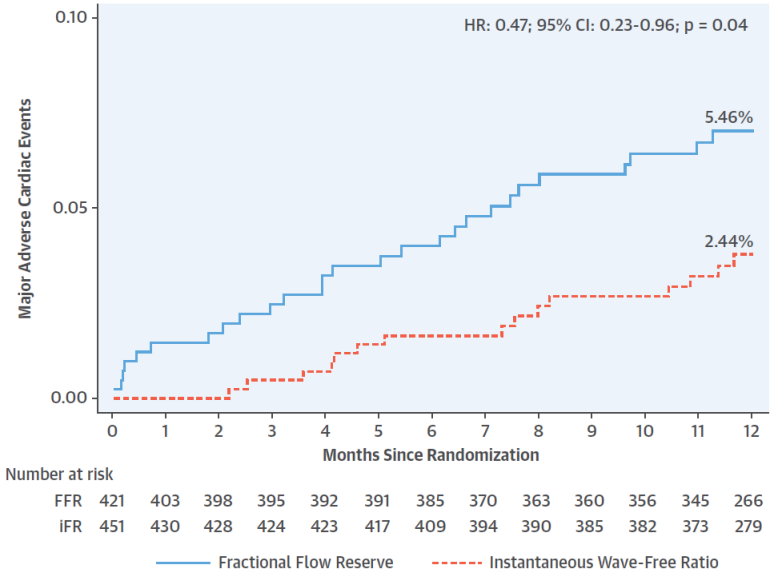
Sen et al., J Am Coll Cardiol 2019;73:444–53

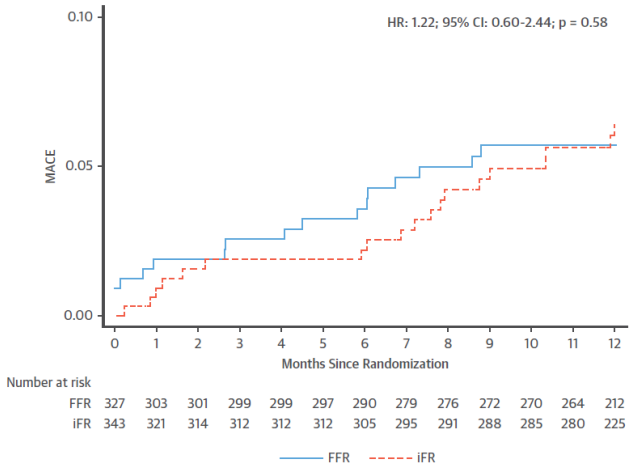
A recent report

FIGURE 1 Flow Chart Outlining Patient Selection









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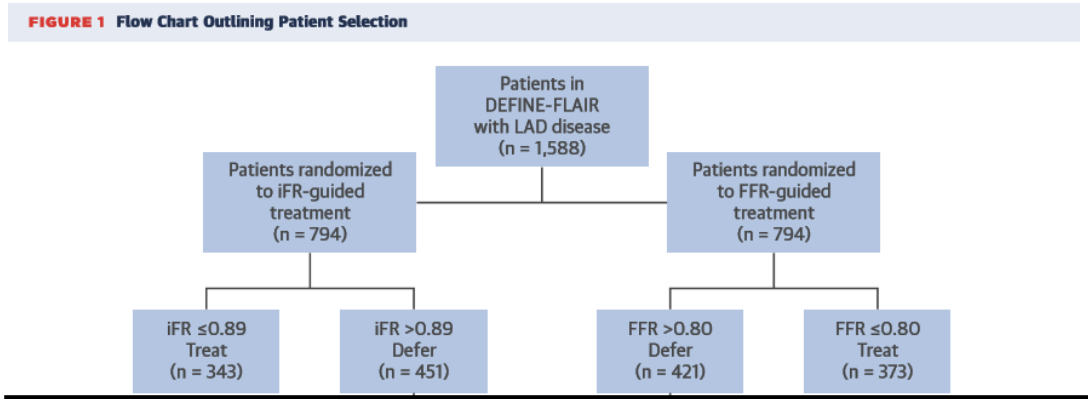
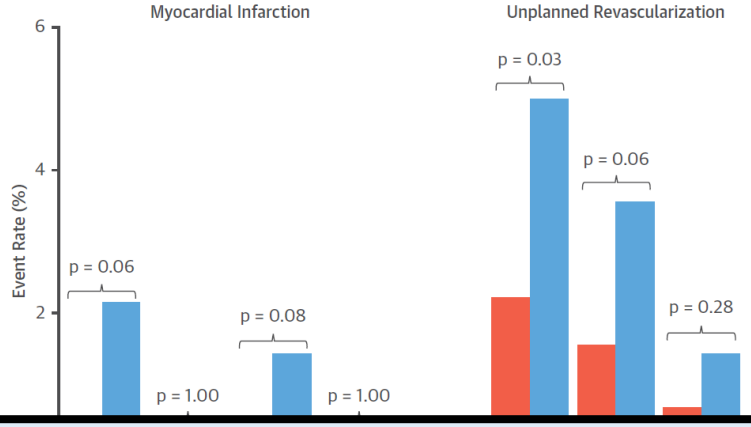
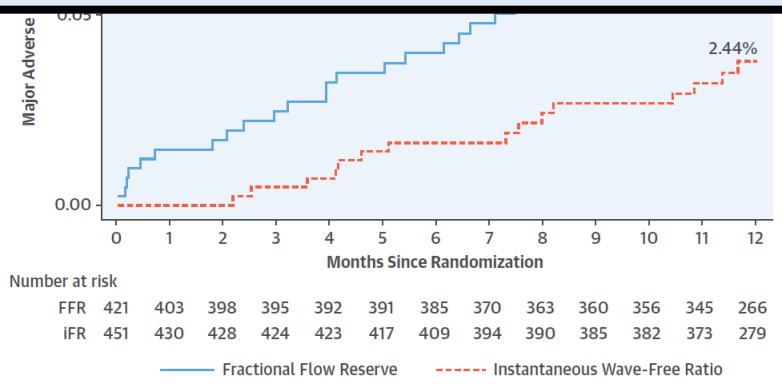
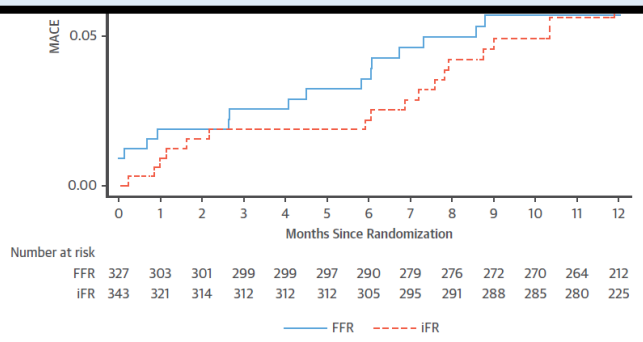
A recent report





iFR-guided deferral appears to be ***safe*** for patients with ***LAD lesions***. Patients in whom iFR-guided deferral was performed had ***statistically significantly lower event rates*** than those with ***FFR-guided deferral***.





Sen et al., J Am Coll Cardiol 2019;73:444–53

Conclusion

Now *iFR* could be first pick for physiologic decision in *LAD* stenosis

- ✓ Supported by theoretical background
- ✓ Supported by clinical evidence

- ✓ More safe
- ✓ More easy
- ✓ More applicable…

Thank You For Your Attention

Jeehoon Kang, MD

I am looking forward to have a more discussion.

E-mail: medikang@gmail.com