

FFR in ACS

Applying clinical data to daily practice

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Disclosure Statement of Financial Interest

Within the past 12+ months, Nils Johnson has had a financial interest/arrangement or affiliation with the organization(s) listed below.

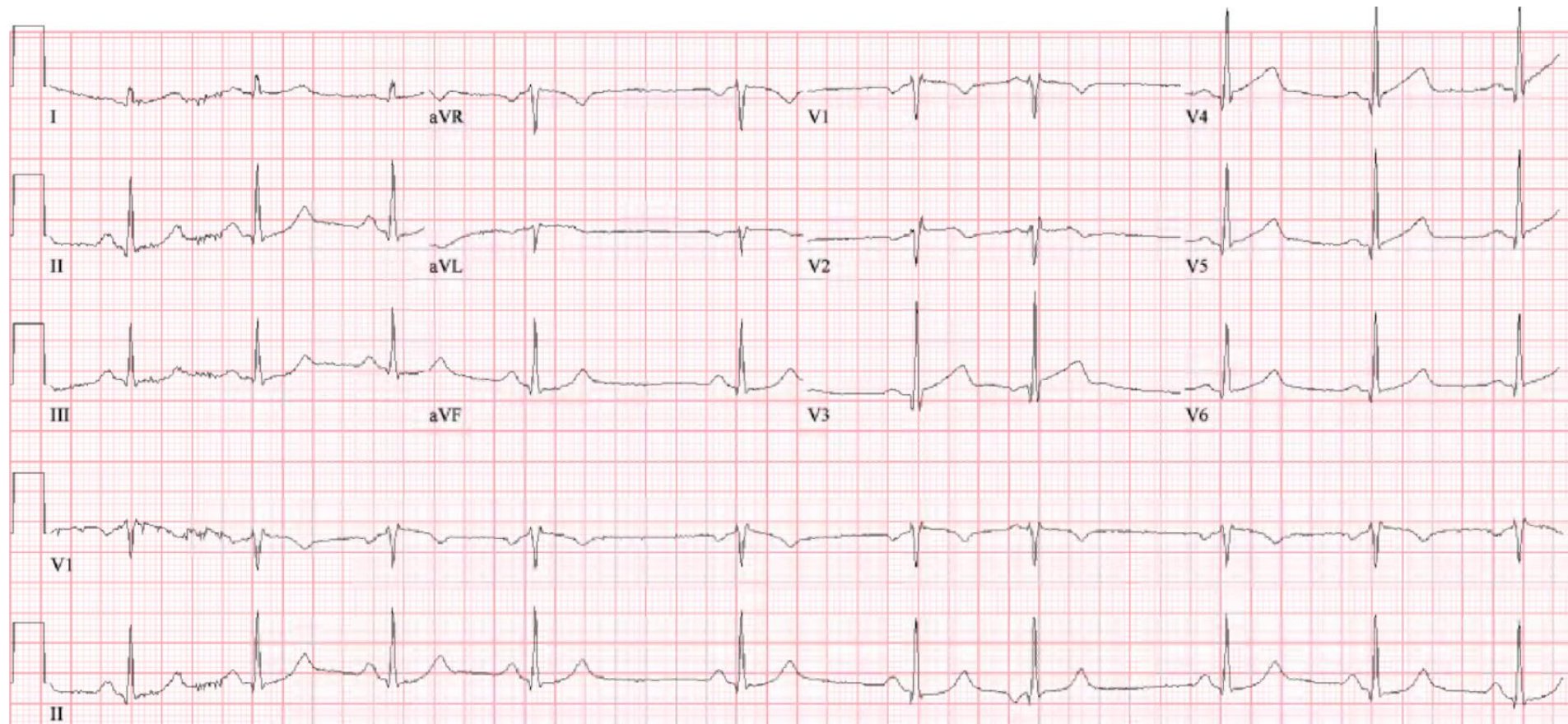
Affiliation/Financial Relationship

- Grant/research support
(to *institution*)
- Licensing and associated consulting
(to *institution*)
- Support for educational meetings/training
(honoraria/fees donated to *institution*)
- PET software 510(k) from FDA
(application by Lance Gould, to *institution*)
- Patent pending
(USPTO serial number 62/597,134)

Organizations (alphabetical)

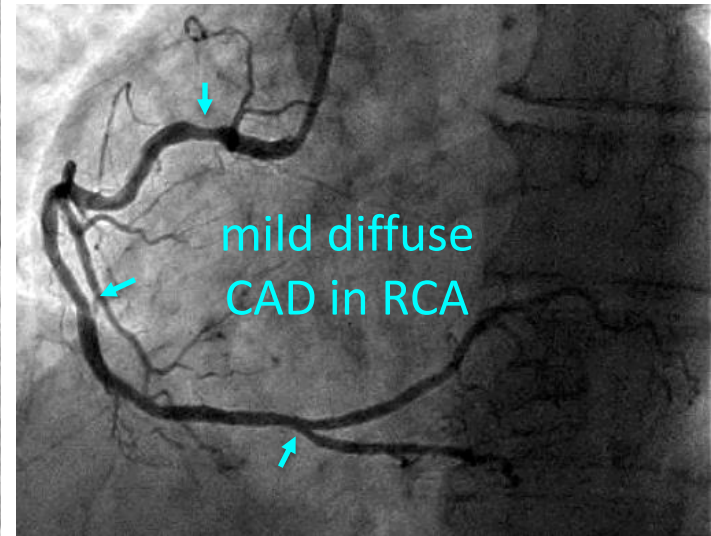
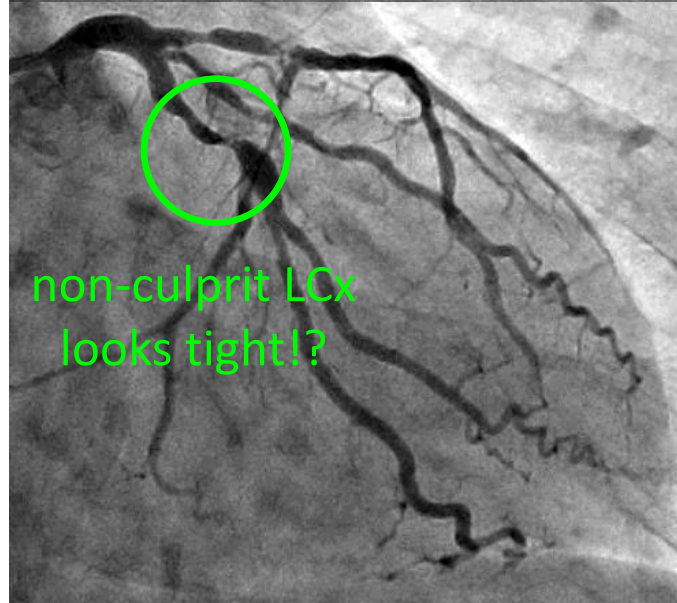
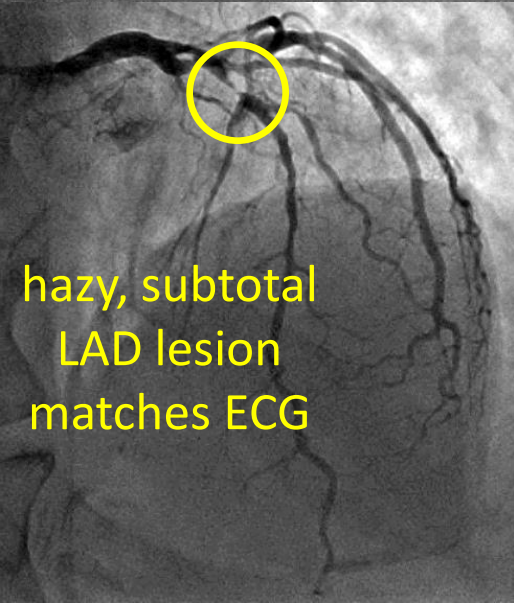
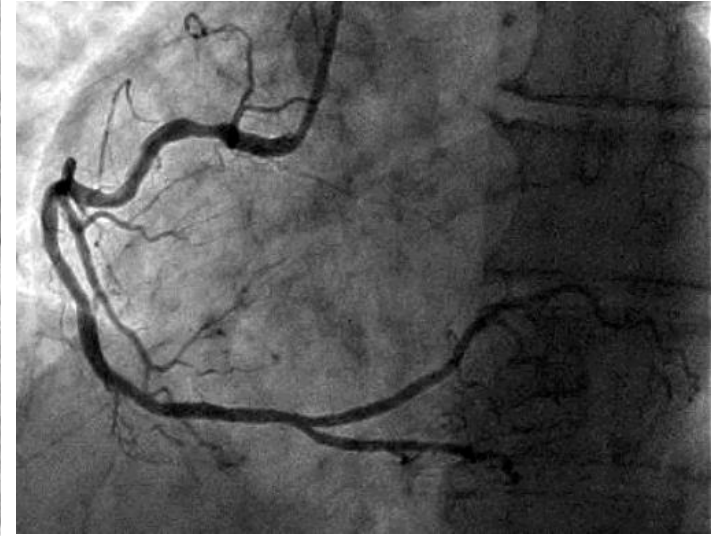
- St Jude Medical (for CONTRAST study)
- Volcano/Philips (for DEFINE-FLOW study)
- Boston Scientific
(for smart-minimum FFR algorithm)
- Various, including academic and industry
- K113754 (cfrQuant, 2011)
- K143664 (HeartSee, 2014)
- K171303 (HeartSee update, 2017)
- SAVI and $\Delta P/Q$ methods

70 year-old man with STEMI



- Sudden onset of substernal chest pressure
- Called ambulance, ECG immediately
- Hemodynamically stable, came to cath lab

STEMI culprit plus non-culprit

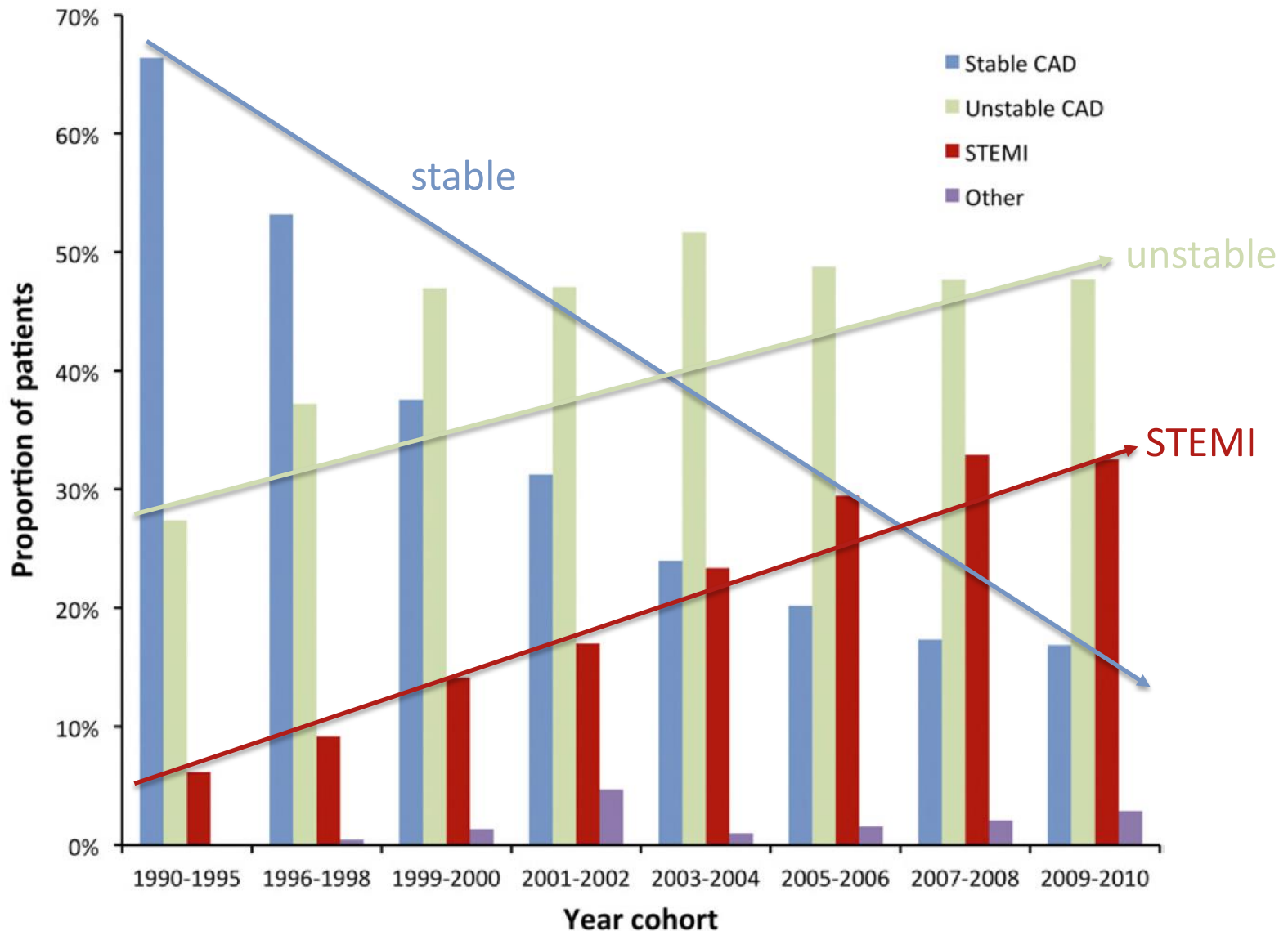


hazy, subtotal
LAD lesion
matches ECG

non-culprit LCx
looks tight!?

mild diffuse
CAD in RCA

Reversal in who receives PCI



Stable patients: most FFR data

TABLE 1 Indications for FFR-Based Decision Making

Vessel	SIHD	NSTE-ACS	STEMI
Clear culprit	Yes	No	No
Nonculprit	Yes	Yes	Yes

FFR = fractional flow reserve; NSTE-ACS = non-ST-segment elevation acute coronary syndrome; SIHD = stable ischemic heart disease; STEMI = ST-segment elevation myocardial infarction.

ACS culprits: avoid FFR!

TABLE 1 Indications for FFR-Based Decision Making

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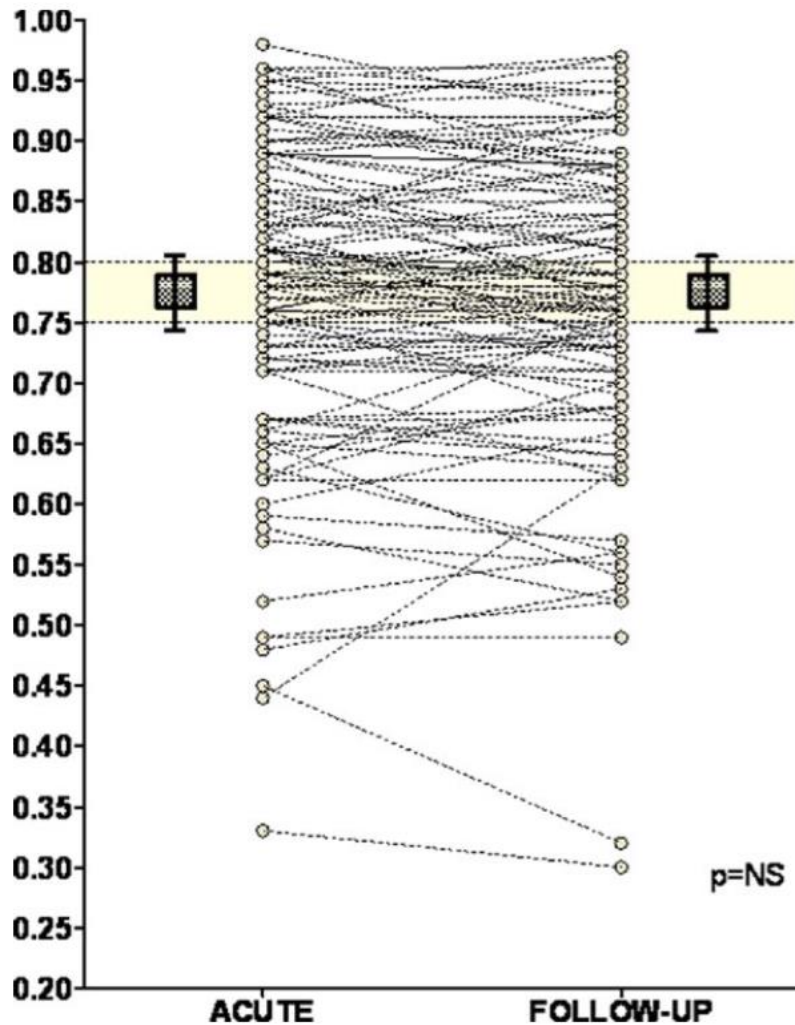
What about FFR of ACS *non-culprit*?

TABLE 1 Indications for FFR-Based Decision Making

Vessel	SIHD	NSTE-ACS	STEMI
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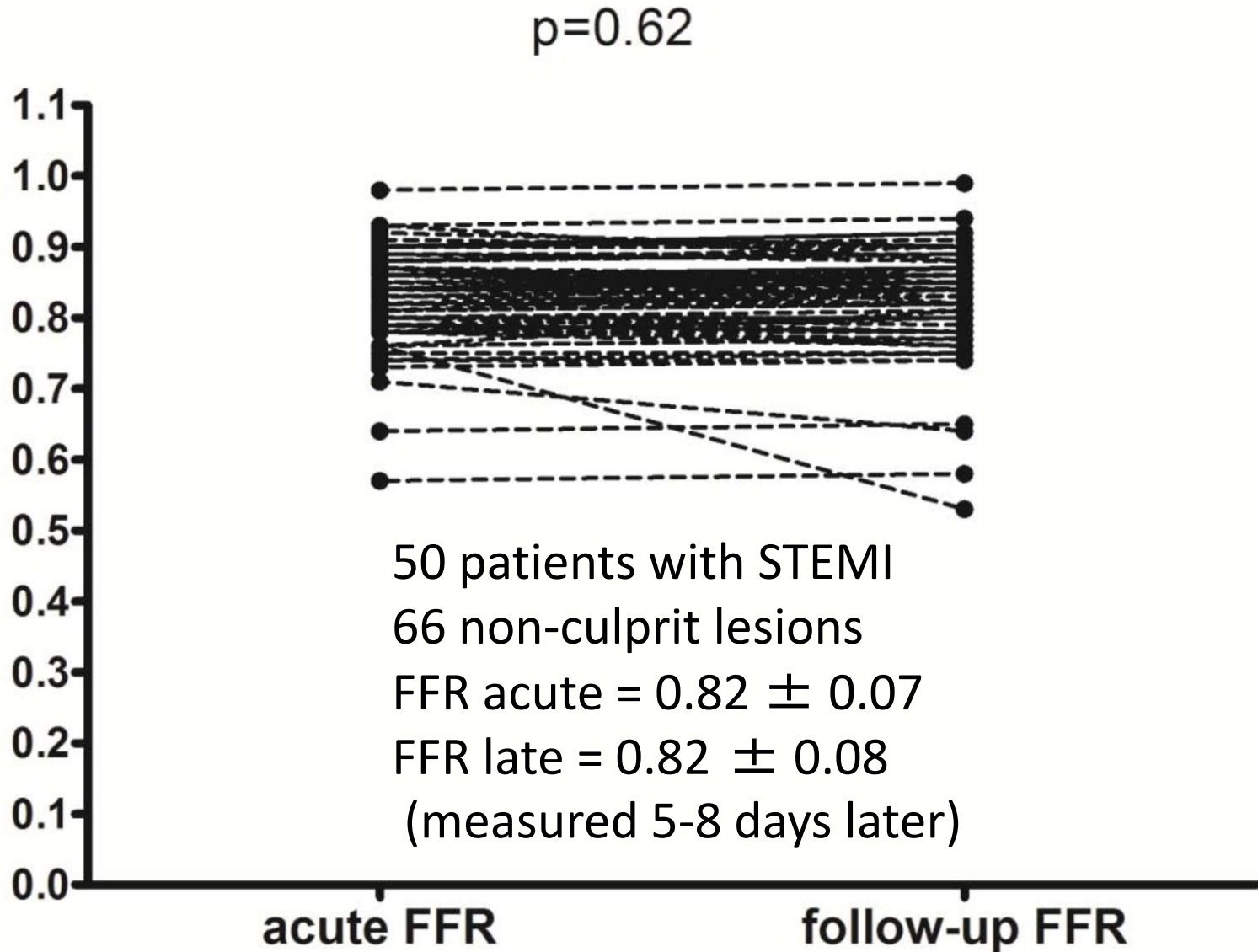
ACS non-culprits: *FFR stable!*



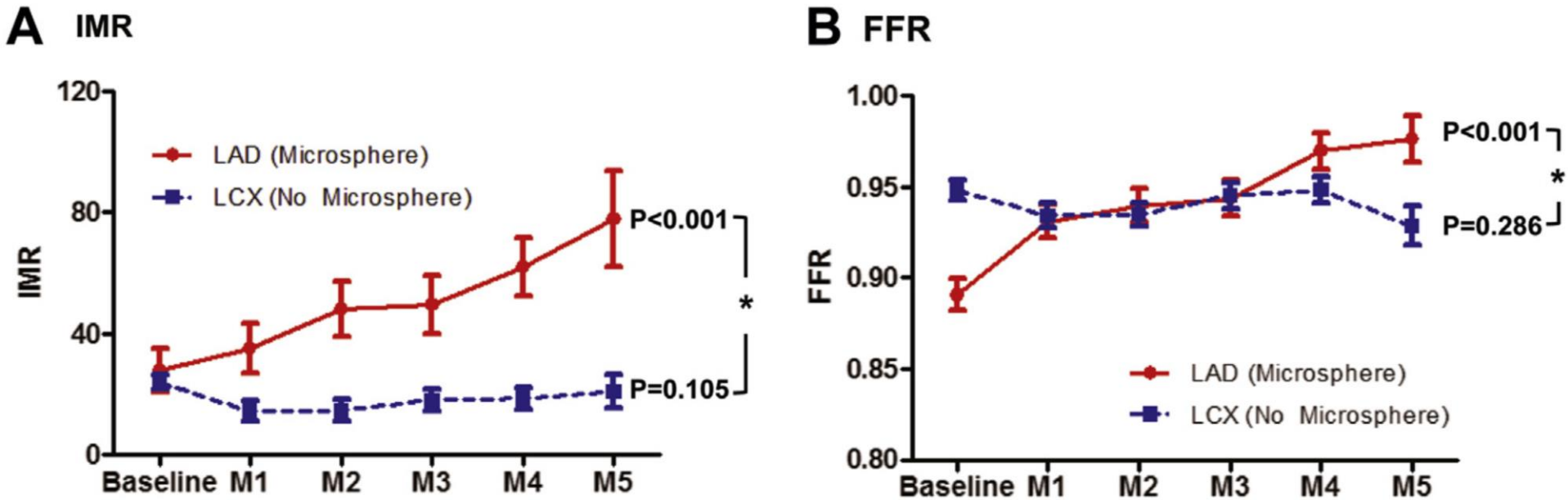
101 patients with ACS
STEMI in 75%
FFR acute = 0.77 ± 0.13
FFR late = 0.77 ± 0.13
(measured 35 days later)
Only 2 changed >0.8 to <0.75

Figure 1. Plot of FFR Values of Nonculprit Coronary Artery Stenoses During the Acute Phase and at Follow-Up

ACS non-culprits: *FFR stable!*



ACS non-culprits: *FFR and IMR stable!*



FFR and IV adenosine safe in ACS

- FAMOUS-NSTEMI
 - 704 of 706 (*99.7%*) had successful FFR
 - 2 of 704 (*0.3%*) had wire-related injury
 - 0 of 350 (*0.0%*) had adenosine-related MACE
- MR-MI (STEMI culprits for IMR)
 - 0 of 298 (*0.0%*) had wire-related injury
 - 0 of 298 (*0.0%*) had adenosine-related MACE
- COMPARE-ACUTE (non-culprit STEMI)
 - 867 of 885 (*98.0%*) had successful FFR
 - 2 of 885 (*0.2%*) had wire-related injury
 - “brief episodes of AV conduction delay”
 - “moderate drops in blood pressure”

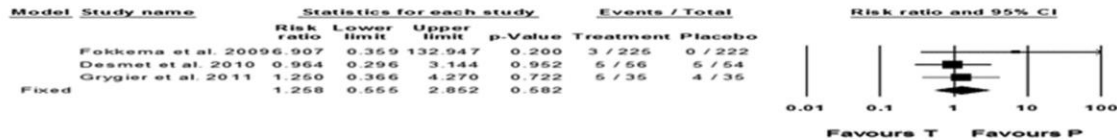
FAMOUS = Layland J, *Eur Heart J*. 2015 Jan 7;36(2):100-11. (Results from Table 2, results section)

MR-MI and FAMOUS = Ahmed N, *Int J Cardiol*. 2016 Jan 1;202:305-10.

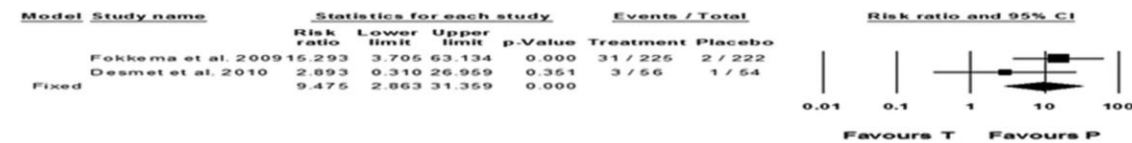
COMPARE-ACUTE = Smits PC, *NEJM*. 2017 Mar 30;376(13):1234-1244. (Results from Table 2, methods)

IC adenosine safe in ACS patients

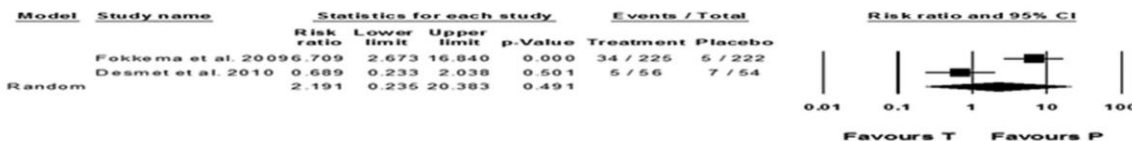
CP: Treatment (T) vs. Placebo (P)



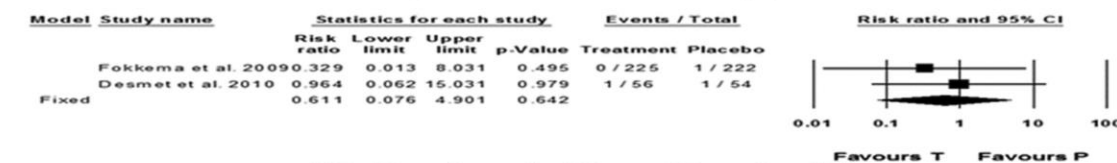
Second Degree AV Block: Treatment (T) vs. Placebo (P)



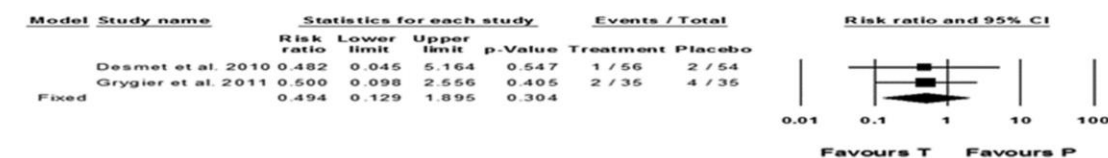
Bradycardia: Treatment (T) vs. Placebo (P)



Ventricular Tachycardia: Treatment (T) vs. Placebo (P)



VF: Treatment (T) vs. Placebo (P)



7 trials in acute MI

1030 subjects

Treated after primary PCI

IC adenosine vs placebo

No difference in: chest pain, bradycardia, VT/VF

Higher rates of 2oAVB

Guidelines *uncertain* for non-culprit

NSTEMI in ESC (2015)

5.6.5.3 Revascularization strategies and outcomes

There is a lack of prospective randomized investigations addressing the type (i.e. complete vs. incomplete) and timing (i.e. simultaneous vs. staged) of revascularization in NSTEMI-ACS. A complete revascularization strategy of significant lesions should be pursued in multivessel disease patients with NSTEMI-ACS based on two considerations.

European = Roffi M, *Eur Heart J*. 2015;37(3):267-315.

American = Amsterdam EA, *JACC*. 2014 Dec 23;64(24):e139-228.

STEMI in ESC (2017)

11. Gaps in the evidence and areas for future research

The best management of non-IRA lesions should be addressed. Unresolved issues are the best criteria to guide PCI (angiography, FFR, or assessment of plaque vulnerability) and the best timing for complete revascularization if indicated (during index PCI or staged, including staged during hospitalization vs. after discharge).

European = Ibanez B, *Eur Heart J*. 2018 Jan 7;39(2):119-177.

American = O'Gara PT, *JACC*. 2013 Jan 29;61(4):e78-140.

NSTEMI in ACC/AHA (2014)

5.1.1. PCI—General Considerations: Recommendation

CLASS IIb

1. A strategy of multivessel PCI, in contrast to culprit lesion–only PCI, may be reasonable in patients undergoing coronary revascularization as part of treatment for NSTEMI-ACS (330,359–364). (Level of Evidence: B)

STEMI in ACC/AHA (2013)

12.6. Approach to Noninfarct Artery Disease

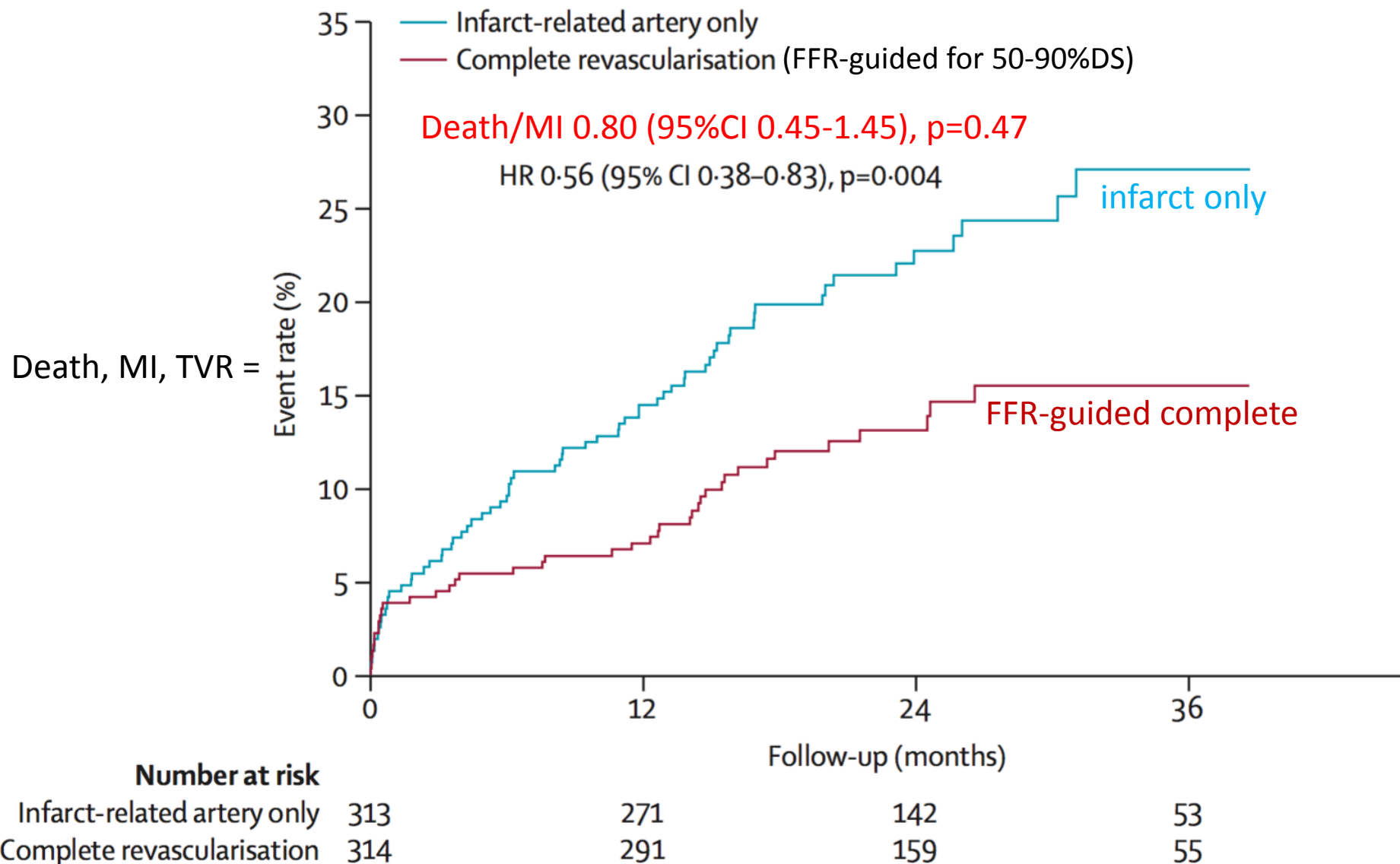
There is great variability in the evaluation and management of nonculprit coronary artery disease in stable patients without HF or shock, both at the time of primary PCI and later during the hospital course.

PRIMULTI: FFR in STEMI non-culprit

Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3—PRIMULTI): an open-label, randomised controlled trial

- bystander lesion *>50% diameter stenosis*
- culprit only arm: only primary PCI
- *FFR arm: 2nd procedure 2 days after index STEMI*
- *69% of FFR-guided lesions were ≤ 0.8*

PRIMULTI: FFR in STEMI non-culprit



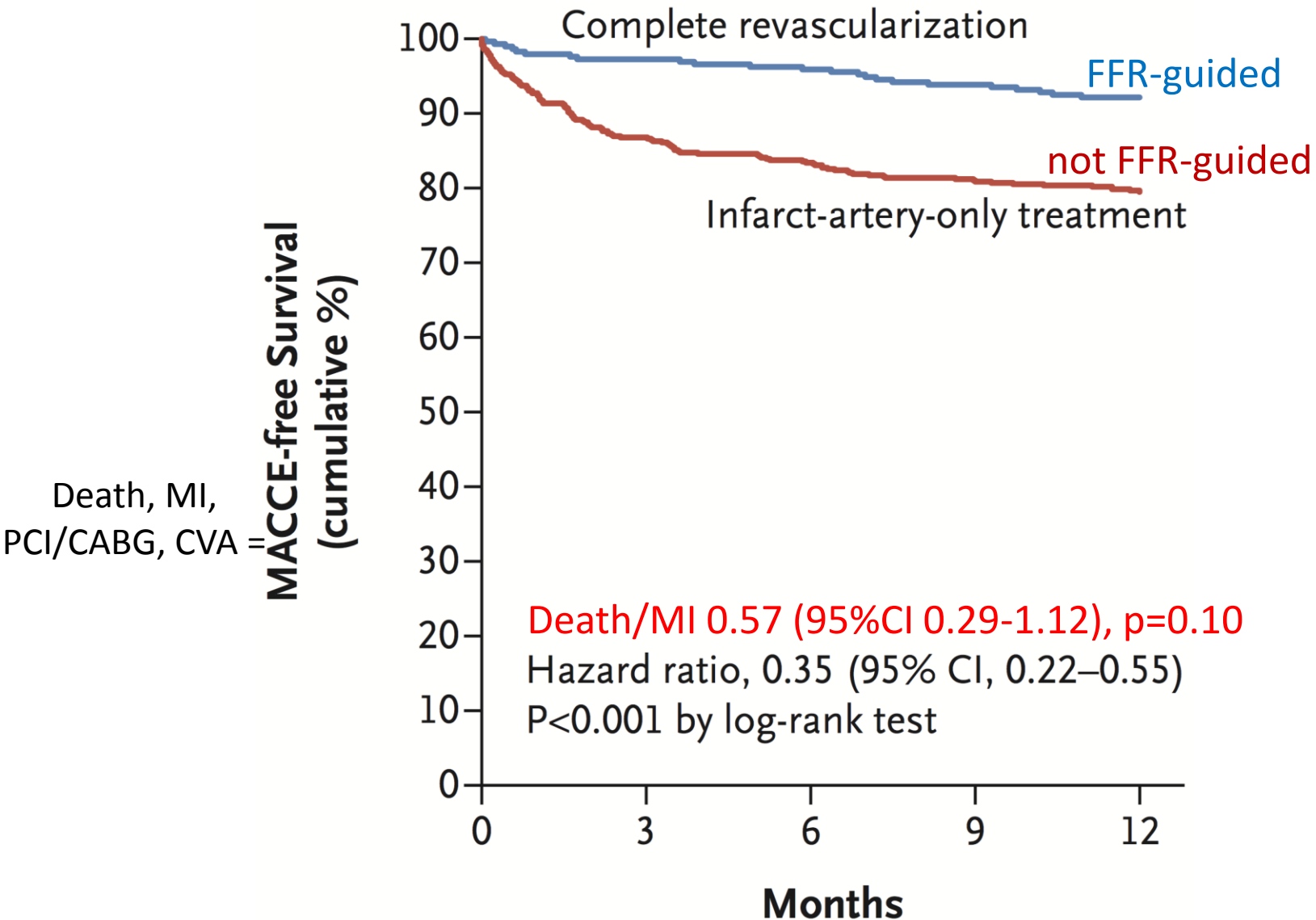
Compare-Acute: FFR in STEMI

ORIGINAL ARTICLE

Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction

- bystander lesion *>50% diameter stenosis*
- culprit only arm: only primary PCI
- *FFR arm: over 80% treated during index STEMI*
- *50% of lesions had $FFR \leq 0.8$*

Compare-Acute: FFR in STEMI



Smits PC, *NEJM*. 2017 Mar 30;376(13):1234-1244. (Figure 2 with annotations and results from Table 3)

Now or later?

In two patients (0.2%), both in the infarct-artery-only group, a serious adverse event related to FFR occurred. In one patient, the FFR wire caused a dissection in the non–infarct-related right coronary artery, with subsequent occlusion, infarction, and in-hospital death. In the other patient, after withdrawal of the FFR wire, the non–infarct-related left anterior descending coronary artery became occluded and the patient had ST-segment elevation and recurrent chest pain. PCI of the artery was performed successfully.

Does FFR reduce or increase PCI?

Non-culprit revascularization higher with FFR-guided treatment

= (follow-up) / N = incidence

- Compare-Acute

- ✓ FFR-guided = (18) / 295 = **6.1%**

- ✓ culprit only = (103) / 590 = **17.4%**

- PRIMULTI

- ✓ FFR-guided = (17) / 314 = **5.4%**

- ✓ culprit only = (52) / 313 = **16.6%**

Non-culprit revascularization appears lower when FFR-guided

FFR increases PCI vs culprit only!

Non-culprit revascularization higher with FFR-guided treatment

= (index + follow-up) / N = incidence

- Compare-Acute
 - ✓ FFR-guided = $(163 + 18) / 295 = 61.4\%$
 - ✓ culprit only = $(1 + 103) / 590 = 17.6\%$
- PRIMULTI
 - ✓ FFR-guided = $(217 + 17) / 314 = 74.5\%$
 - ✓ culprit only = $(2 + 52) / 313 = 17.3\%$

But only when discounting index revascularization!

FULL REVASC: FFR in STEMI

FULL  REVASC

For patients | For new centers | Who we are | Documents



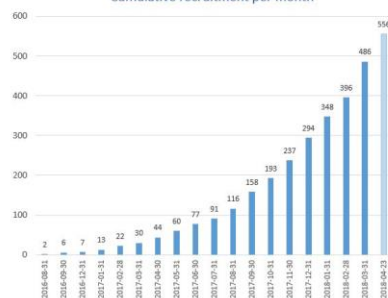
Recruitment update 23-April-2018

Active sites	Principal Investigator	No. of subjects randomized until 2018-04-23	Change since last week
DK01 Copenhagen	Thomas Engström (NC)	81	3
DK02 Aarhørg	Leif Thuesen	12	1
DK04 Aarhus	Evald Hej Christiansen	18	0
FI01 Helsinki	Mika Laine (NC)	8	0
FI02 Tampere	Olli Kajander	17	0
LV01 Riga	Andrejs Erglis (NC)	1	0
RS01 Belgrade Cc Serbia	Goran Stankovic (NC)	15	2
RS02 Belgrade Cc Zemun	Aleksandar Neskovic	1	1
RS03 Sremska Kamenica	Ilija Srdanovic	34	11
SE01 Stockholm KS Solna	Andreas Rück (NC)	54	0
SE02 Uppsala	Stefan James	33	2
SE03 Stockholm KS Huddinge	Brynjólfur Mogensen	17	0
SE04 Stockholm Danderyd	Rickard Linder	22	0
SE05 Stockholm Capio St Göran	Pontus Lindroos	6	0
SE06 Stockholm Södersjukhuset	Nils Witt	17	1
SE07 Örebro	Thomas Kellerth	31	1
SE08 Eskilstuna	Mehmet Hamid	39	0
SE09 Umeå	Jonas Andersson	25	0
SE10 Linköping (Norrköping)	Dario Hauer	46	2
SE11 Lund	David Erlinge	2	0
SE13 Jönköping	Jörg Laueremann	34	0
SE14 Göteborg SU Sahlgrenska	Oskar Angerås	15	0
SE16 Sundsvall	Bo Lindvall	6	0
SE17 Östersund	Anders Ulvenstam	7	2
SE18 Falun	Kristina Hambræus	6	0
SE19 Västerås	Martin Lindholm	3	0
SE20 Gävle	Robert Kästberg	6	0
Total of 27 active sites		556	26

Registry RCT

- STEMI or high-risk NSTEMI
- **4052 subjects**
- **556 enrolled (14%)**
- FFR-guided PCI during index admission
- No shock, LM, or prior CABG
- **Endpoint: all-cause death or MI**

Cumulative recruitment per month



American guidelines now favoring FFR

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<http://dx.doi.org/10.1016/j.jacc.2016.10.034>

CLINICAL DOCUMENT

ACC/AATS/AHA/ASE/ASNC/SCAI/ SCCT/STS 2016 Appropriate Use Criteria for Coronary Revascularization in Patients With Acute Coronary Syndromes

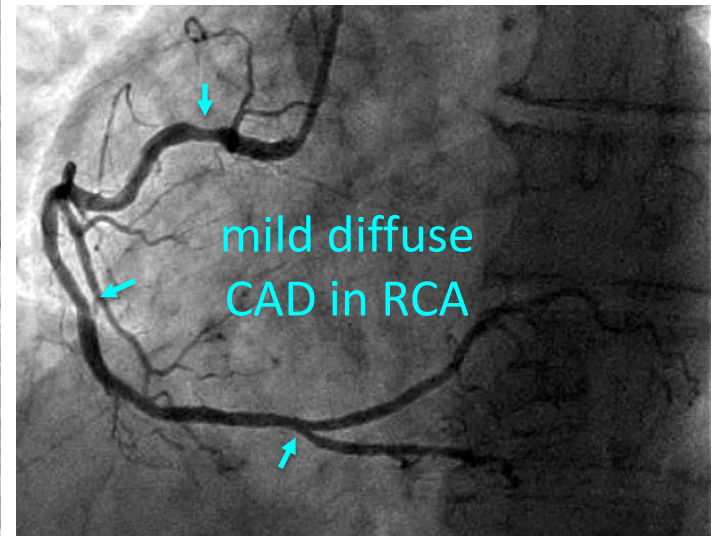
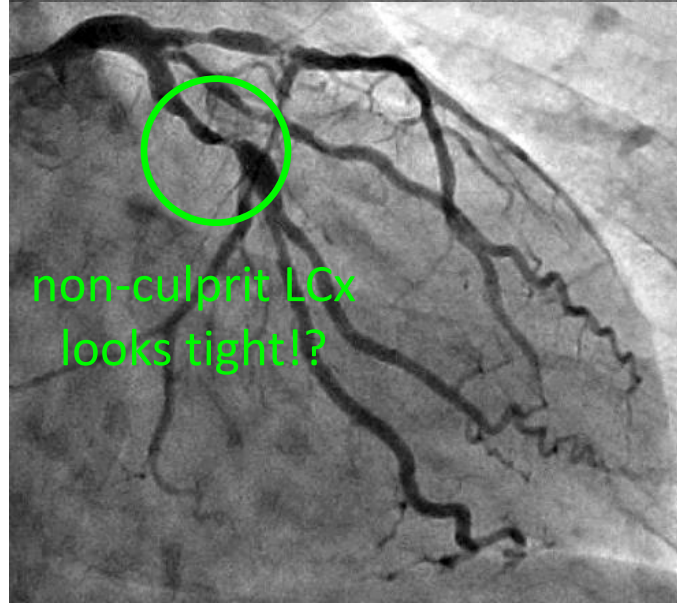
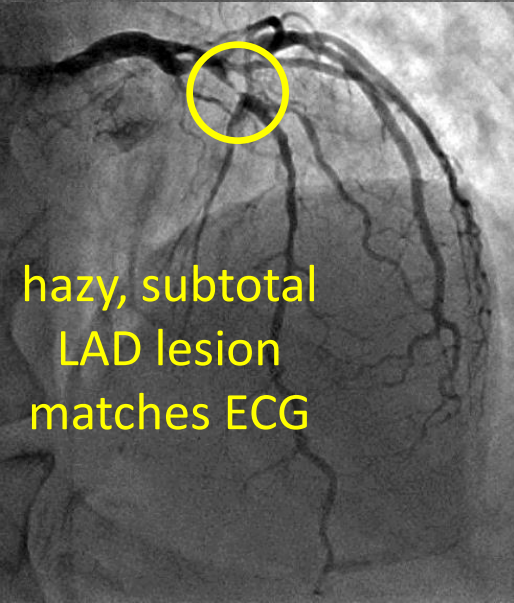
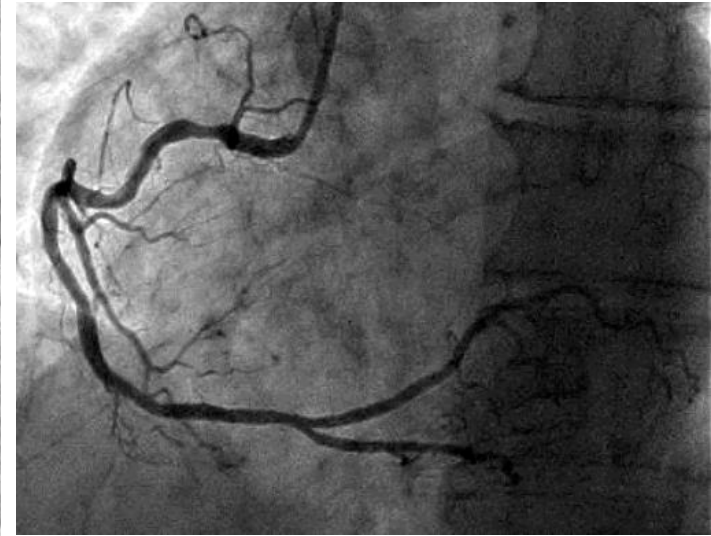


TABLE 1.3 STEMI—Revascularization of Nonculprit Artery During the Initial Hospitalization

Indication	Appropriate Use Score (1-9)
Successful Treatment of the Culprit Artery by Primary PCI or Fibrinolysis Revascularization of 1 or More Nonculprit Arteries During the Same Hospitalization	
Revascularization by PCI or CABG	
14. <ul style="list-style-type: none">■ Asymptomatic■ One or more additional intermediate (50%-70%) stenoses■ FFR performed and ≤ 0.80	A (7)

A = appropriate for PCI/CABG

STEMI culprit plus non-culprit

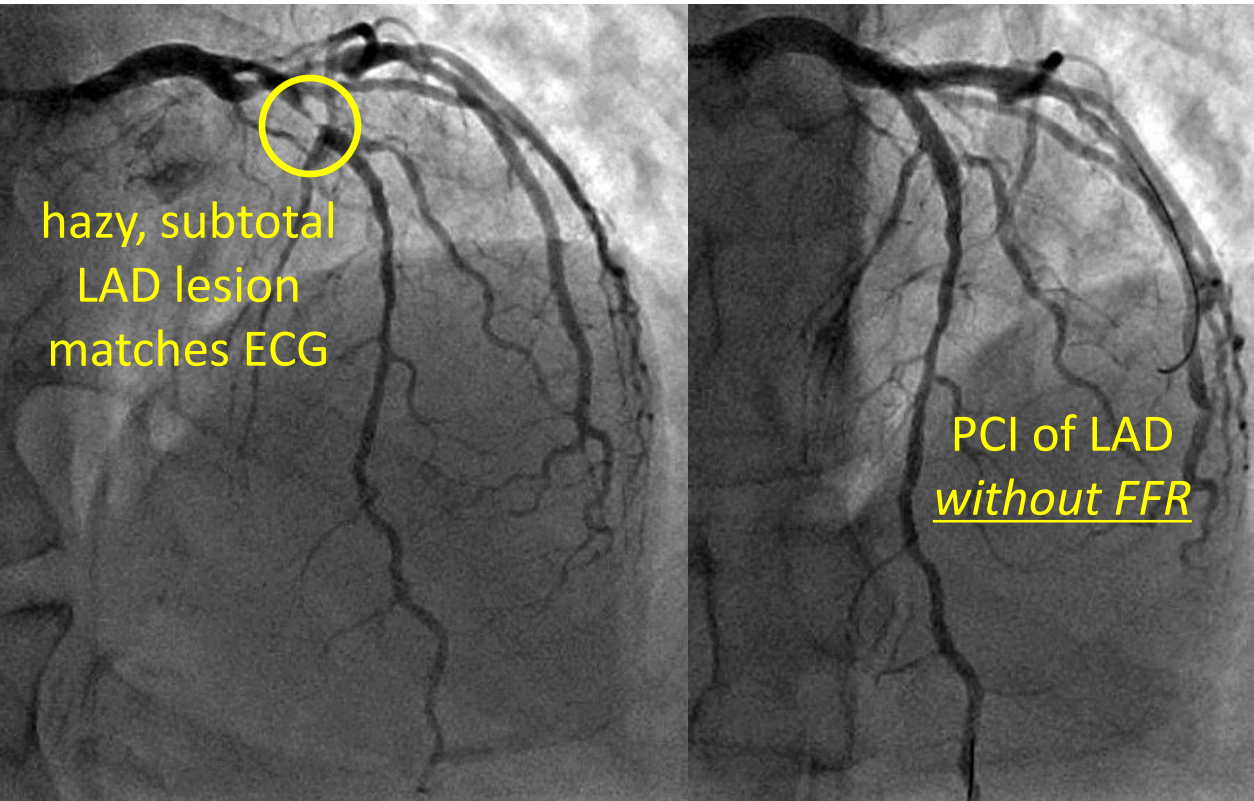


hazy, subtotal
LAD lesion
matches ECG

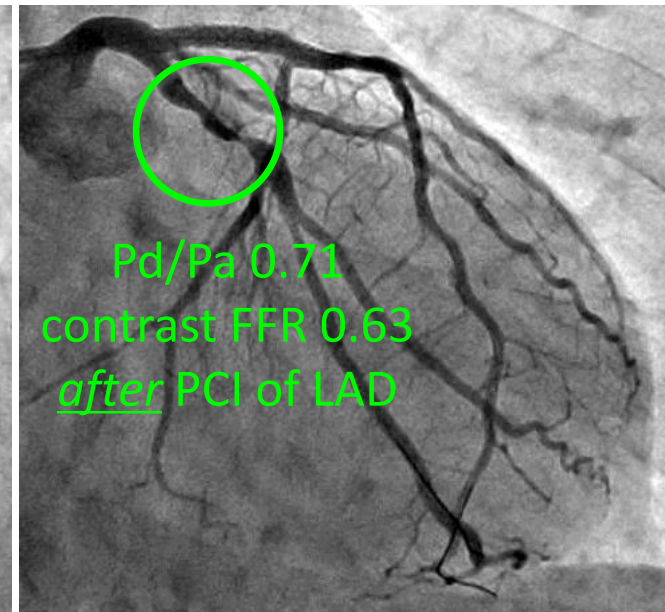
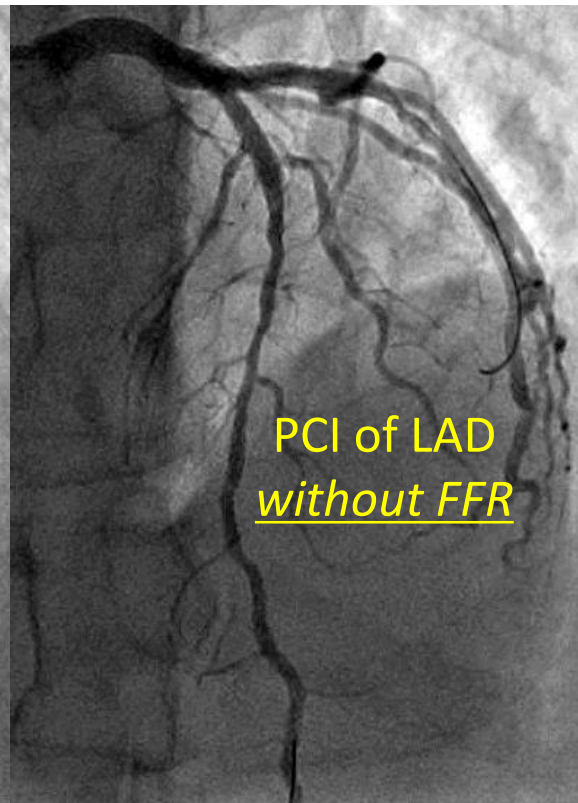
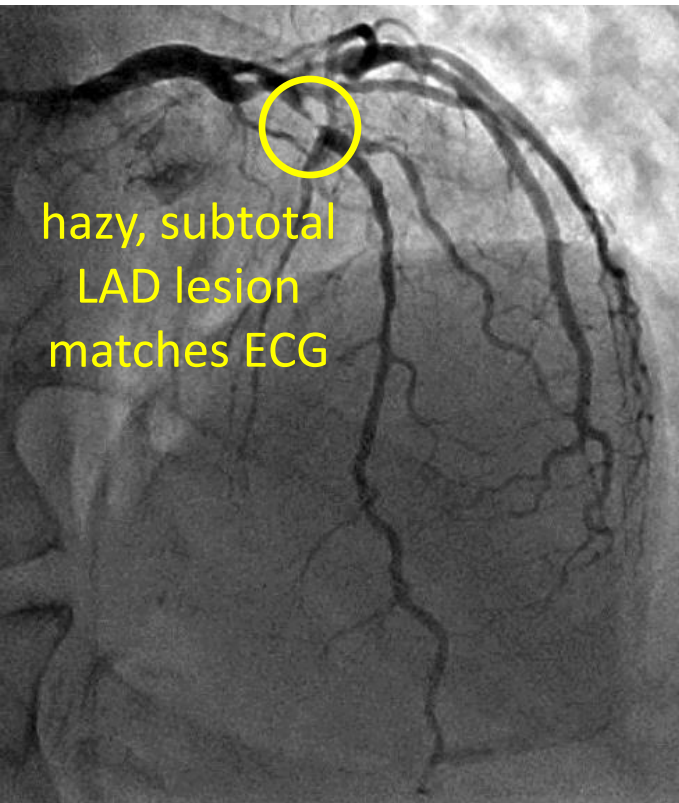
non-culprit LCx
looks tight!?

mild diffuse
CAD in RCA

1st = PCI of culprit (no FFR needed)



2nd = FFR-guided PCI of non-culprit



When can we use FFR?

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