8th IMAGING & PHYSIOLOGY SUMMIT2015

Review in 2015

Physiology

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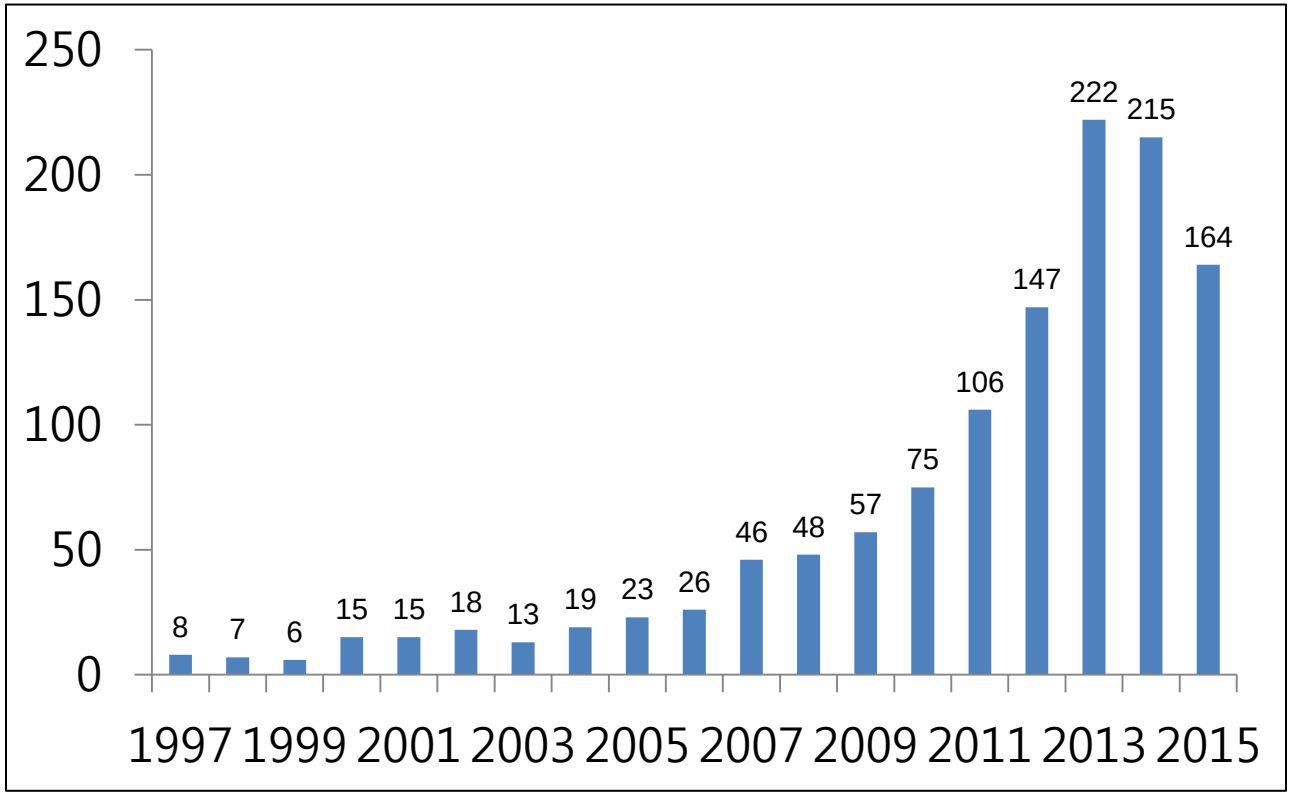
FFR Publications in 2015

- Key word search for “fractional flow reserve, myocardial” at Pubmed (2015.12.4)



DEFER 15 Year-FU

The DEFER study was a multicenter, international, randomized controlled trial performed in 12 European and 2 Asian centres between 1997 and 1998 (N=325).

	Defer group (n = 91)	Perform group (n = 90)	Reference group (n = 144)	*P*-value	
				Defer vs. Perform	Defer and perform vs. Reference
Mortality					
All cause	30 (33.0%)	28 (31.1%)	52 (36.1%)	0.789	0.441
Cardiac	5 (5.5%)	4 (4.4%)	15 (10.4%)	1.000	0.062
Unknown	13 (14.3%)	11 (12.2%)	10 (6.9%)	0.682	0.065
Non-cardiac	12 (13.2%)	13 (14.4%)	27 (18.8%)	0.806	0.228
MI					
All	2 (2.2%)	9 (10.0%)	18 (12.5%)	0.033	0.044
Target vessel[a]	1 (1.1%)	8 (8.9%)	12 (8.3%)	0.018	0.221
Revascularization					
All	39 (42.9%)	31 (34.4%)	64 (44.4%)	0.245	0.294
Target vessel	33 (36.3%)	25 (27.8%)	51 (35.4%)	0.221	0.522

Conclusions

Deferral of PCI of a functionally non-significant stenosis is associated with a favourable very long-term follow-up without signs of late ‘catch-up’ phenomenon.

Frederik M. Zimmermann et al. *Eur Heart J* doi:10.1093/eurheartj/ehv452

FAME 5 Year-FU

The FAME study was a multicenter trial done in Belgium, Denmark, Germany, the Netherlands, Sweden, the UK, and the USA in 1005 patient with multivessel disease.

	Angiography-guided PCI (n=496)	Fractional flow reserve-guided PCI (n=509)	p value
Total events	210	185	
Events per patient	0·42 (0·76)	0·36 (0·67)	0·28
Endpoints			
All-cause mortality	49 (10%)	44 (9%)	0·50
Cardiac mortality	28 (6%)	21 (4%)	0·26
Myocardial infarction	60	49	
Revascularisation	101	92	
Combined endpoints			
Major adverse cardiac events (primary endpoint)	154 (31%)	143 (28%)	0·31
All-cause mortality or myocardial infarction	98 (20%)	86 (17%)	0·24
Cardiac mortality or myocardial infarction	78 (16%)	66 (13%)	0·21

The number of stents/patient

- 2.7 in CAG guided group
- 1.9 in FFR guided group

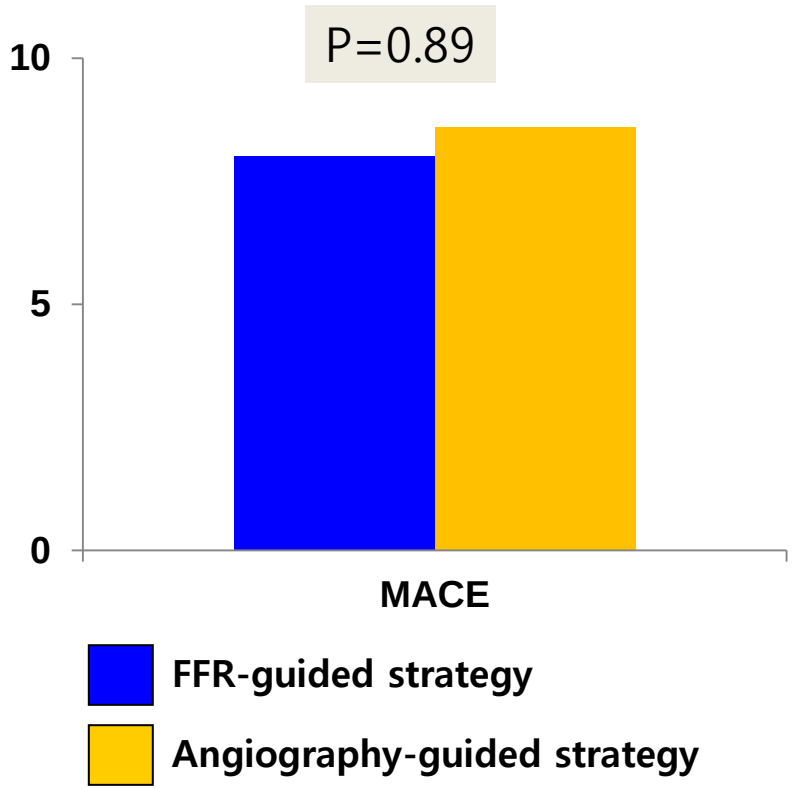
Conclusions

The results confirm the long-term safety of FFR-guided PCI in patients with multivessel disease. This clinical outcome in the FFR-guided group was achieved with a lower number of stented arteries and less resource use.

Lokien X van Nunen et al *Lancet* 2015; 386: 1853–60

FAMOUS-NSTEMI

Participants with NSTEMI were randomized to an FFR-guided strategy (n = 176) vs. a coronary angiography-guided strategy (n = 174).



Results

- Proportion of patients medically treated: **22.7% in the FFR group** vs. **13.2% in the angiography group** (p = 0.022)
- MACE at 12 months: 8.0% vs. 8.6% (p = 0.89), respectively
- Freedom from revascularization at 12 months: 21.0% vs. 13.2% (p = 0.054)

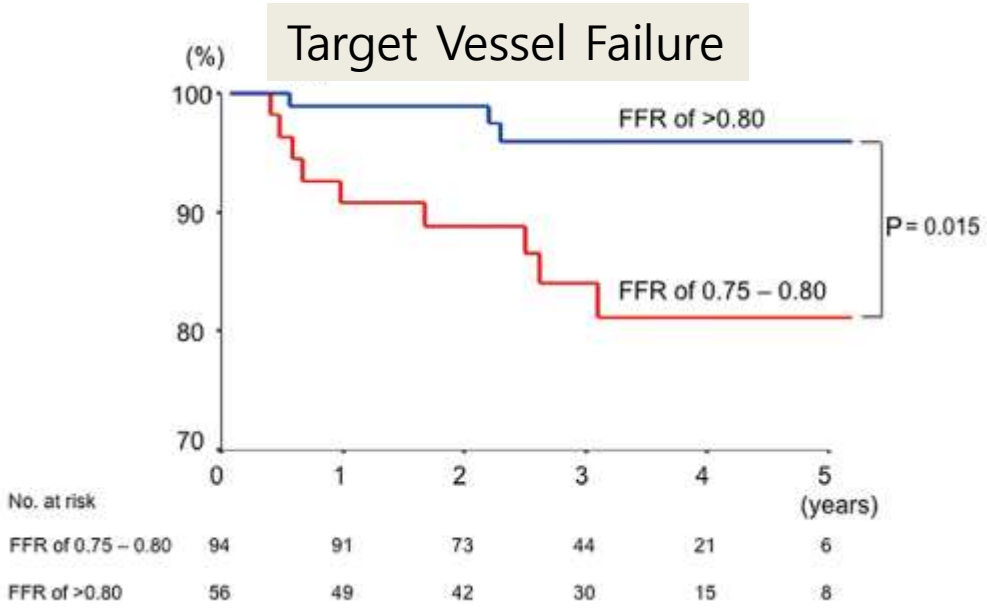
Conclusions

- Among NSTEMI patients, an FFR-guided strategy was feasible, resulting in a larger proportion of patients treated medically
- FFR-guided strategy was associated with similar MACE, but a marginal reduction in revascularization

JamieLayland et al. *Eur Heart J* (2015) 36, 100–111

Outcome of Deferred Lesion with FFR Gray Zone

This study enrolled 155 patients from the FFR registry who had a de novo target lesion with an angiographically intermediate stenosis (percent diameter stenosis, 30–70%) and who had PCI deferred based on FFR ≥0.75.



Conclusions

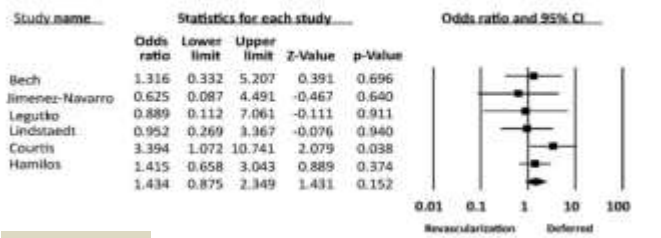
Patients with FFR 0.75–0.80 were at higher risk of TVF mainly due to TVR than those with FFR>0.80.

Yasutsugu Shiono et al. *Circ J* 2015; **79:** 91 – 95

Meta-analysis (I):
FFR Guided Treatment of LM:

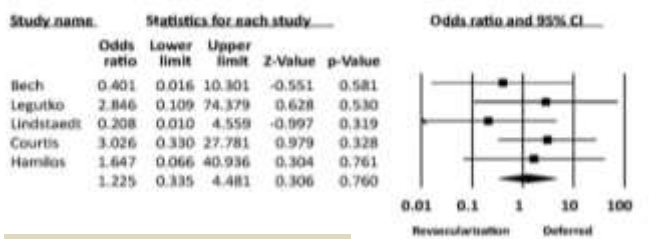
6 prospective cohort studies involving 525 patients met the inclusion criteria

Death, MI, Revascularization



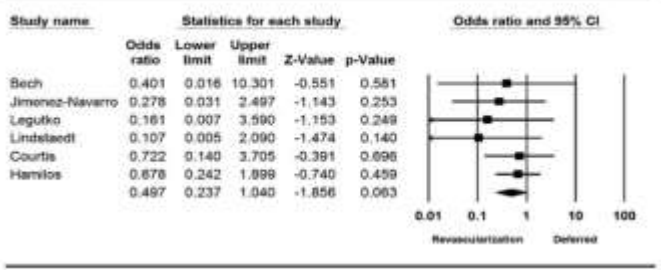
Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Bech	1.316	0.332	5.207	0.391	0.696
Jimenez-Navarro	0.625	0.087	4.491	-0.467	0.640
Legutko	0.889	0.112	7.061	-0.111	0.911
Lindstaedt	0.952	0.269	3.367	-0.076	0.940
Courtis	3.394	1.072	10.741	2.079	0.038
Hamilos	1.415	0.658	3.043	0.889	0.374
	1.434	0.875	2.349	1.431	0.152

MI



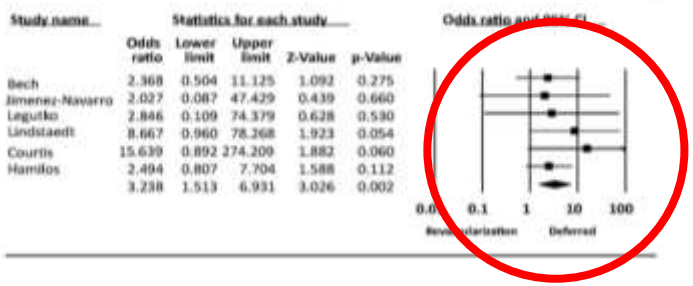
Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Bech	0.401	0.016	10.301	-0.551	0.581
Legutko	2.846	0.109	74.379	0.628	0.530
Lindstaedt	0.208	0.010	4.559	-0.997	0.319
Courtis	3.026	0.330	27.781	0.979	0.328
Hamilos	1.647	0.066	40.936	0.304	0.761
	1.225	0.335	4.481	0.306	0.760

Death



Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Bech	0.401	0.016	10.301	-0.551	0.581
Jimenez-Navarro	0.278	0.031	2.497	-1.143	0.253
Legutko	0.161	0.007	3.590	-1.153	0.249
Lindstaedt	0.107	0.005	2.090	-1.474	0.140
Courtis	0.722	0.140	3.705	-0.391	0.696
Hamilos	0.676	0.242	1.899	-0.740	0.459
	0.497	0.237	1.040	-1.856	0.063

Revascularization



Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Bech	2.368	0.504	11.125	1.092	0.275
Jimenez-Navarro	2.027	0.087	47.429	0.439	0.660
Legutko	2.846	0.109	74.379	0.628	0.530
Lindstaedt	8.667	0.960	78.368	1.923	0.054
Courtis	15.639	0.892	274.209	1.882	0.060
Hamilos	2.494	0.807	7.704	1.588	0.112
	3.238	1.513	6.931	3.026	0.002

Conclusions

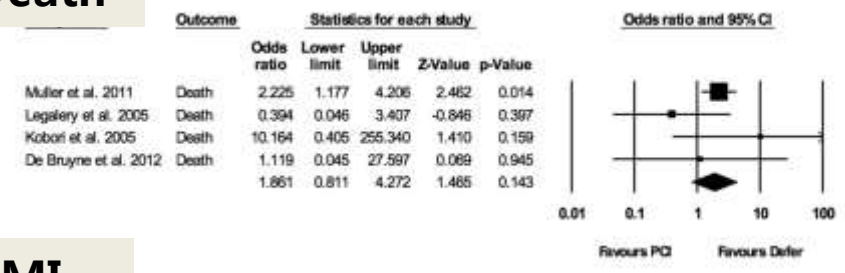
The long term clinical outcomes in patients with ambiguous LMCA stenosis for whom revascularization is deferred based on FFR are favorable and similar to the revascularized group in terms of overall mortality and MI

Jaya Mallidi et al. Catheterization and Cardiovascular Interventions 86:12–18 (2015)

Meta-analysis (II): Deferral vs. Performance After FFR

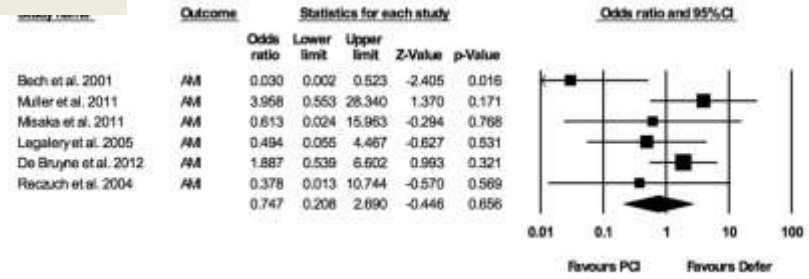
Nineteen studies were included, totaling 3,097 patients (3,796 lesions).

Death



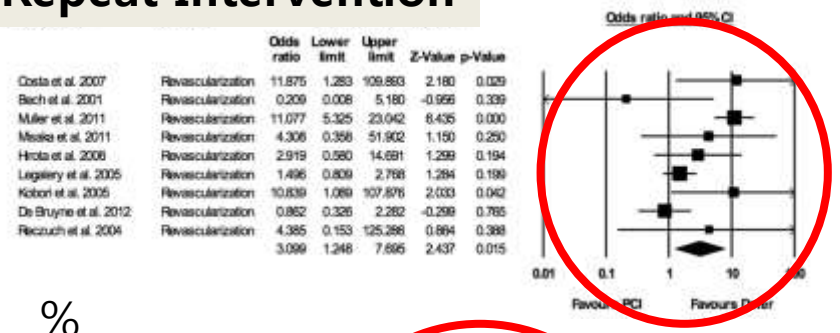
Outcome		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Muller et al. 2011	Death	2.225	1.177	4.206	2.462	0.014
Legalery et al. 2005	Death	0.394	0.046	3.407	-0.846	0.397
Kobori et al. 2005	Death	10.164	0.405	255.340	1.410	0.159
De Bruyne et al. 2012	Death	1.119	0.045	27.597	0.069	0.945
		1.861	0.811	4.272	1.465	0.143

AMI

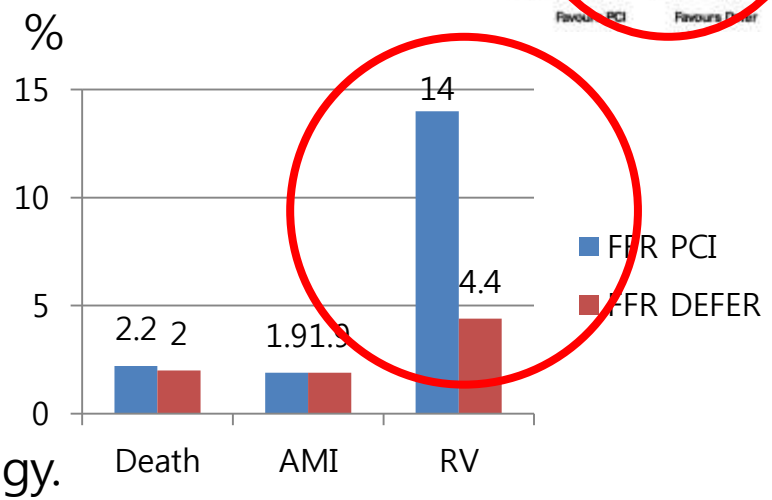


Outcome		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Bech et al. 2001	AMI	0.030	0.002	0.523	-2.405	0.016
Muller et al. 2011	AMI	3.958	0.553	28.340	1.370	0.171
Misaka et al. 2011	AMI	0.613	0.024	15.963	-0.294	0.768
Legalery et al. 2005	AMI	0.494	0.055	4.467	-0.627	0.531
De Bruyne et al. 2012	AMI	1.887	0.539	6.602	0.993	0.321
Reczuch et al. 2004	AMI	0.378	0.013	10.744	-0.570	0.569
		0.747	0.208	2.690	-0.446	0.656

Repeat Intervention



		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Costa et al. 2007	Revascularization	11.875	1.283	109.893	2.180	0.029
Bech et al. 2001	Revascularization	0.209	0.008	5.180	-0.956	0.339
Muller et al. 2011	Revascularization	11.077	5.325	23.042	6.435	0.000
Misaka et al. 2011	Revascularization	4.306	0.358	51.902	1.150	0.250
Hirota et al. 2006	Revascularization	2.919	0.560	14.681	1.299	0.194
Legalery et al. 2005	Revascularization	1.496	0.809	2.768	1.284	0.199
Kobori et al. 2005	Revascularization	10.839	1.089	107.876	2.033	0.042
De Bruyne et al. 2012	Revascularization	0.852	0.326	2.282	-0.299	0.765
Reczuch et al. 2004	Revascularization	4.385	0.153	125.286	0.864	0.388
		3.099	1.248	7.695	2.437	0.015



Conclusions

Deferral of PCI based on FFR is a safe strategy.

Bruno R. Nascimento et al. Am J Cardiol 2015;115:385e391

Meta-analysis (III): Deferral vs. Performance After FFR

Four prospective and three retrospective studies involving 49 517 patients were included.

Results

FFR-guided PCI was associated with lower

1) MACE (OR: 1.71, 95% CI 1.31 to 2.23)
2) Death (OR: 1.64, 95% CI 1.37 to 1.96)
3) MI (OR: 2.05, 95% CI 1.61 to 2.60)
4) Repeat revascularisation (OR: 1.25, 95% CI 1.09 to 1.44)
5) Death or MI (OR: 1.84, 95% CI 1.58 to 2.15)

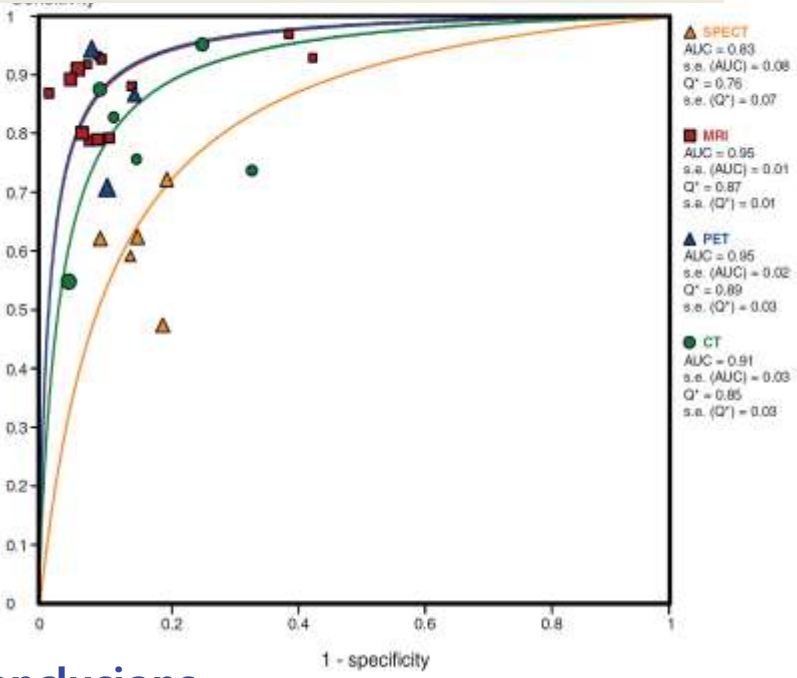
Than angiography-guided PCI strategy

Zhang D, et al. Heart 2015;101:455–462

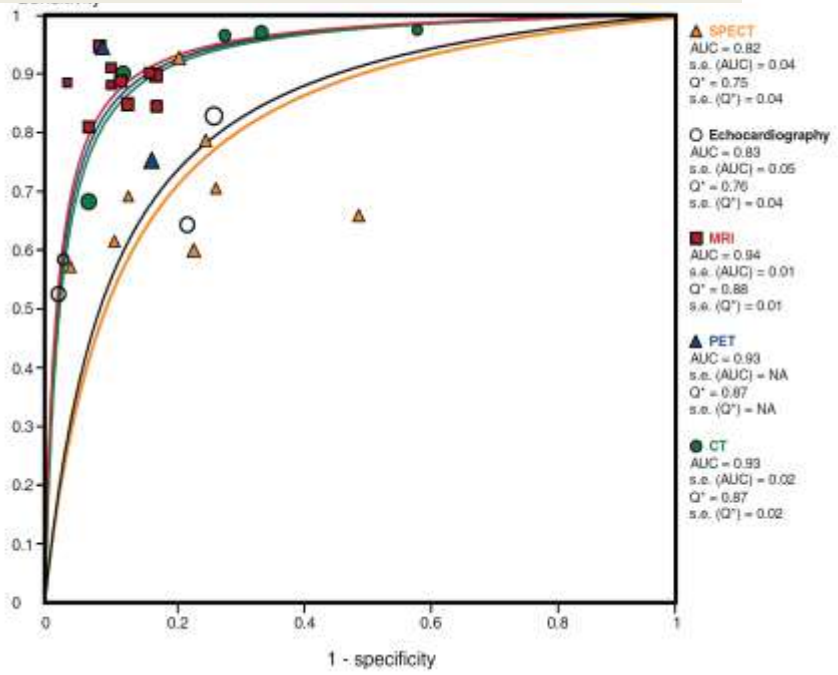
Diagnostic Accuracy of Noninvasive Functional Study Compared with FFR: Meta-anlaysis (IV)

Thirty-seven studies, reporting on 4721 vessels and 2048 patients, were included

Per-Vessel Level



Per-Patient Level



Conclusions

MRI, CT, or PET can accurately rule out hemodynamically significant coronary artery disease and can act as a gatekeeper for invasive revascularization. SPECT and Echo are less suited for this purpose.

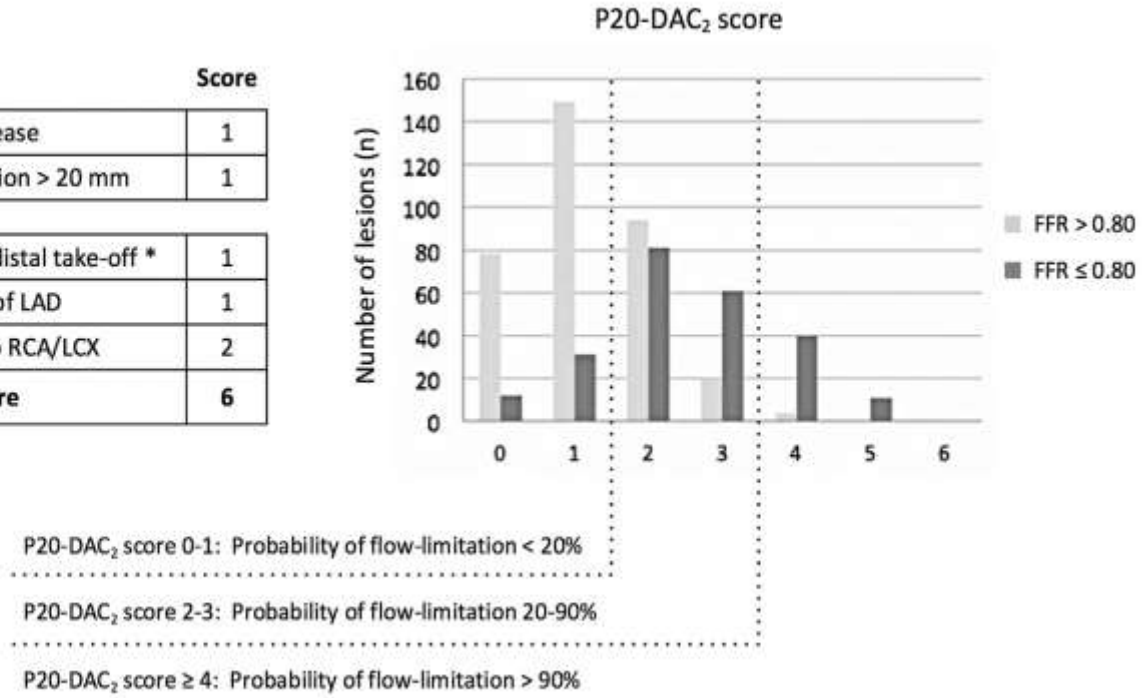
Richard A.P. Takx, et al. *Circ Cardiovasc Imaging*. 2015;8:e002666

Prediction Model for LAD FFR ≤0.80 (I)

583 intermediate LAD stenosis

		Score
P	Proximal disease	1
20	Length of lesion > 20 mm	1

D	Diagonals – distal take-off *	1
A	Apical wrap of LAD	1
C	Collaterals to RCA/LCX	2
	Maximal score	**6**



Luigi Biasco et al. Am J Cardiol 2015;115:1475e1480

Prediction Model for FFR (II)

A total of 260 consecutive patients (362 lesions) who underwent FFR testing

Table 3. Angiographic Independent Predictors of Positive FFR

	OR	95% CI	P-value
Stenosis	8.43	4.71–15.64	<0.0001
Lesion length >20 mm	5.40	2.17–14.89	0.0002
Tandem	4.00	2.14–7.68	<0.0001
True bifurcation	2.42	1.10–5.50	0.028
Distance from ostium <20 mm	1.94	1.07–3.53	0.028
Calcification	1.58	0.69–3.65	0.28
LAD	1.53	0.82–2.91	0.18

CI, confidence interval; FFR, fractional flow reserve; LAD, left anterior descending; OR, odds ratio.

Table 4. Calculation of STABLED Score

Independent predictors of positive FFR	Points
Stenosis diameter >50%	2
Tandem lesions	1
Bifurcation lesions	1
Lesion length >20 mm (diffuse lesions)	1
Distance from ostium <20 mm (proximal lesions)	1
Total STABLED Score	6

FFR, fractional flow reserve.

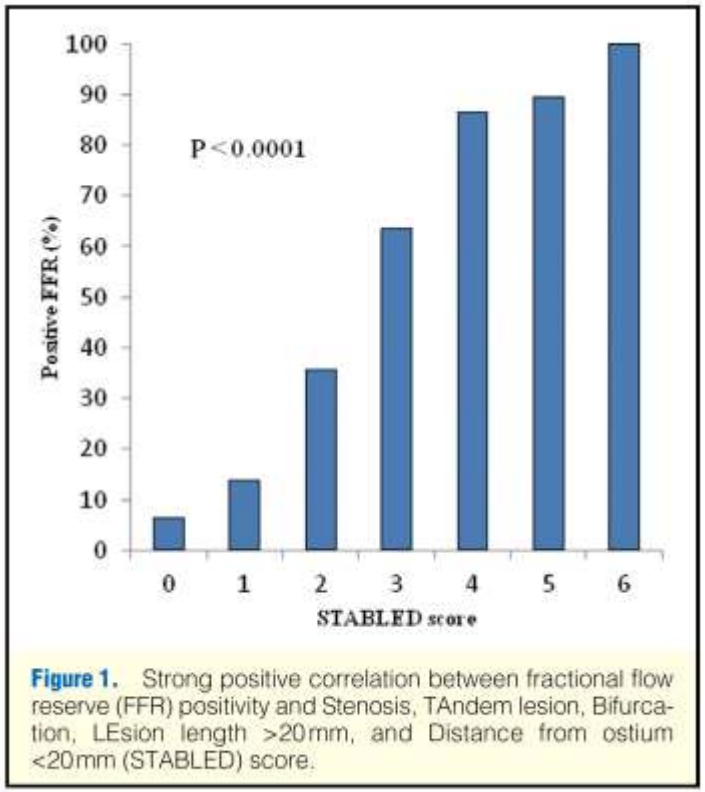


Figure 1. Strong positive correlation between fractional flow reserve (FFR) positivity and Stenosis, TAndem lesion, Bifurcation, LEsion length >20 mm, and Distance from ostium <20 mm (STABLED) score.

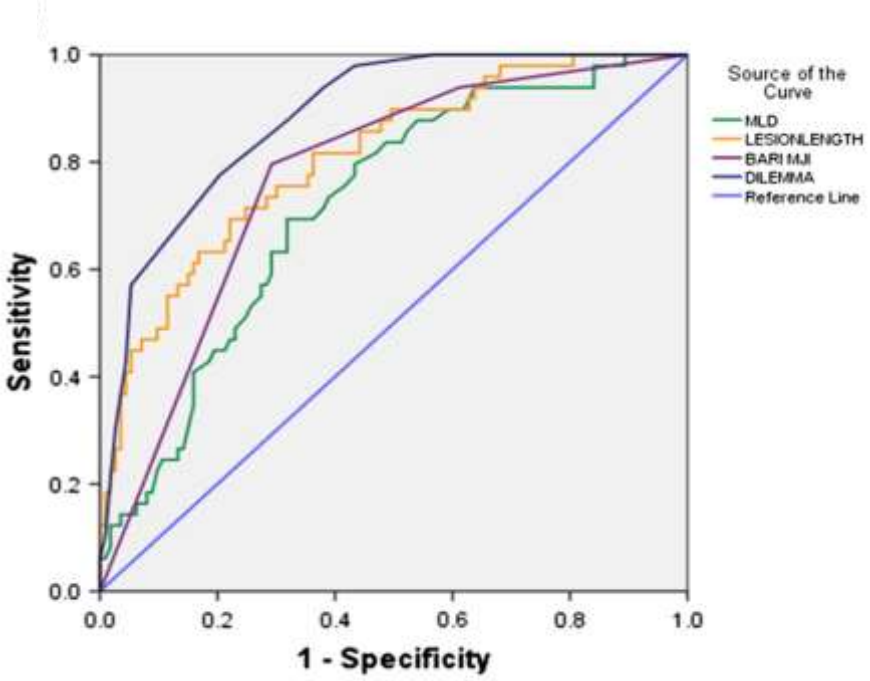
Makoto Natsumeda et al. *Circ J* 2015; **79:** 802 – 807

Prediction Model for FFR (III)

A total of 296 patients were included

DILEMMA Score

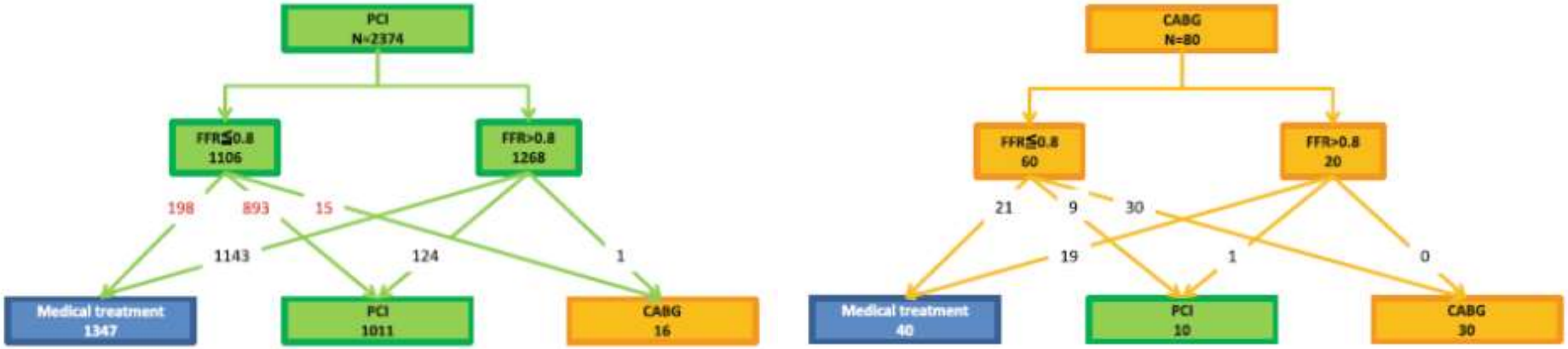
Variable	Value	Points
MLD (mm)	<1.1	4
	1.1-1.5	1
	>1.5	0
Lesion length (mm)	>18	3
	9-18	1
	<9	0
Jeopardy index (%)	>35	5
	18-35	1
	<18	0
Total		Maximum = 12



Dennis T. L. Wong et al. Am Heart J 2015;169:564-571.e4

Modification of Treatment Strategy after FFR CVIT-DEFER Registry

The CVIT-DEFER registry (N=3093) is a prospective multicenter registry enrolling consecutive patients with angiographically intermediate coronary stenosis for whom FFR measurement is clinically indicated.



Conclusions

Reclassification of the treatment at the patient level was done in 39.0 % of the patients. Revascularization was frequently switched to medical treatment after FFR

Masato Nakamura et al. Cardiovasc Interv and Ther (2015) 30:12–21

NXT Trial: $_{FFR}$CT

This prospective multicenter trial included 254 patients scheduled to undergo clinically indicated ICA for suspected CAD.

Per Patient Diagnostic Accuracy

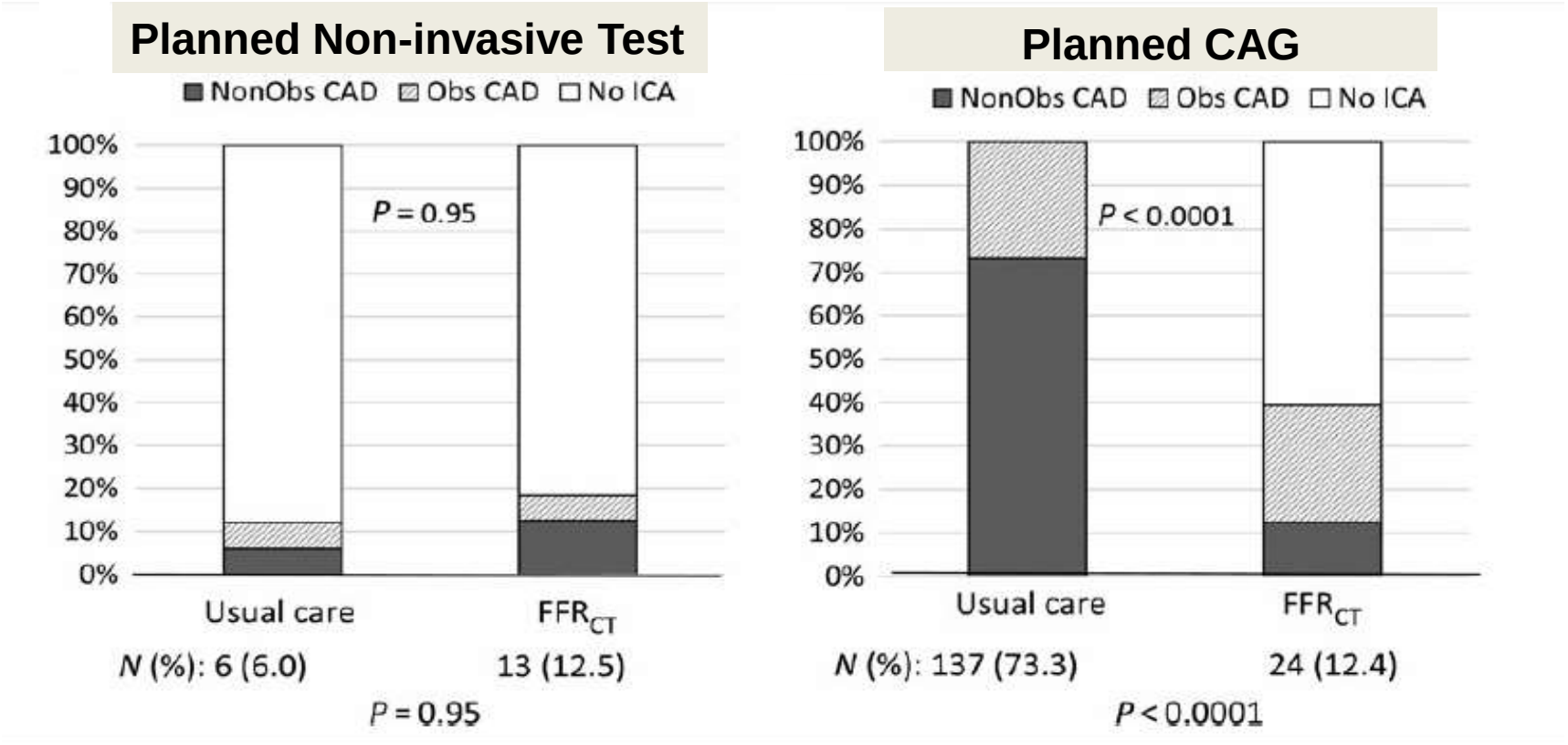
	$FFR_{CT} \leq 0.80$	Coronary CTA Stenosis >50%	p Value
Accuracy	80 (75–85)	51 (44–57)	<0.0001
Sensitivity	85 (74–91)	93 (85–97)	0.058
Specificity	79 (72–84)	32 (26–40)	<0.0001
PPV	63 (53–72)	37 (31–44)	<0.0001
NPV	92 (87–96)	91 (81–96)	0.42

FFRCT provides high diagnostic accuracy and discrimination for the diagnosis of hemodynamically significant CAD with invasive FFR as the reference standard. When compared with anatomic testing by using coronary CTA, FFRCT led to a marked increase in specificity.

Bjarne L. Nørgaard, et al. J Am Coll Cardiol 2014;63:1145–55

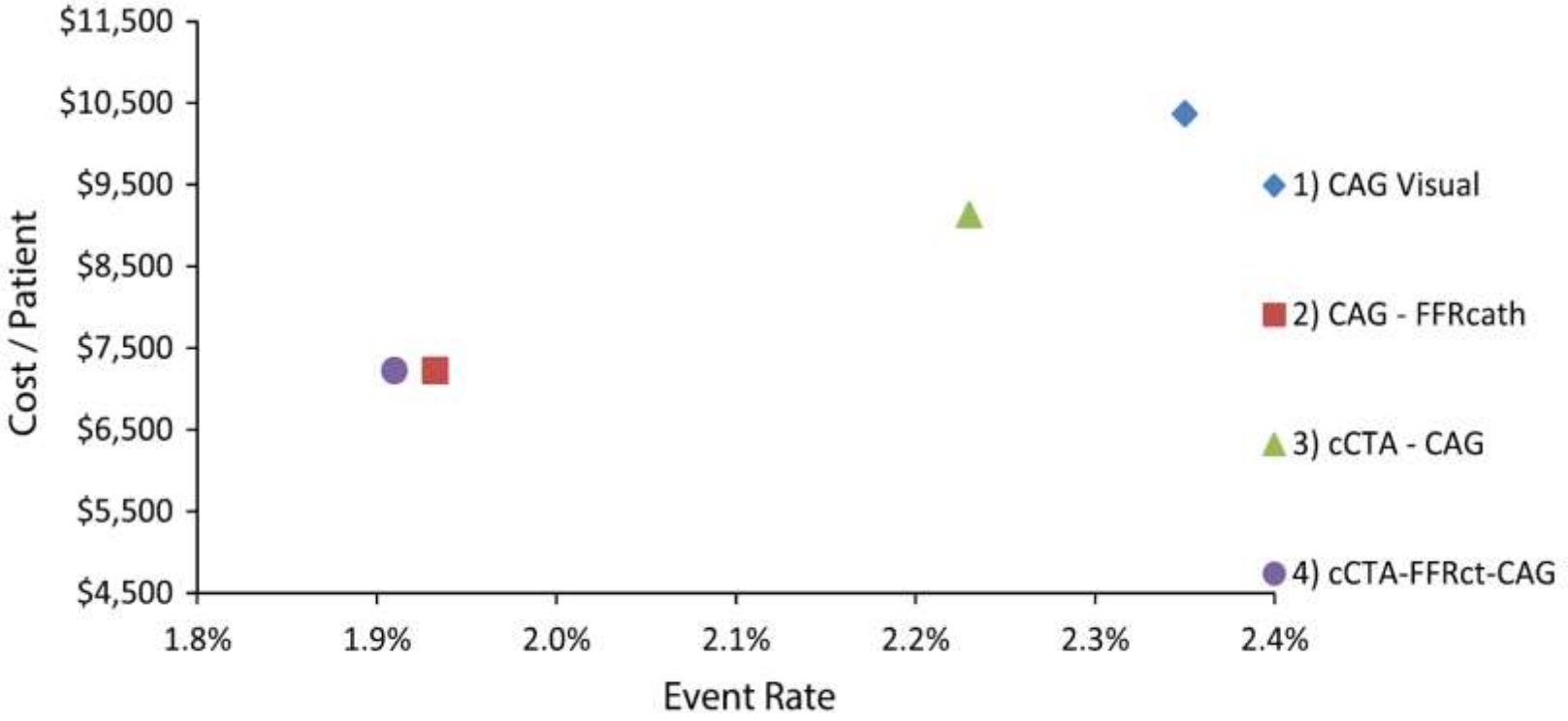
Platform Study: FFR CT

At 11 sites, 584 patients with new onset chest pain were prospectively assigned to receive either usual testing (n=287) or CTA/FFRCT (n=297).



Douglas PS et al. *Eur Heart J*. 2015 Sep 1. pii: ehv444. [Epub ahead of print]

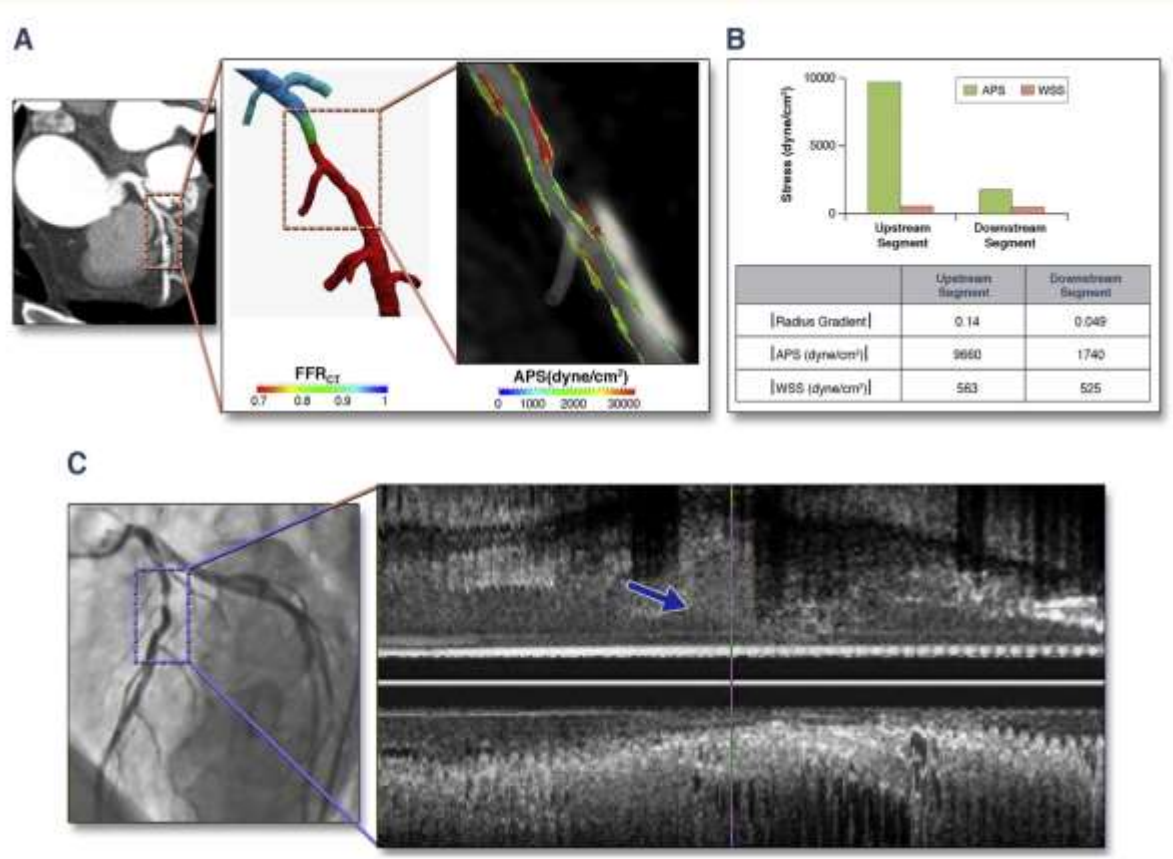
FFRCT Cost Analysis in Japan



Use of the cCTA-FFRCT strategy to select patients for PCI would result in 32 % lower costs and 19 % fewer cardiac events at 1 year compared to the most commonly used CAG-visual strategy

Takeshi Kimura, et al. Cardiovasc Interv and Ther (2015) 30:38–44

New CFD Parameter: Axial Plaque Stress

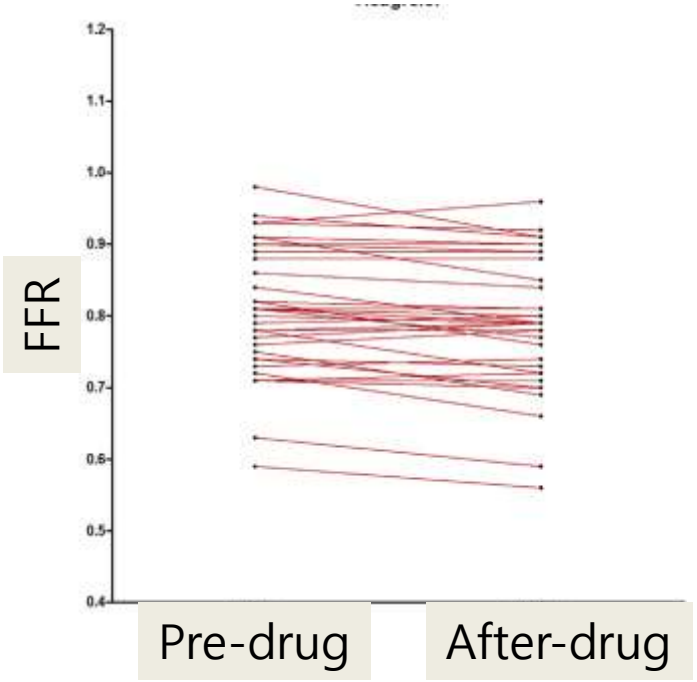


Although there were no differences in FFRCT,%diameter stenosis, and wall shear stress pattern, the distribution of APS was different between upstream- and downstream-dominant lesions.

Gilwoo Choi, et al. J Am Coll Cardiol Img 2015;8:1156–66

Ticagrelor Loading and FFR

Background: Increased adenosine plasma levels have been described in patients 6 hours after receiving ticagrelor LD attributed to inhibition of adenosine uptake by the erythrocytes.



Conclusions

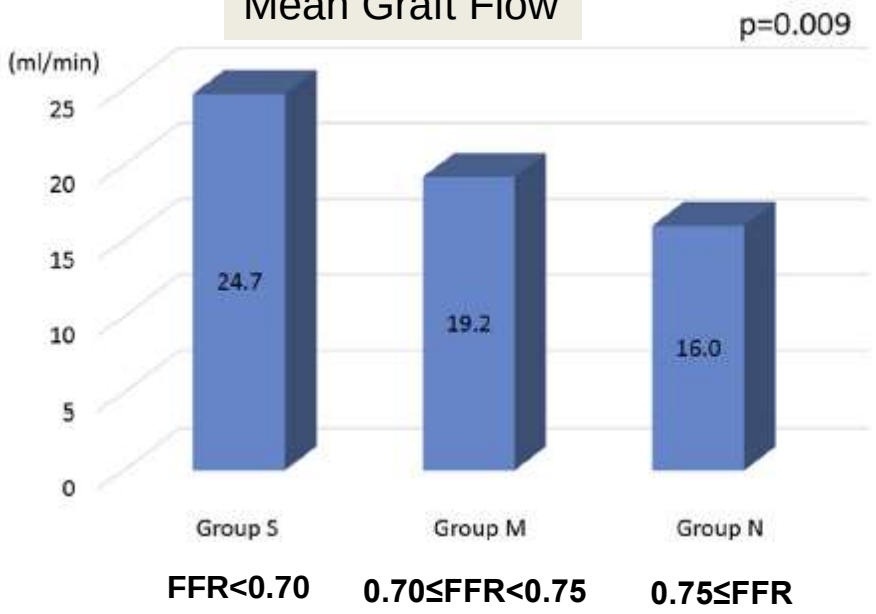
Ticagrelor LD resulted in a greater absolute and relative change (reduction) in sFFR compared with thienopyridine LD, although the magnitude of change was small, (ii) rate of reclassification of treatment decision based on sFFR was not affected by ticagrelor versus thienopyridine

Dimitrios Alexopoulos et al *Am J Cardiol* 2015 in press

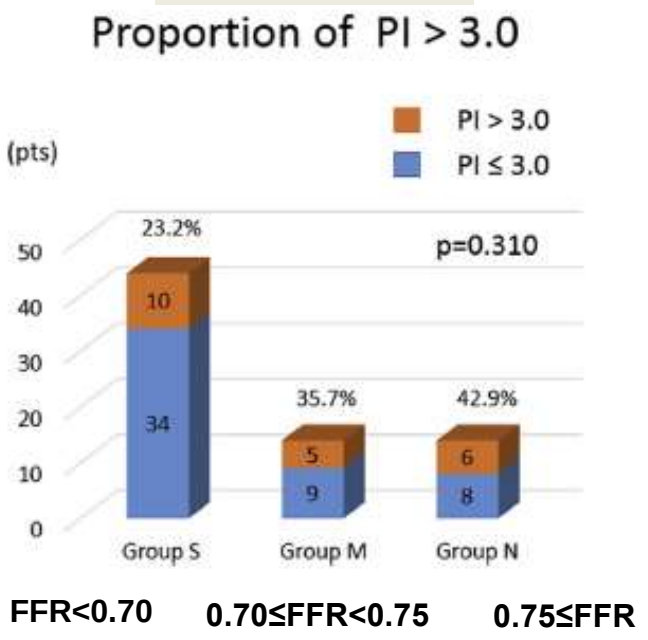
FFR and Graft Flow after CABG

In all, 72 patients underwent CABG were enrolled in this retrospective study

Mean Graft Flow



Pulsatile Index

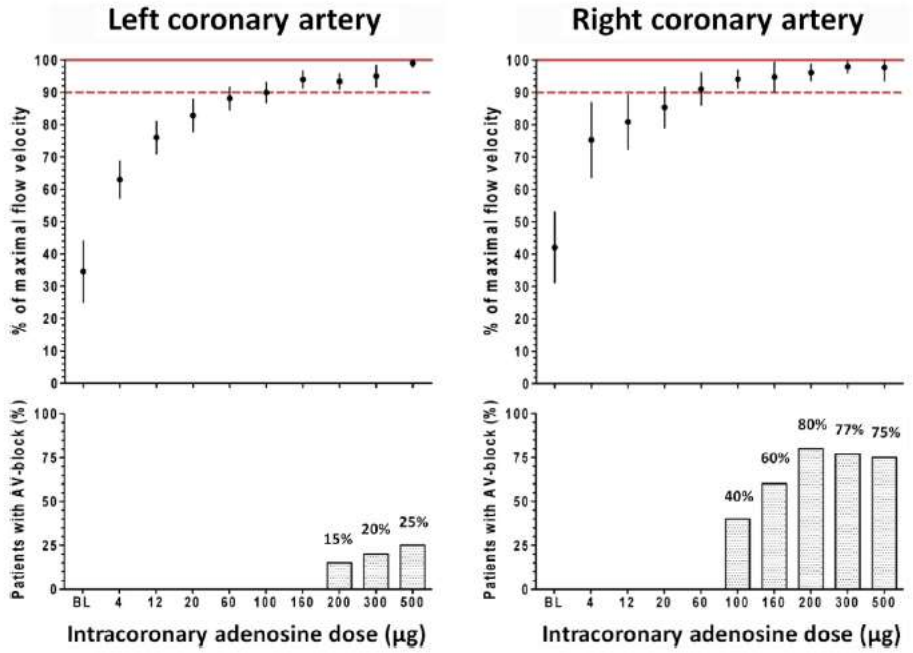


In mild coronary artery stenosis, the chance of flow competition between the native coronary artery and the bypass graft increased

Kentaro Honda, et al. J Thorac Cardiovasc Surg 2015;149:1622-8

IC Adenosine Dose Response Relationship

In 30 patients, Doppler-derived flow velocity measurements were obtained in 10 RCAs and 20 LCAs free of stenoses>20% in diameter.



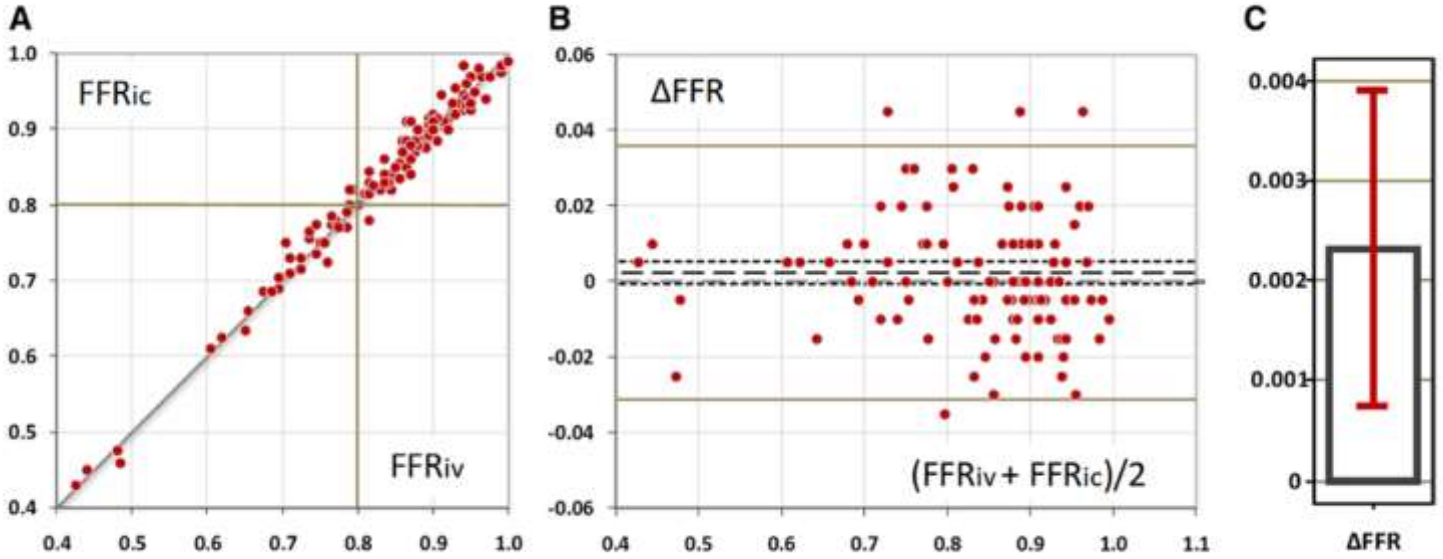
Conclusions

This wide-ranging, dose-response study indicates that an IC adenosine bolus injection of **100 mg** in the RCA and **200 mg** in the LCA induces maximum hyperemia while being associated with minimal side effects

Julien Adjedj, et al. J Am Coll Cardiol Intv 2015;8:1422–30

IC and IV adenosine

- Study included 114 patients with an intermediate degree of stenosis.
- IC injection of adenosine is insufficiently validated against continuous intravenous infusion.
- 40 µg for the right and 80 µg for the left coronary artery

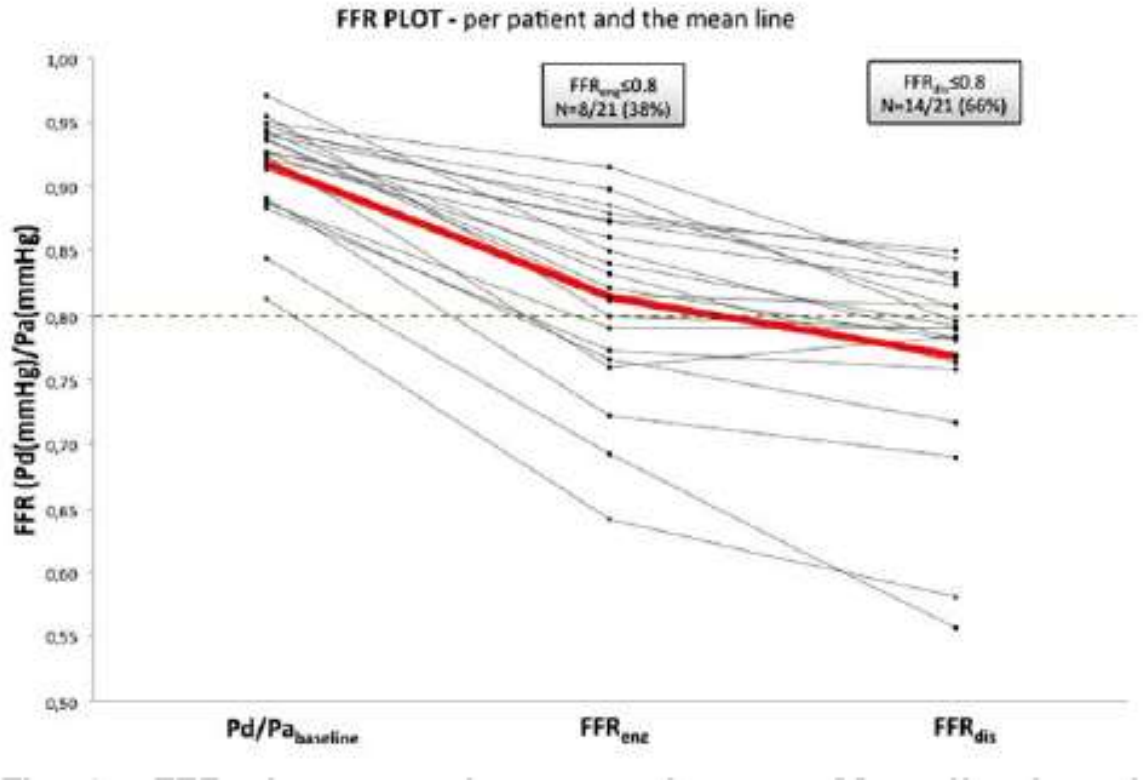


IC injection of adenosine yields identical FFR results compared with intravenous infusion (140 µg/kg per minute), while requiring less time and offering superior patient comfort

Christian Schlu, et al. Circ Cardiovasc Interv. 2015;8:e001781

Guiding Catheter Disengagement

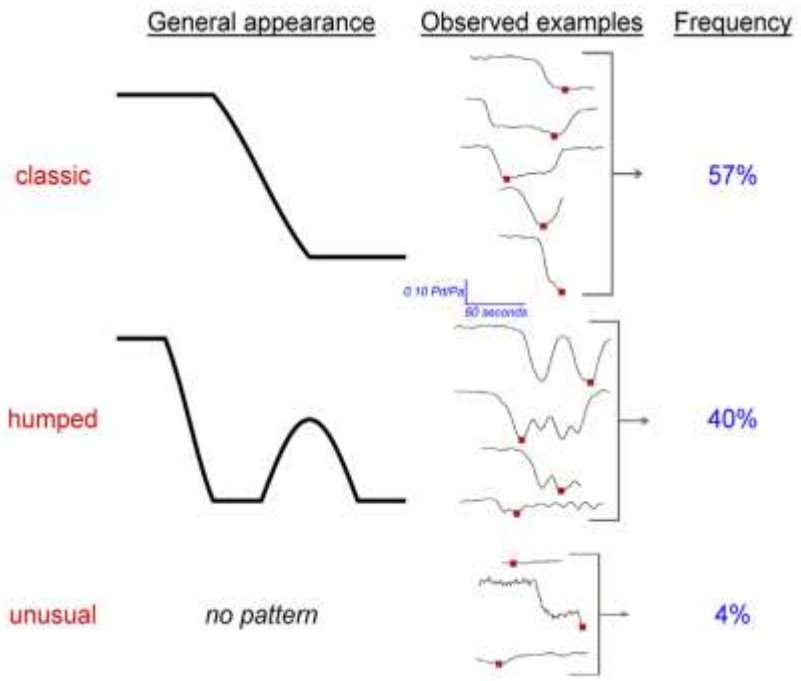
Measurements of FFR were performed in 21 patients with an isolated intermediate lesion of the proximal LAD



During FFR assessment of isolated intermediate proximal LAD lesions, guiding catheter disengagement is associated with a decrease in mean FFR values.

Adel Aminian, et al. CCI 85:595–601 (2015)

Patterns of Pd/Pa Response and FFR repeatability

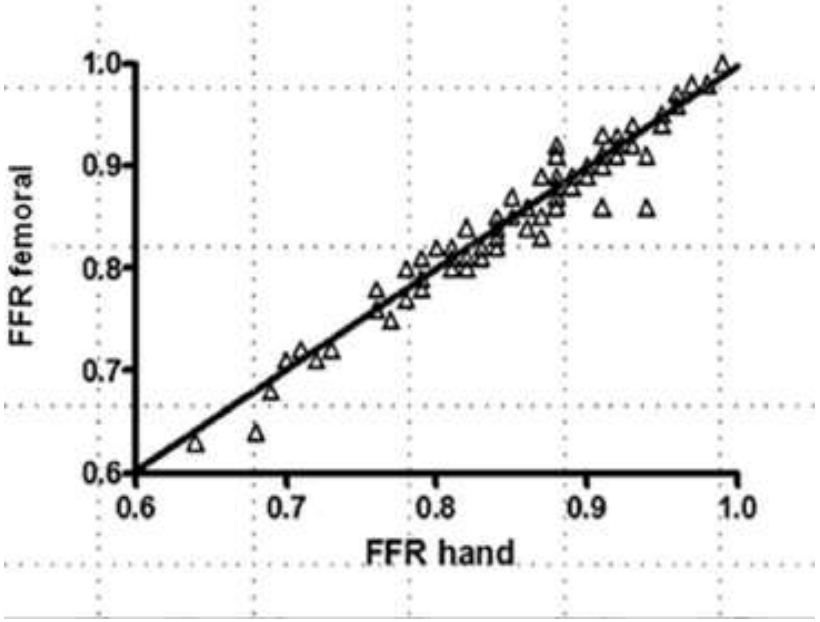


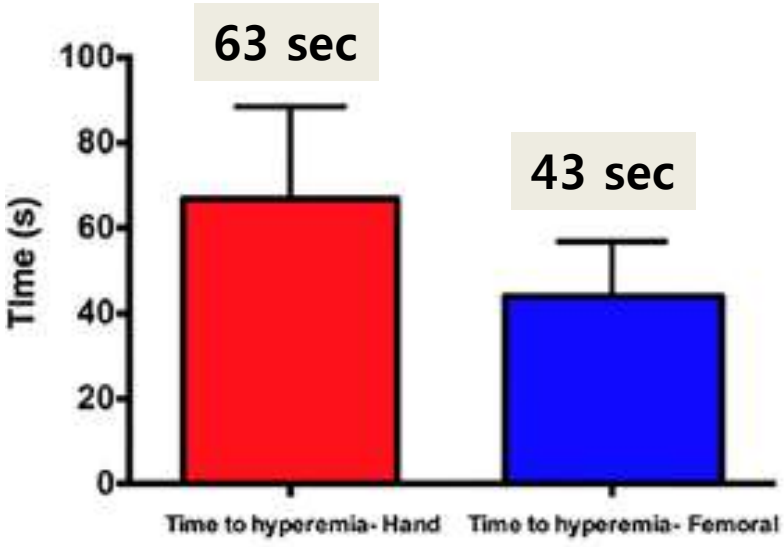
Despite variability of Pd/Pa during the hyperemic period, the **"smart minimum" FFR** demonstrated excellent repeatability (bias 0.001, SD 0.018, paired p ¼ 0.93, r2 ¼ 98.2%, coefficient of variation ¼ 2.5%).

Nils P. Johnson, et al. J Am Coll Cardiol Intv 2015;8:1018–27

Hand vs. Femoral Route for Adenosine

Paired (hand and femoral adenosine) recordings taken from 84 vessels in 61 patients were suitable for blinded analysis.





- Hand vein adenosine infusion produced FFR values very similar to those obtained using central femoral vein adenosine administration
- Time to peak hyperemia was longer on average with hand-administered adenosine compared with femoral adenosine administration

Peter Scott, et al. J Am Coll Cardiol Intv 2015;8:527–35