Post-PCI physiology: more important?

replace post-PCI imaging?

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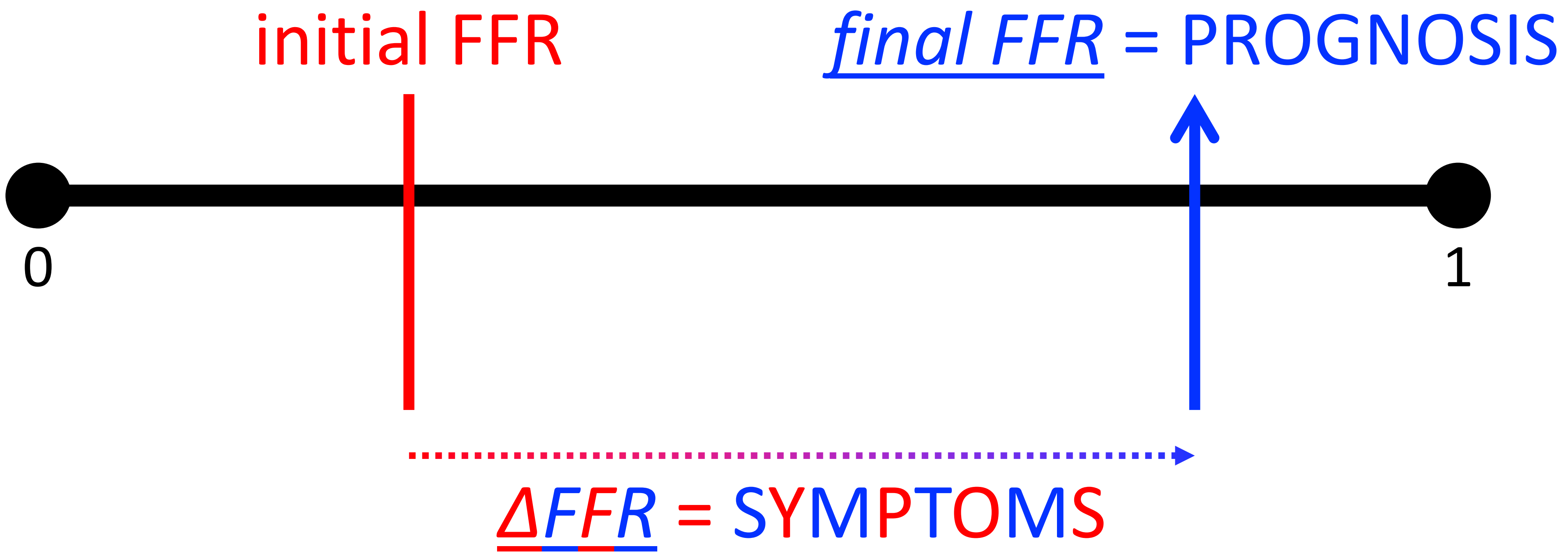
Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship	Organizations (chronologic)
• Grant/research support (to <ins>*institution*</ins>)	• St Jude Medical (CONTRAST, NCT02184117) • Volcano/Philips (DEFINE-FLOW, NCT02328820) • CoreAalst (PPG registry, NCT04789317) • Abiomed (local "DPTI" study)
• Licensing and associated consulting (to <ins>*institution*</ins>)	• Boston Scientific (smart-minimum FFR, 510(k) K191008)
• Support for educational meetings/training (honoraria/fees donated to <ins>*institution*</ins>)	• Various, including academic and industry
• PET software 510(k) from FDA (application by Lance Gould, to <ins>*institution*</ins>)	• K113754 (cfrQuant, 2011) • K143664 (HeartSee, 2014) • K171303 (HeartSee update, 2017) • K202679 (HeartSee update, 2020)
• Patents filed (USPTO serial numbers 62/597,134 + 62/907,174)	• SAVI and ΔP/Q methods • Correction of fluid-filled catheter signal

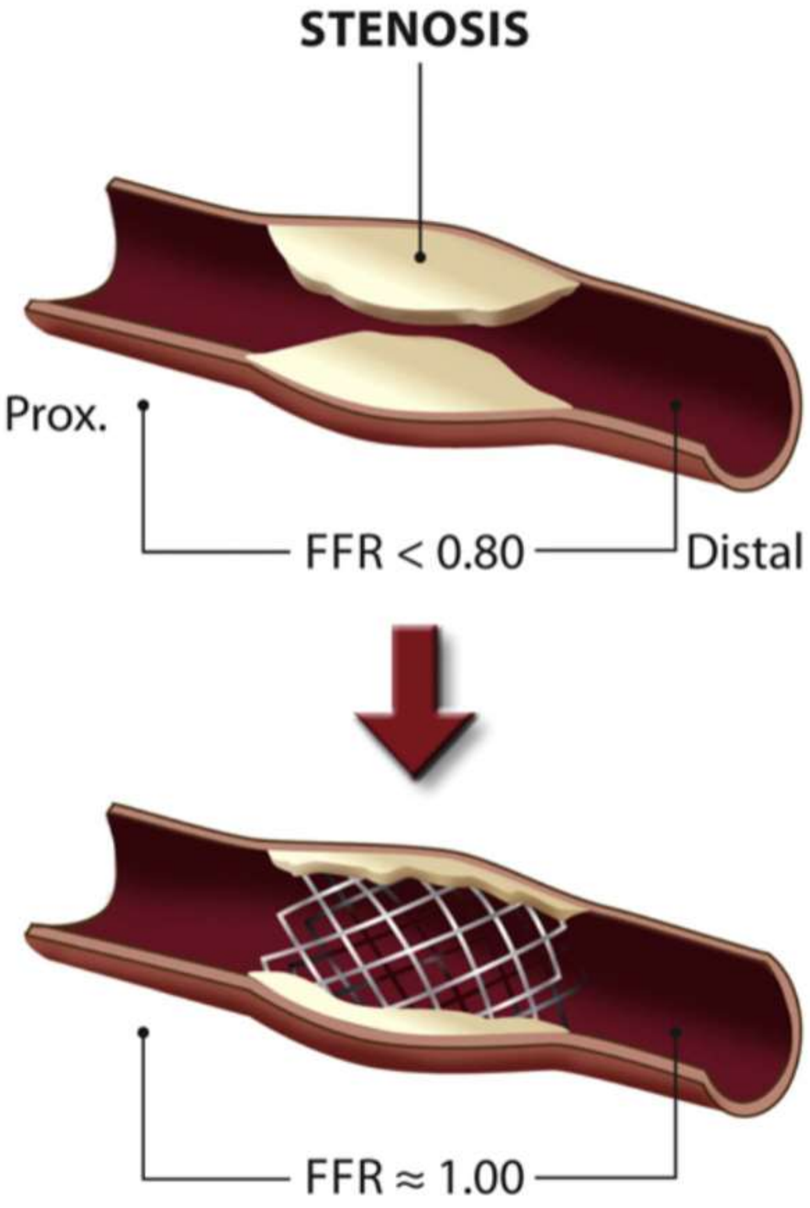
Key concept



final FFR

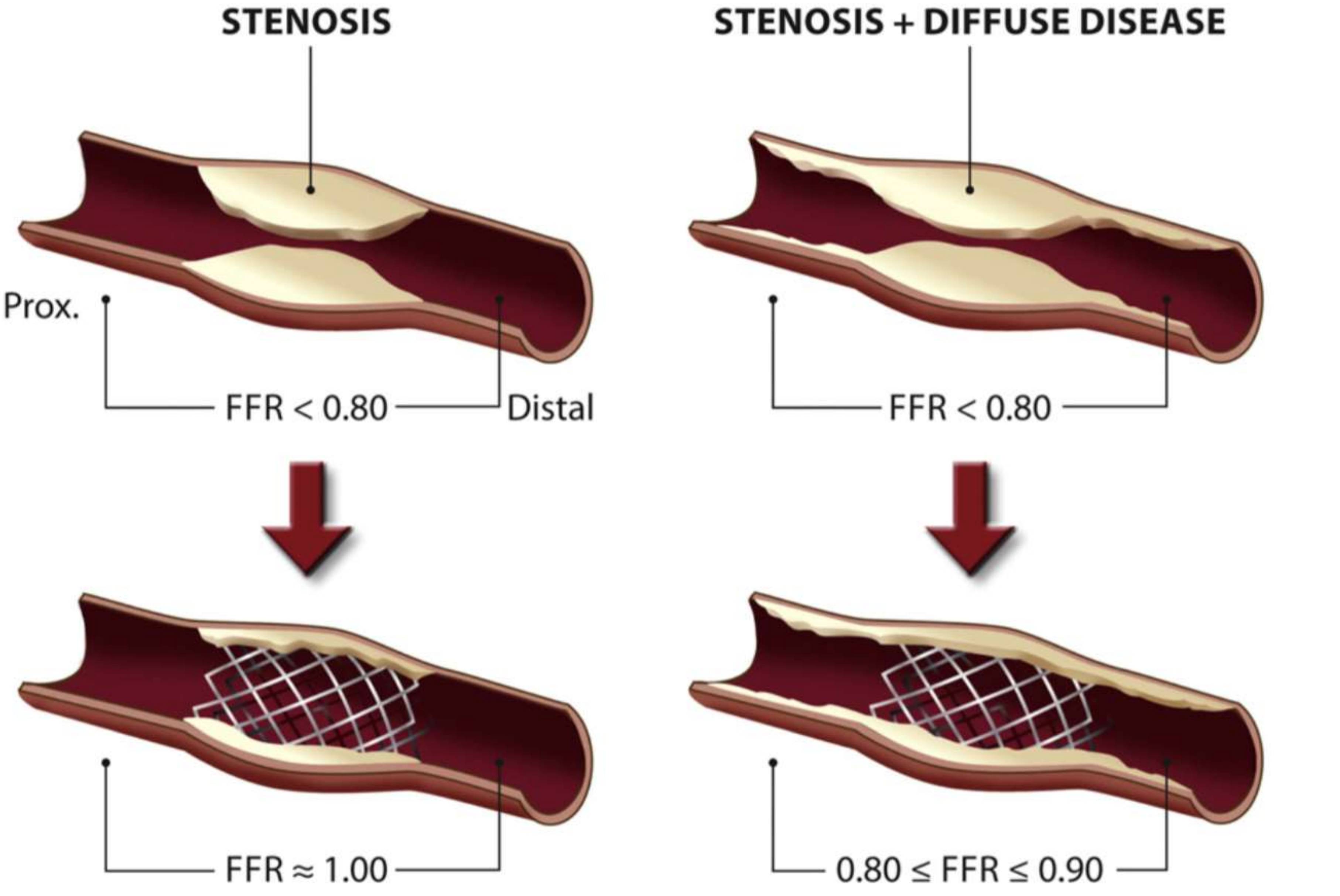
= prognosis

FFR could be perfect for a focal lesion



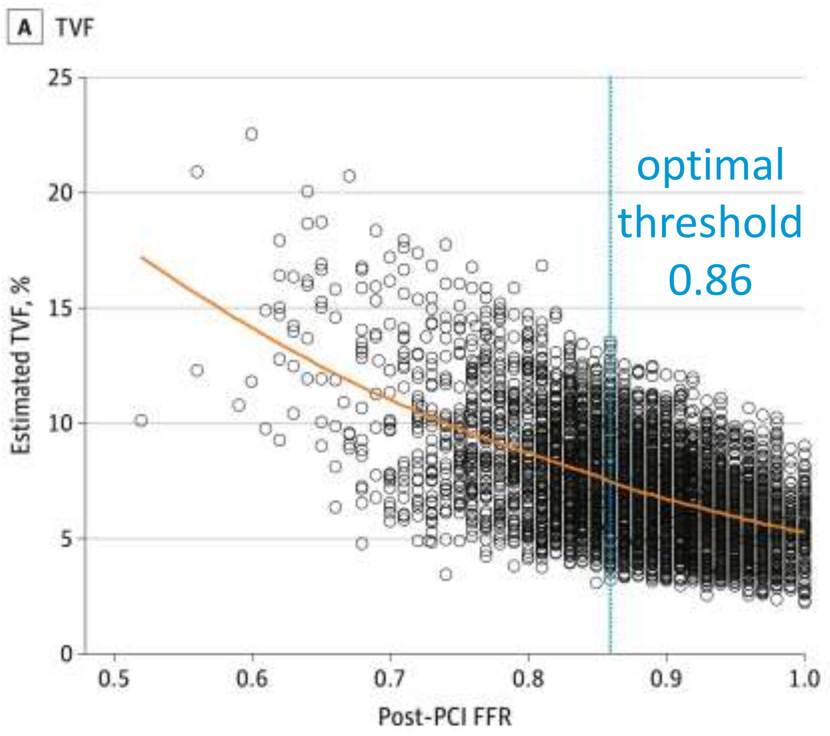
Rimac G, *Am Heart J*. 2017 Jan;183:1-9. (Figure 7)

Post-PCI FFR ≈ diffuse disease burden



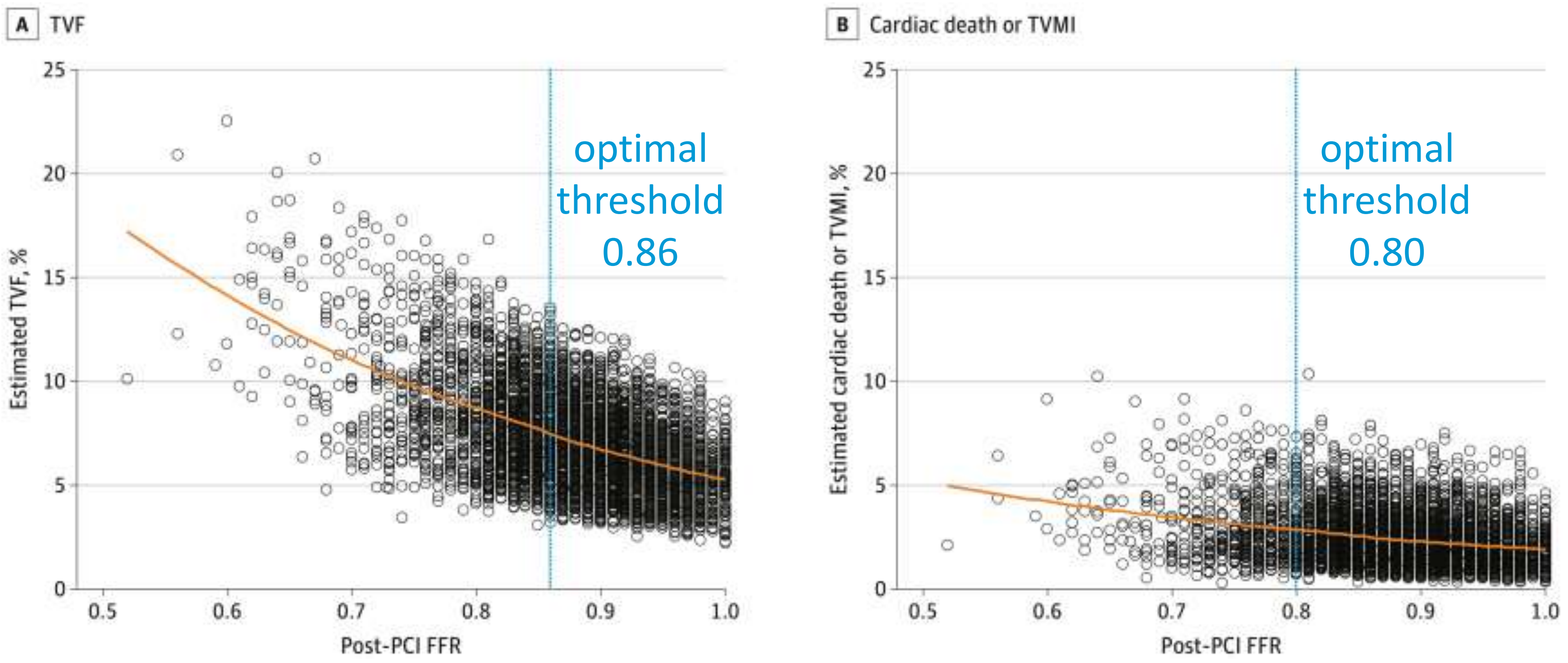
Rimac G, *Am Heart J*. 2017 Jan;183:1-9. (Figure 7)

FFR after modern DES in 5869 vessels



Hwang D, *JAMA Netw Open*. 2022 Sep 1;5(9):e2232842. (Figure 3 *annotated* and part of Table with *highlights*)

FFR after modern DES in 5869 vessels



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FFR after modern DES in 5869 vessels

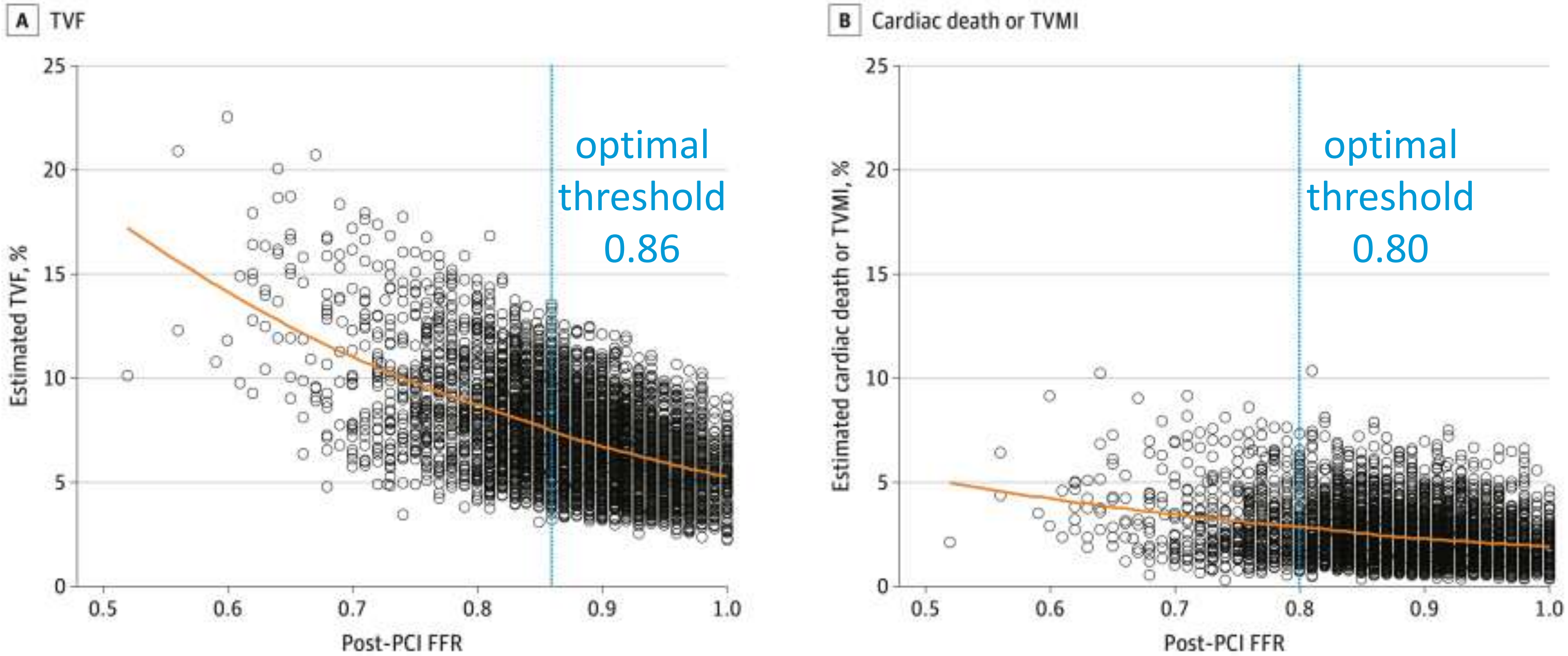


Table. Risk of Clinical Events at 2 Years per Post-PCI FFR 0.01 Decrease

Event	Total events, No. (%)	Adjusted HR (95% CI)	*P* value
Target vessel failure	340/5204 (7.2)	1.035 (1.020-1.051)	<.001
Cardiac death or TVMI	111/5204 (2.4)	1.034 (1.001-1.068)	.049
Cardiac death	64/5274 (1.4)	1.045 (1.011-1.081)	.009
TVMI	57/5207 (1.2)	1.018 (0.973-1.066)	.44
TVR	285/5276 (6.0)	1.034 (1.015-1.052)	<.001

Hwang D, *JAMA Netw Open*. 2022 Sep 1;5(9):e2232842. (Figure 3 *annotated* and part of Table with *highlights*)

TVF in multivariable Cox, 2438 vessels

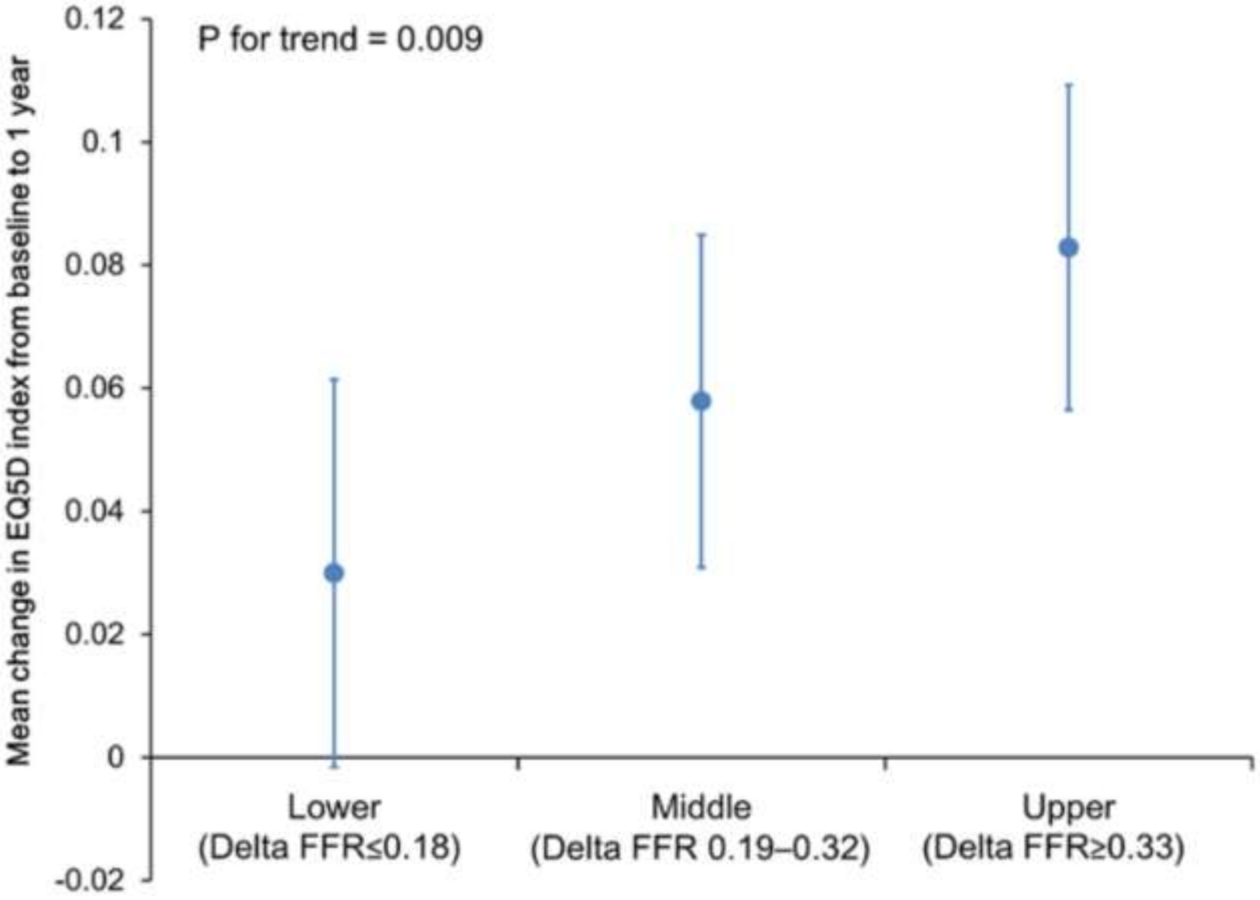
Variables	Adjusted HR (95% CI)	p-value
Age	1.01 (1 - 1.03)	0.130
Hypertension	1.06 (0.71 - 1.57)	0.789
Dyslipidemia	1.3 (0.9 - 1.87)	0.157
Diabetes mellitus	1.09 (0.82 - 1.45)	0.536
FFR post-PCI per 0.10	0.64 (0.51 - 0.8)	<0.001
FFR pre-PCI per 0.10	0.93 (0.84 - 1.03)	0.180
Vessel type (non-LAD)	0.99 (0.73 - 1.35)	0.963
Number of stents	1.14 (0.84 - 1.57)	0.400
Total stent length	1 (0.98 - 1.01)	0.796

Collet C, under journal review. (Table S7 with highlights)

Δ FFR

= symptoms

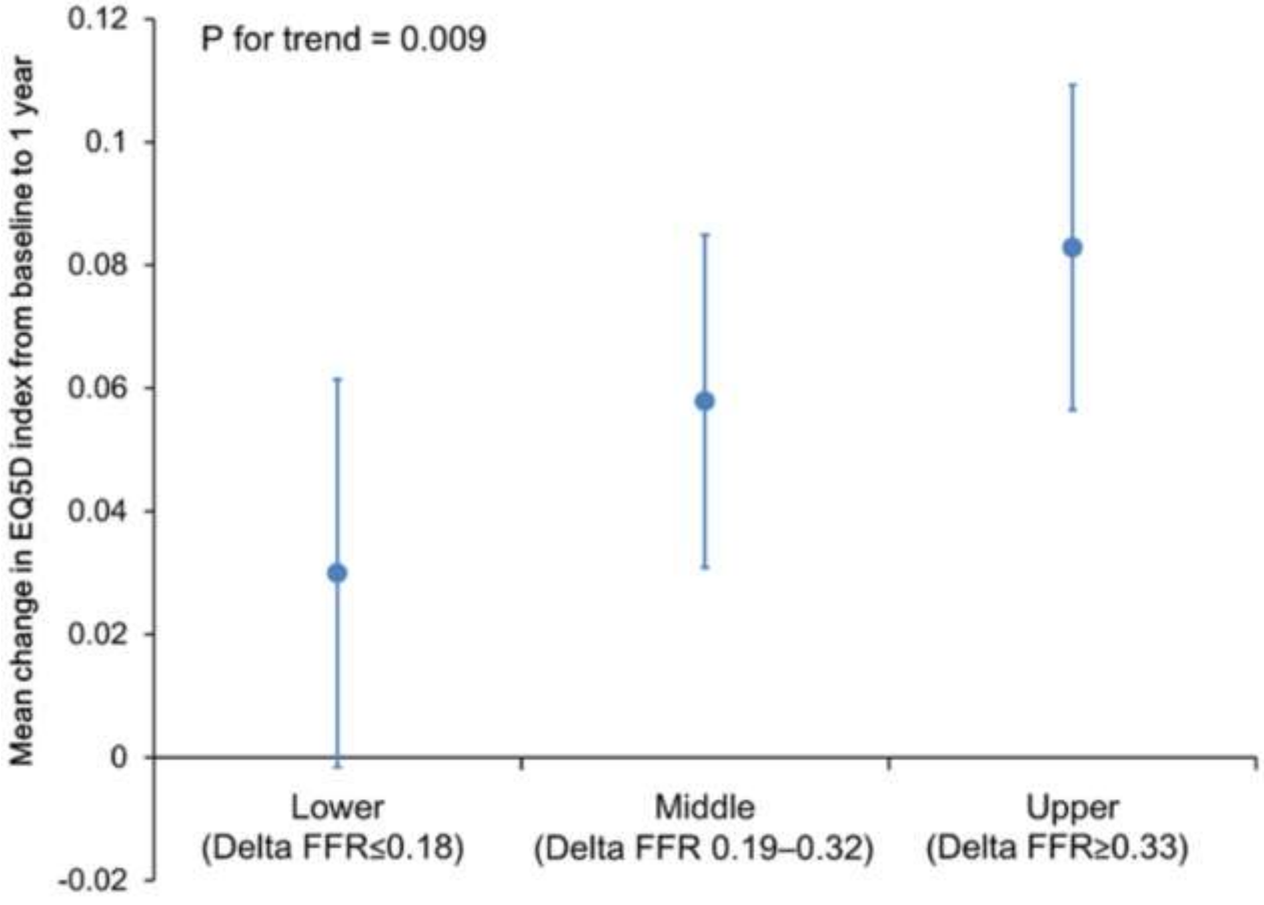
FFR improvement ≈ symptom improvement



n = 507 patients
in FAME 1 + 2
average FFR Δ +0.28

FAME 1+2 = Nishi T, *Circulation*. 2018 Oct 23;138(17):1797-1804. (Figure 5)

FFR improvement ≈ symptom improvement



n = 507 patients
in FAME 1 + 2
average FFR Δ +0.28

FFR Δ tertile	*SAQ summary*
lower	74.5
middle	81.5
upper	88.2

more angina ↓ less angina

p = 0.01
n = 162 patients
in TARGET-FFR
SAQ at 3 months

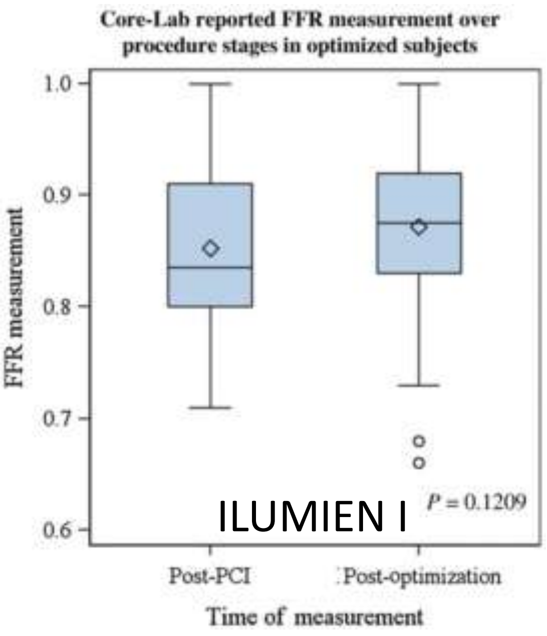
FAME 1+2 = Nishi T, *Circulation*. 2018 Oct 23;138(17):1797-1804. (Figure 5)
TARGET-FFR = Collison D, *EHJ*. 2021 Dec 1;42(45):4656-4668. (data taken from Table 5)

final FFR

optimize?

Does optimization with Δ<0.05 reduce TVF?

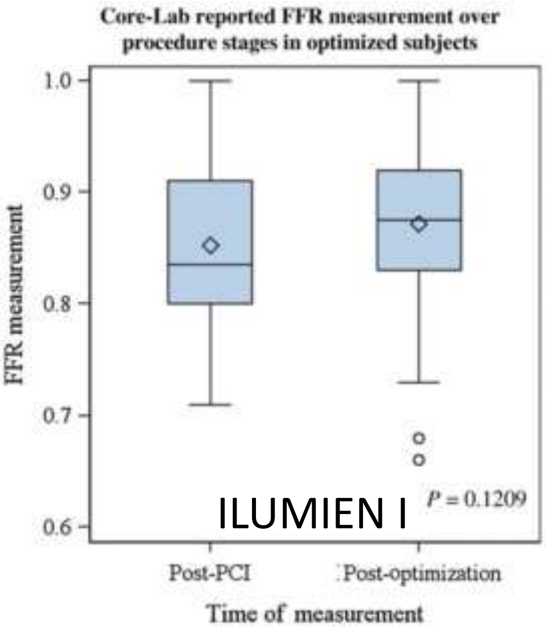
study	*N*	*tool*	*routine FFR*	*optimized*	*Δ*
ILUMIEN I	70	OCT	0.86	0.90	0.04

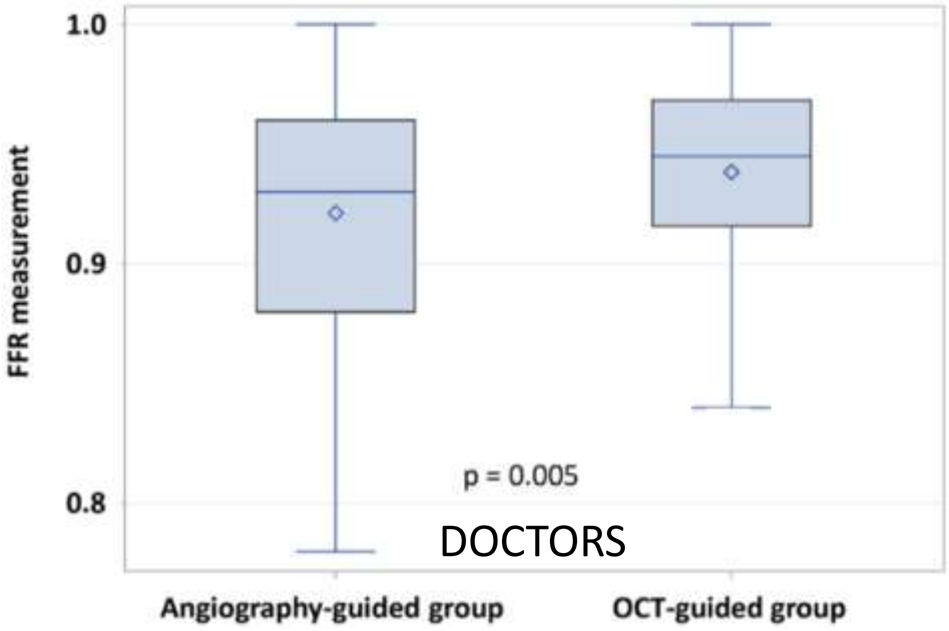


ILUMIEN I = Wijns W, *EHJ*. 2015 Dec 14;36(47):3346-55. (Figure 3B)

Does optimization with Δ<0.05 reduce TVF?

study	*N*	*tool*	*routine FFR*	*optimized*	*Δ*
ILUMIEN I	70	OCT	0.86	0.90	0.04
DOCTORS	240	OCT	0.92	0.94	0.02
TARGET-FFR	260	PIOS	0.85	0.86	0.01





ILUMIEN I = Wijns W, *EHJ*. 2015 Dec 14;36(47):3346-55. (Figure 3B)
DOCTORS = Meneveau N, *Circulation*. 2016 Sep 27;134(13):906-17. (Figure 2A)
TARGET-FFR = Collison D, *EHJ*. 2021 Dec 1;42(45):4656-4668. (from Table 3 for control vs PIOS "final")

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study	*N*	*tool*	*routine FFR*	*optimized*	*Δ*
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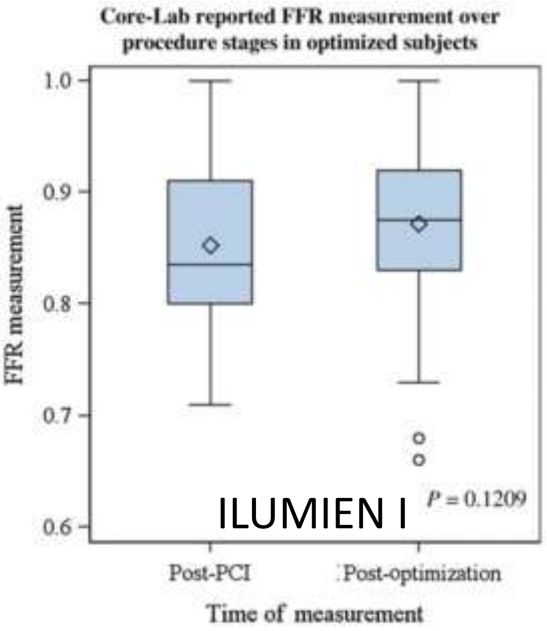

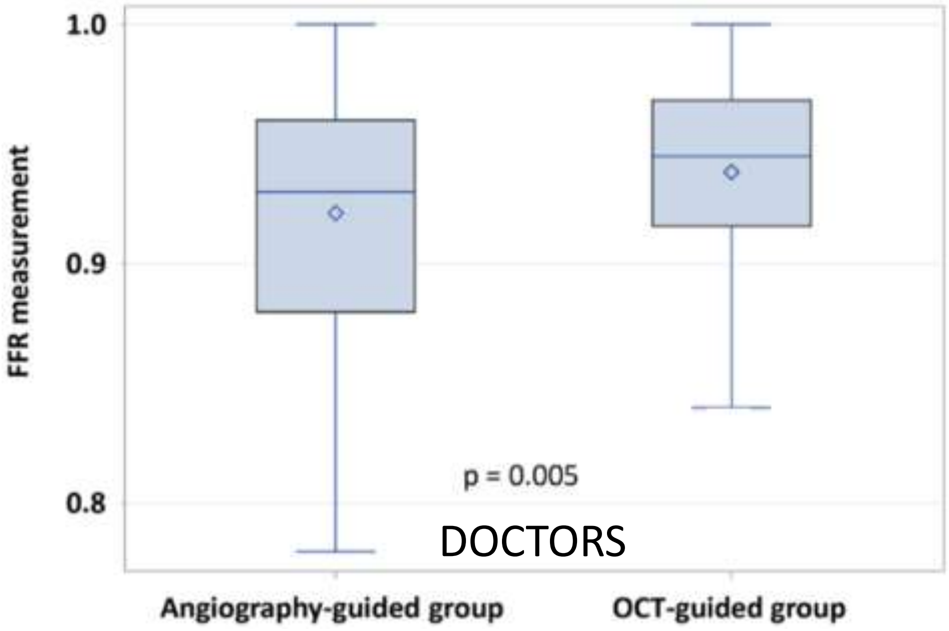

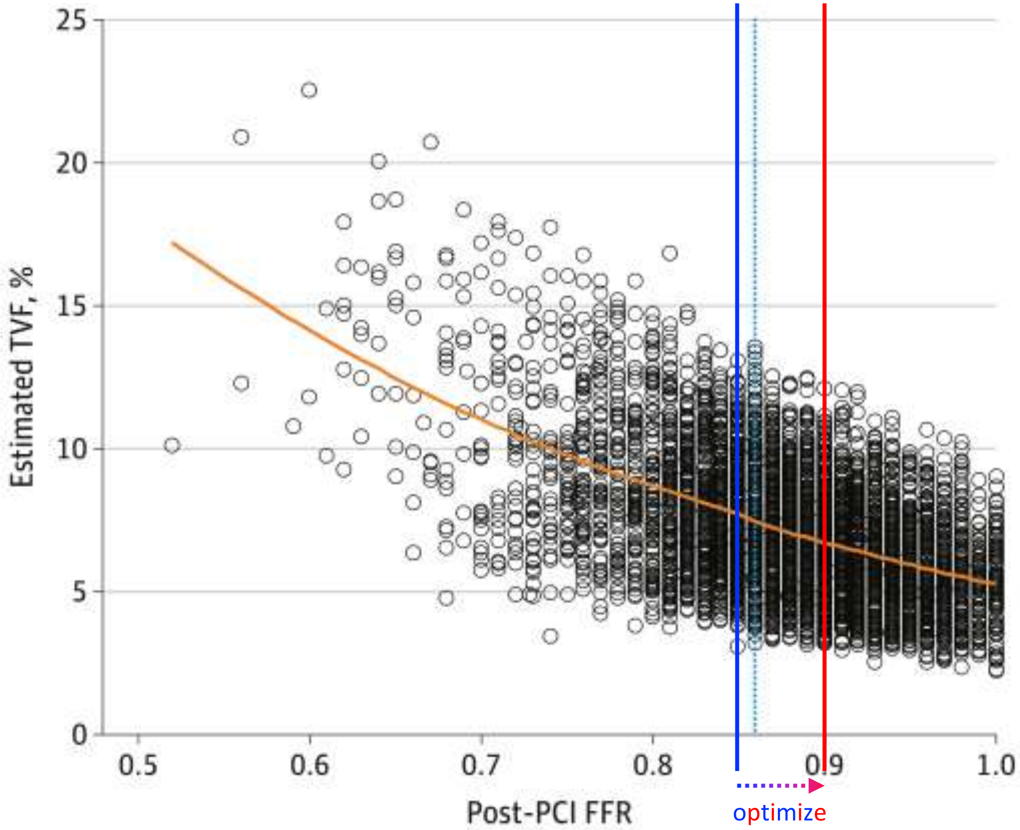

0.85 = 7.7% TVF

0.90 = 6.7% TVF

Δ +0.05 = -1.0%

ILUMIEN I = Wijns W, *EHJ*. 2015 Dec 14;36(47):3346-55. (Figure 3B)

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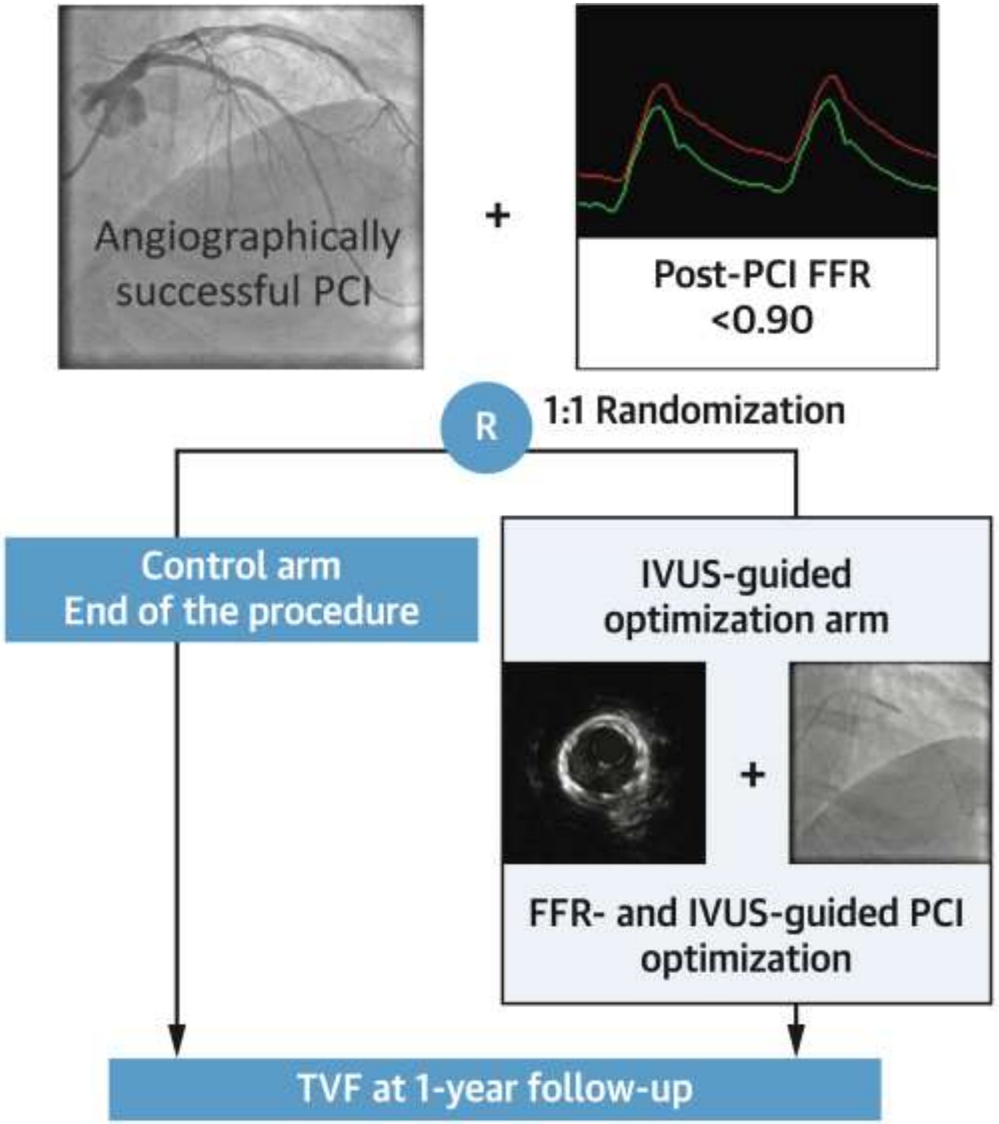
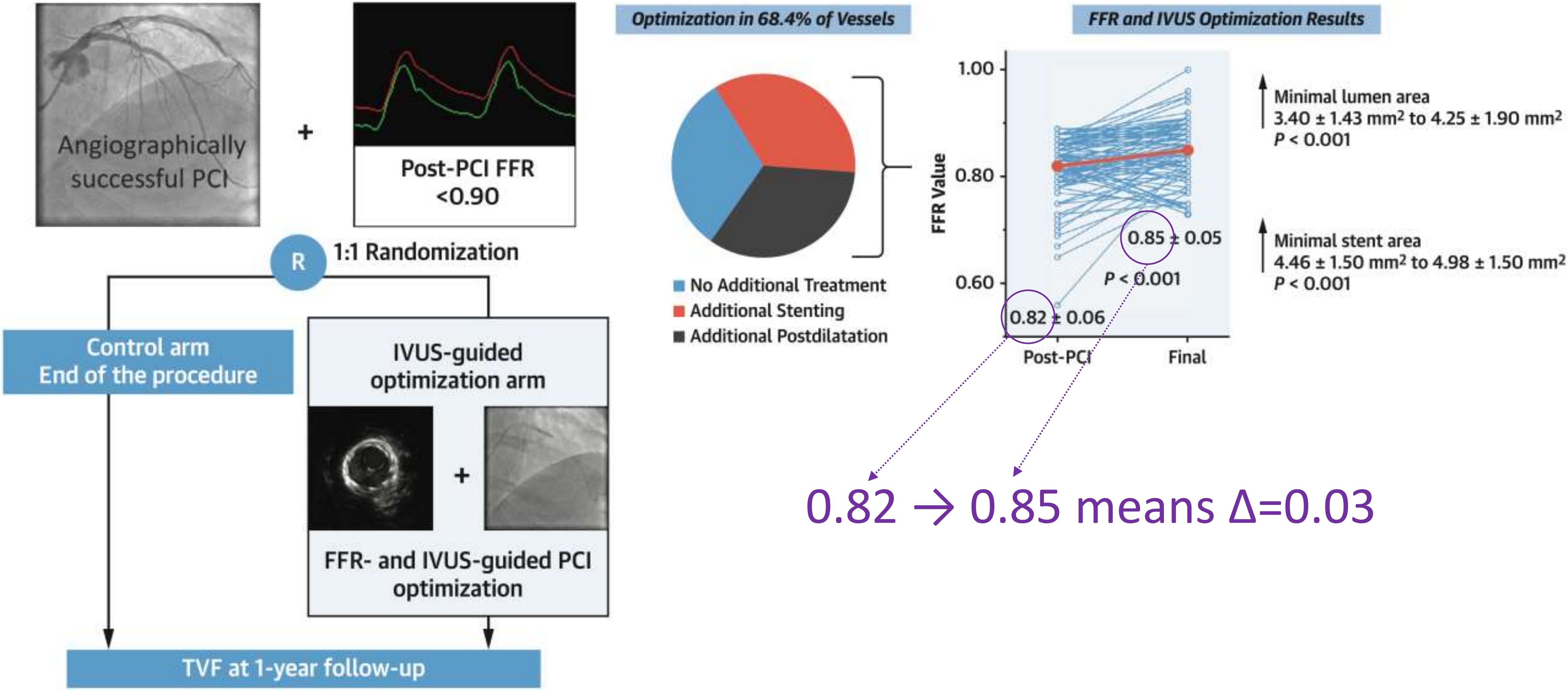
FFR-REACT trial confirms small change in TVF



N = 291

Neleman T, *JACC Cardiovasc Interv*. 2022 Aug 22;15(16):1595-1607. (Central Illustration excerpts)

FFR-REACT trial confirms small change in TVF



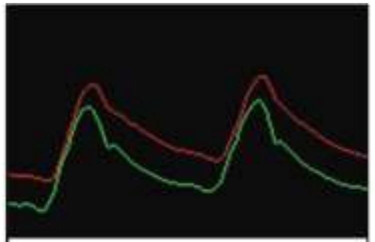
0.82 → 0.85 means Δ=0.03

N = 291

Neleman T, *JACC Cardiovasc Interv*. 2022 Aug 22;15(16):1595-1607. (Central Illustration excerpts with *annotations*)

FFR-REACT trial confirms small change in TVF

+

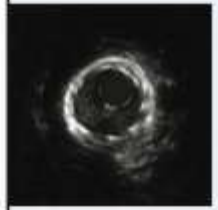


Post-PCI FFR
<0.90

R 1:1 Randomization

Control arm
End of the procedure

IVUS-guided
optimization arm



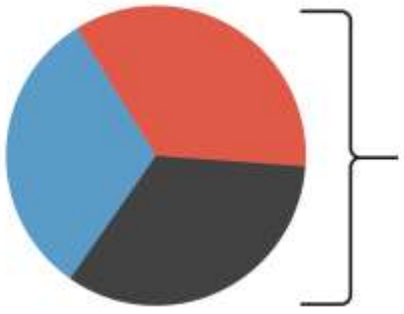
+

FFR- and IVUS-guided PCI
optimization

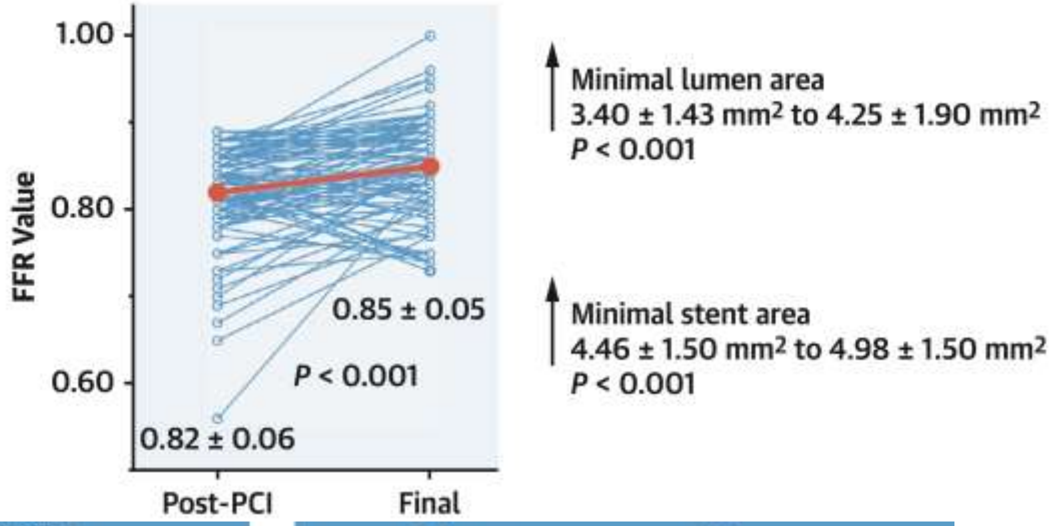
TVF at 1-year follow-up

N = 291

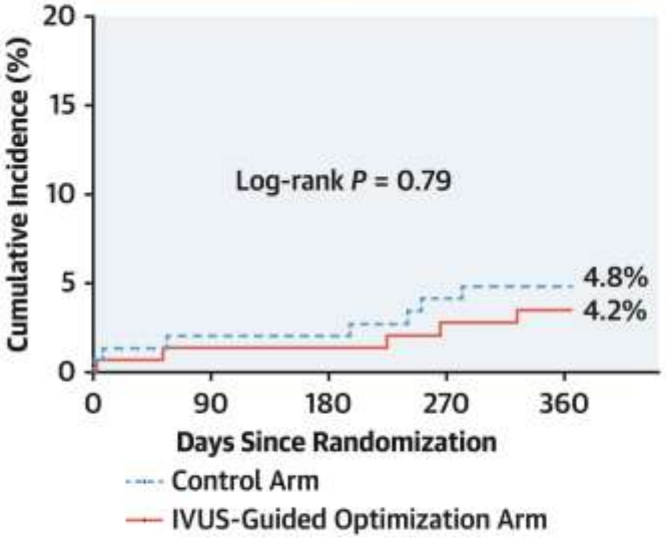
Optimization in 68.4% of Vessels



FFR and IVUS Optimization Results



Primary Endpoint
1-Year Target Vessel Failure



1-Year Follow-Up	HR (95% CI)	*P* Value
Target Vessel Failure	0.86 (0.29-2.57)	0.79
Cardiac Death	4.06 (0.45-36.34)	0.17
Target Vessel Myocardial Infarction	0.41 (0.08-2.09)	0.26
Target Vessel Revascularization	0.17 (0.02-1.40)	0.06

Neleman T, *JACC Cardiovasc Interv*. 2022 Aug 22;15(16):1595-1607. (Central Illustration excerpts)

Optimizing FFR has minimal impact on TVF

study	*N*	*tool*	*routine FFR*	*optimized*	*ΔFFR*	*ΔTVF*
ILUMIEN I	70	OCT	0.86	0.90	0.04	
DOCTORS	240	OCT	0.92	0.94	0.02	
TARGET-FFR	260	PIOS	0.85	0.86	0.01	0%
FFR-REACT	291	IVUS	0.82	0.85	0.03	-0.6%

ILUMIEN I = Wijns W, *EHJ*. 2015 Dec 14;36(47):3346-55.

DOCTORS = Meneveau N, *Circulation*. 2016 Sep 27;134(13):906-17.

TARGET-FFR = Collison D, *EHJ*. 2021 Dec 1;42(45):4656-4668.

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DOCTORS	240	OCT	0.92	0.94	0.02	
TARGET-FFR	260	PIOS	0.85	0.86	0.01	0%
FFR-REACT	291	IVUS	0.82	0.85	0.03	-0.6%

thus final FFR will not replace IVUS/OCT

ILUMIEN I = Wijns W, *EHJ*. 2015 Dec 14;36(47):3346-55.
DOCTORS = Meneveau N, *Circulation*. 2016 Sep 27;134(13):906-17.
TARGET-FFR = Collison D, *EHJ*. 2021 Dec 1;42(45):4656-4668.
FFR-REACT = Neleman T, *JACC Cardiovasc Interv*. 2022 Aug 22;15(16):1595-1607.

FFR = 1.0

why not?

How is *diffuse disease* ***different***?

	P3		
	diffuse	focal	
N	74	39	
Diabetes	24%	22%	↑
LAD	**90%**	**46%**	↑
Lesion (mm)	25.6	19.9	↑
Stent (mm)	37.2	29.7	↑
FFR start	0.70	0.58	↑
FFR after PCI	0.86	0.91	↓
ΔFFR	0.16	0.33	↑

P3 = Mizukami T, *J Am Heart Assoc*. 2022 Dec 6;11(23):e026960. (Tables 1-3 extract)

LAD has *lower FFR's* due to *higher flow*

		LAD	*LCx*	*RCA*
FFR	mean	0.92	0.96	0.96
	median	0.93	0.97	0.96
	lower 5%	0.88	0.88	0.92
	upper 95%	0.94	1.00	0.99
Flow (mL/min)	mean	293	204	197
	median	297	208	207

flow = **mass** * perfusion

mL/min = **g** * mL/min/g

- 25 patients with normal coronaries
- age 57±11 years, normal EF
- no coronary atherosclerosis
- FFR in LAD was lower 0.92 vs 0.96
- 5-95% bounds for FFR_{LAD} 0.88 to 0.94

left = Fournier S, *EuroIntervention*. 2021 Jul 20;17(4):e309-e316. (data from Supplement Table 2)

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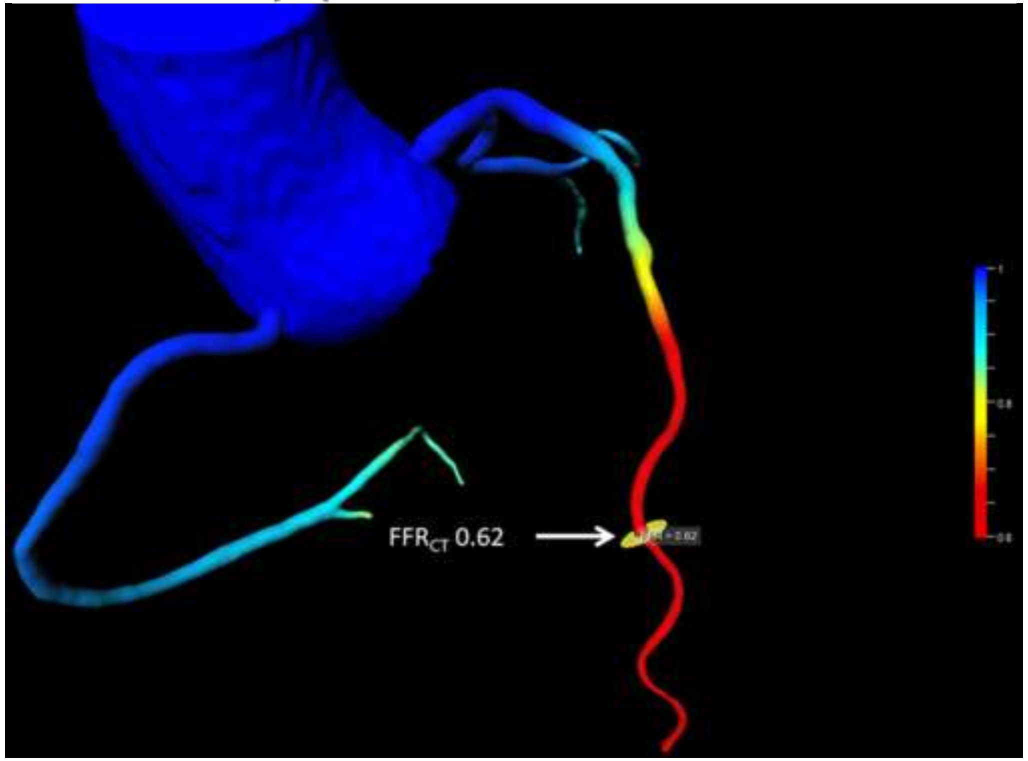
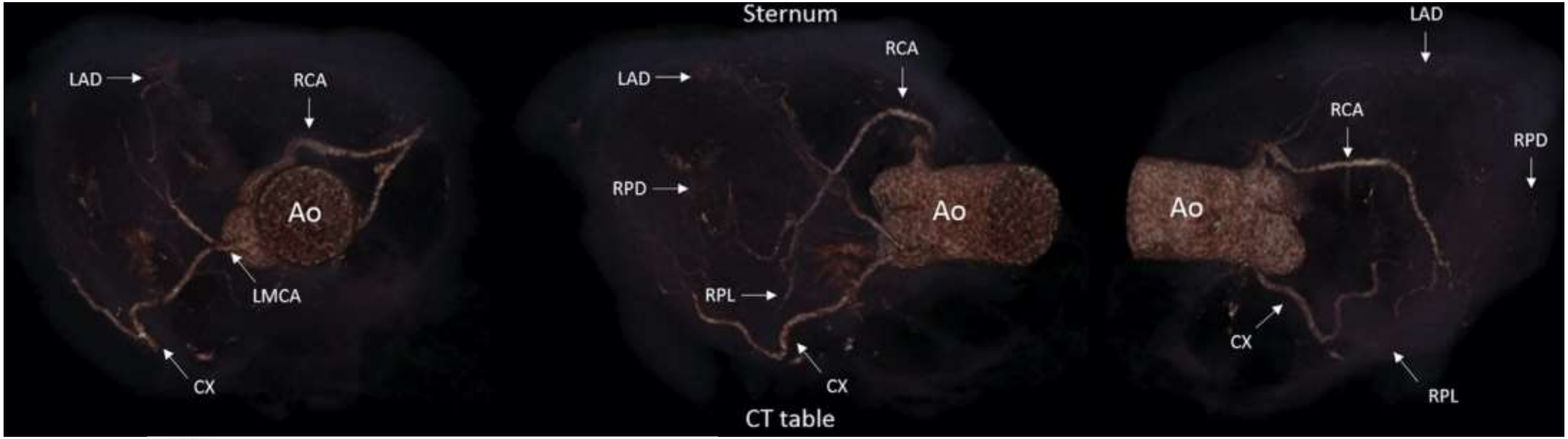
Prevalence of pathological FFR_{CT} values without coronary artery stenosis in an asymptomatic marathon runner cohort

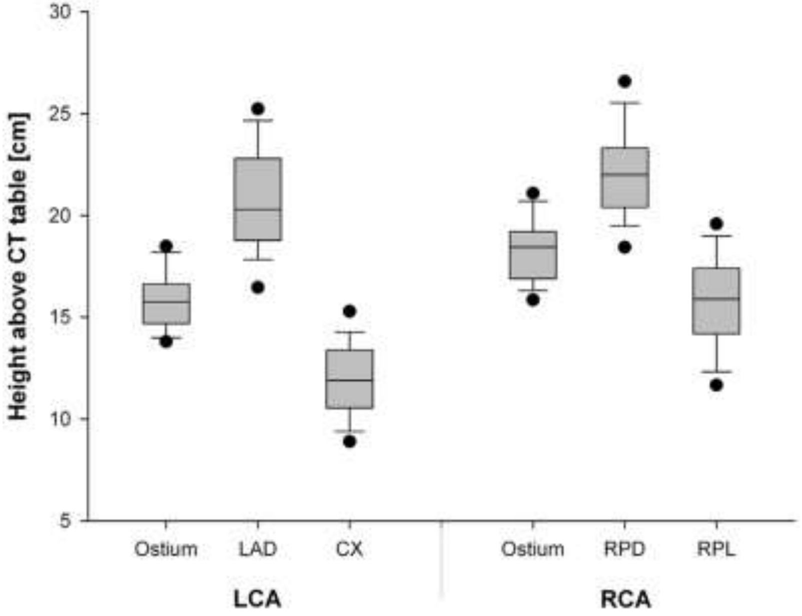


- 59 marathon runners
- age >45 years, asymptomatic
- no coronary atherosclerosis
- FFR_{CT}≤0.8 in 22 people (37%)
- 19 of 22 by mid/distal LAD

left = Fournier S, *EuroIntervention*. 2021 Jul 20;17(4):e309-e316. (data from Supplement Table 2)
right = Gassenmaier S, *Eur Radiol*. 2021 Dec;31(12):8975-8982. (Figure 2 plus results)

LAD has *lower FFR's* due to *hydrostatics*





LCA to LAD max

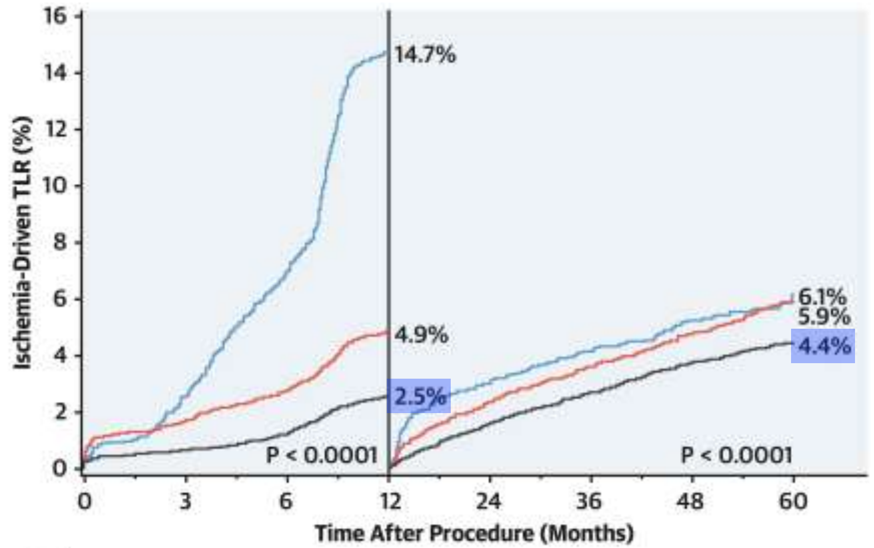
- mean 4.9 cm higher when supine
- median 4.6 cm higher
- 1/13.6*10 = 0.74
- 4 cm $H_2O \approx 3$ mm Hg

➥ LAD pressure 3-4 mmHg lower
(rest *and* stress, regardless of flow)

Härle T, *JACC Cardiovasc Interv*. 2017 Apr 24;10(8):764-773. (Figures 3 and 4 plus results from Table 2)

LAD is a *risk factor for TVF*

	P3		
	diffuse	focal	
N	74	39	
Diabetes	24%	22%	↑
LAD	90%	46%	↑
Lesion (mm)	25.6	19.9	↑
Stent (mm)	37.2	29.7	↑
FFR start	0.70	0.58	↑
FFR after PCI	0.86	0.91	↓
ΔFFR	0.16	0.33	↑



Number at risk:

BMS	3,449	3,317	3,145	2,768	2,615	2,316	1,851	663
DES1	7,804	7,556	7,428	6,992	6,648	5,572	3,660	1,758
DES2	13,380	13,206	13,074	12,502	12,059	11,191	5,913	3,580

	Target Lesion Failure	
	RR (95% CI)	**p Value**
Through 1 yr		
Diabetes mellitus	1.40 (1.20-1.60)	<0.0001
LM or LAD disease	1.20 (1.10-1.40)	0.0006
Lesion length (per 10 mm)	1.20 (1.10-1.30)	<0.0001
Between 1 and 5 yrs		
Diabetes mellitus	1.50 (1.30-1.70)	<0.0001
LM or LAD disease	1.10 (0.92-1.20)	0.48
Lesion length (per 10 mm)	1.10 (0.99-1.10)	0.11

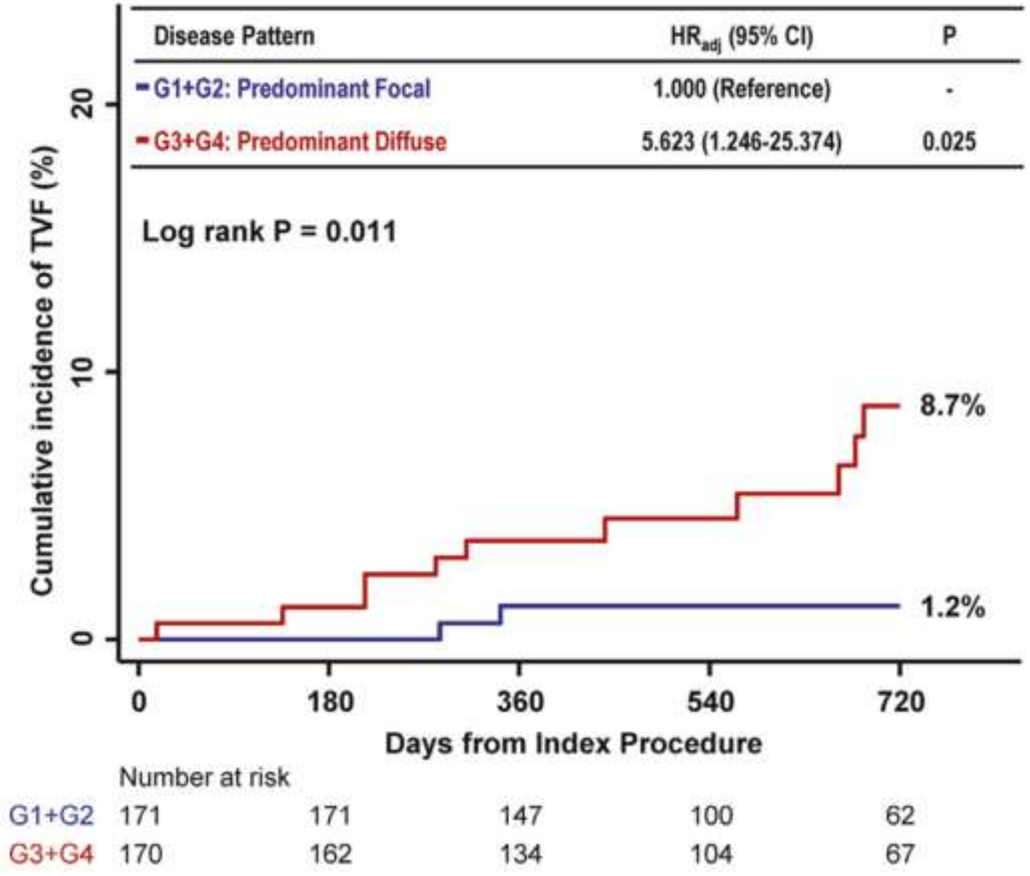
P3 = Mizukami T, *J Am Heart Assoc*. 2022 Dec 6;11(23):e026960. (Tables 1-3 extract)
Madhavan MV, *JACC*. 2020 Feb 18;75(6):590-604. (Figure 1A and Table 5 portion with *annotations*)

Low final FFR = diffuse disease, especially LAD

	P3			Korea		TARGET		ORBITA	
	diffuse	focal		*diffuse*	focal	*diffuse*	focal	*diffuse*	focal
N	74	39		55	150	52	51	81	83
Diabetes	24%	22%	↑	56%	44%	25%	16%	20%	17%
LAD	**90%**	46%	↑	**82%**	71%	**87%**	39%	**82%**	60%
Lesion (mm)	25.6	19.9	↑	24.5	20.6	12.3	10.9	15.2	13.9
Stent (mm)	**37.2**	29.7	↑	**34.0**	30.4	**47.7**	37.4	**26.2**	27.7
FFR start	0.70	0.58	↑	0.71	0.69	0.64	0.59	0.78	0.60
FFR after PCI	0.86	0.91	↓	0.83	0.87	0.83	0.87	0.89	0.90
ΔFFR	**0.16**	0.33	↑	**0.12**	0.18	**0.19**	0.28	**0.11**	0.30

P3 = Mizukami T, *J Am Heart Assoc*. 2022 Dec 6;11(23):e026960. (Tables 1-3 extract)
Korea = Shin D, *JACC Cardiovasc Interv*. 2021 Aug 23;14(16):1771-1785. (Table 1 extract for “Diffuse Without” versus “Focal With” columns)
TARGET = Collet C, *JACC Cardiovasc Interv*. 2022 Dec 26;15(24):2506-2518. (Tables 1-2 extract)
ORBITA = Rajkumar CA, *Circ Cardiovasc Interv*. 2021 Aug;14(8):e009891. (Tables 1-2 extract)

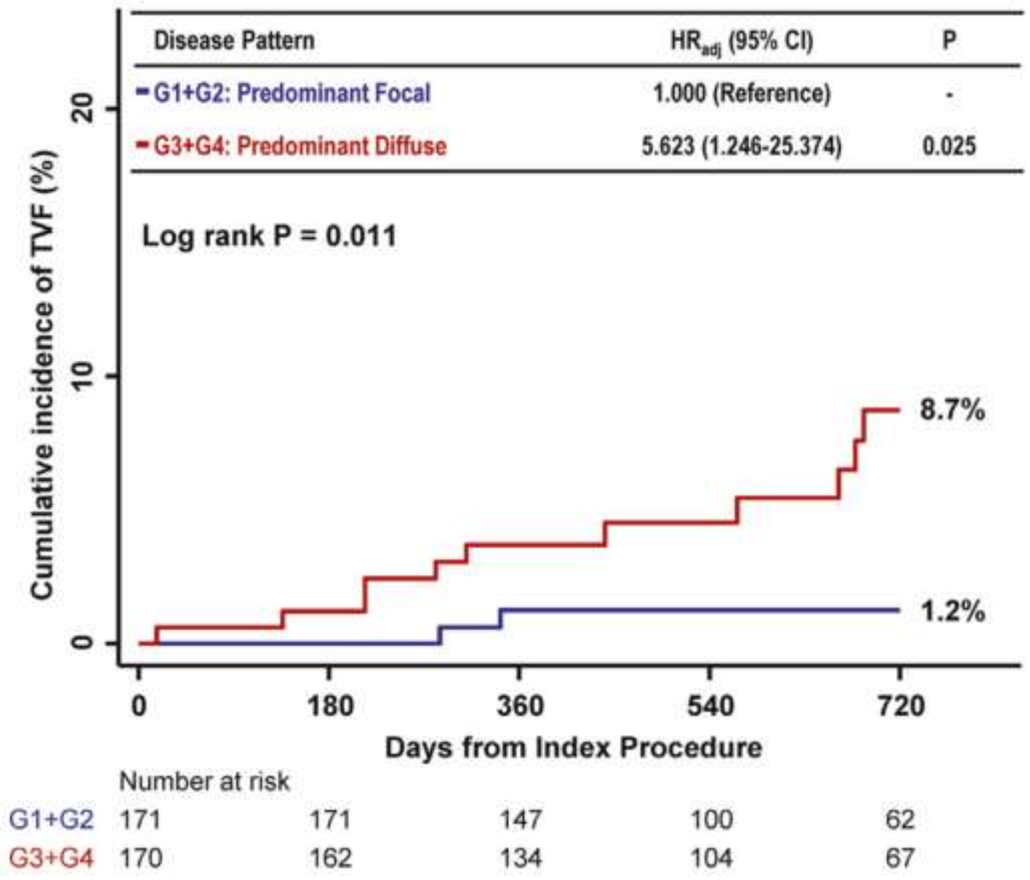
Does *diffuse disease* respond to PCI?

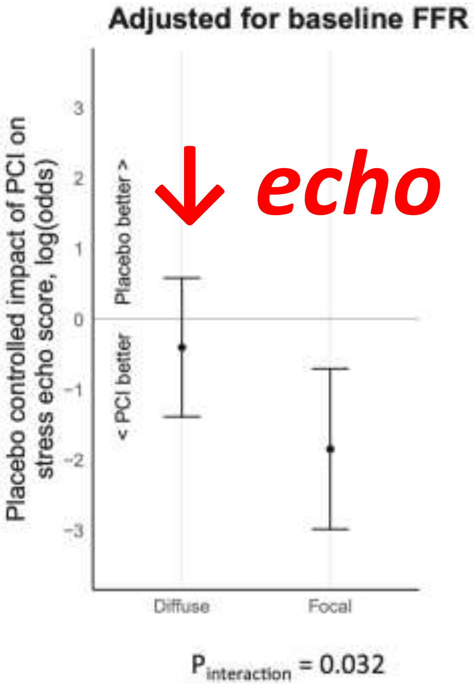


↑ ***TVF***

outcomes = Shin D, *JACC Cardiovasc Interv*. 2021 Aug 23;14(16):1771-1785. (Figure 6A)

Does *diffuse disease* respond to PCI?





↓ ***echo***

↑ ***TVF***

outcomes = Shin D, *JACC Cardiovasc Interv*. 2021 Aug 23;14(16):1771-1785. (Figure 6A)
echo = Rajkumar CA, *Circ Cardiovasc Interv*. 2021 Aug;14(8):e009891. (Figure 1 B(ii))

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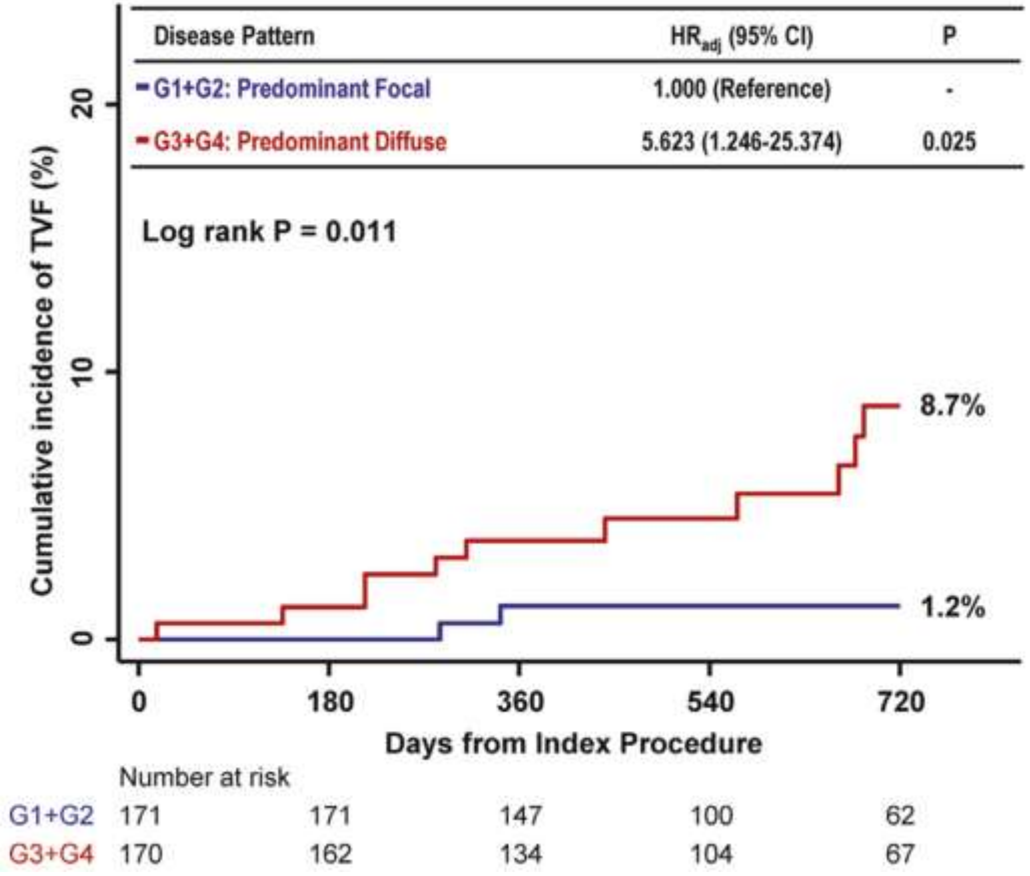
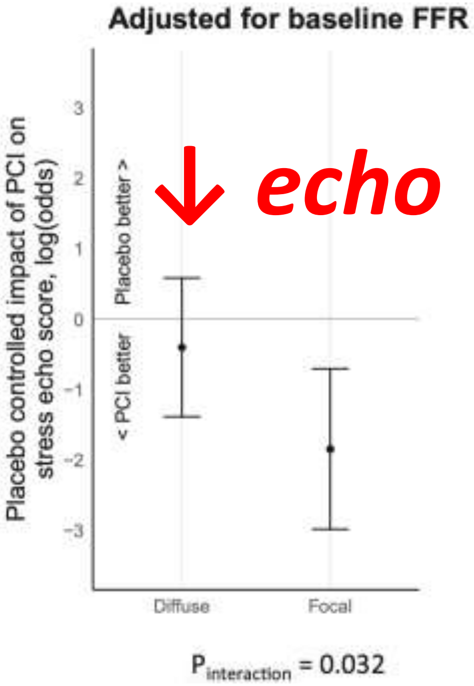
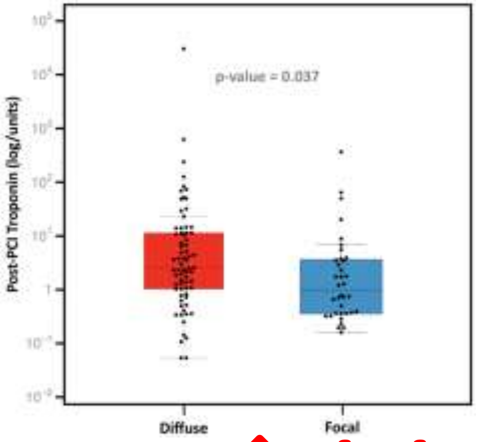


↑ ***TVF***



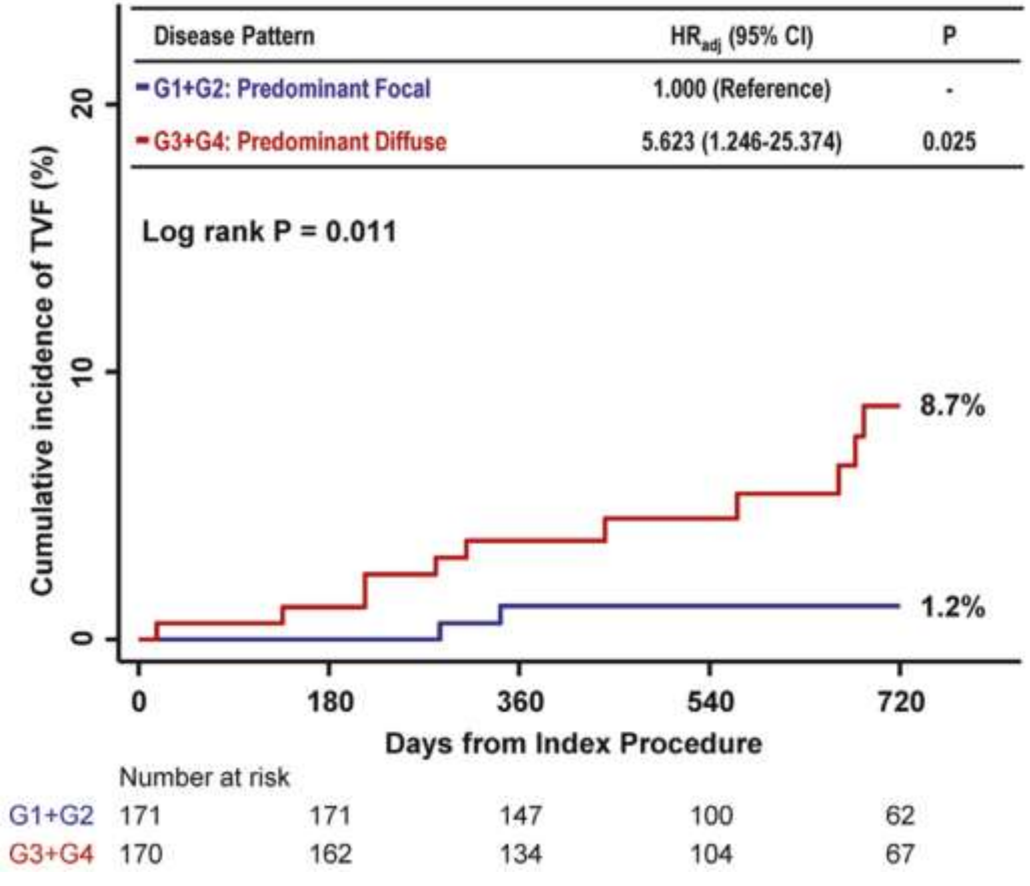
↓ ***echo***



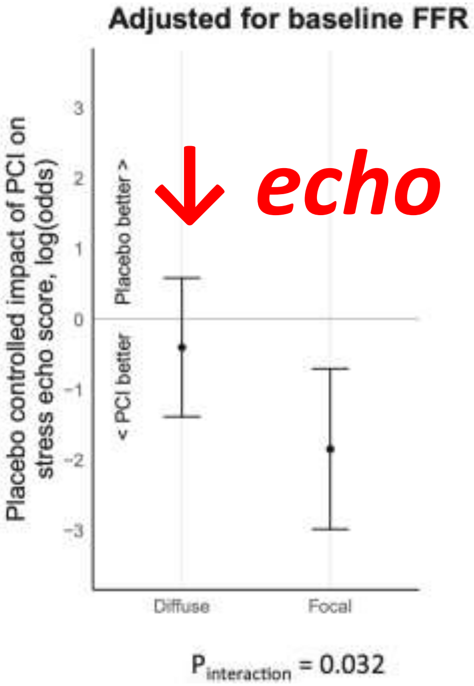
↑ ***injury***

injury = Mizukami T, *J Am Heart Assoc*. 2022 Dec 6;11(23):e026960. (Figure S4)
outcomes = Shin D, *JACC Cardiovasc Interv*. 2021 Aug 23;14(16):1771-1785. (Figure 6A)
echo = Rajkumar CA, *Circ Cardiovasc Interv*. 2021 Aug;14(8):e009891. (Figure 1 B(ii))

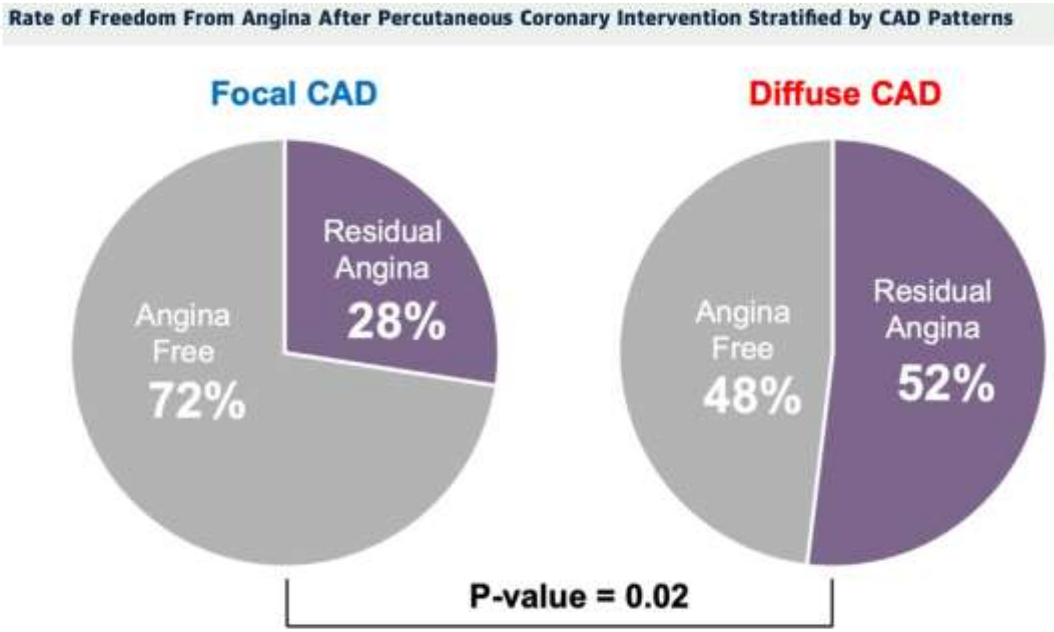
Does *diffuse disease* respond to PCI?



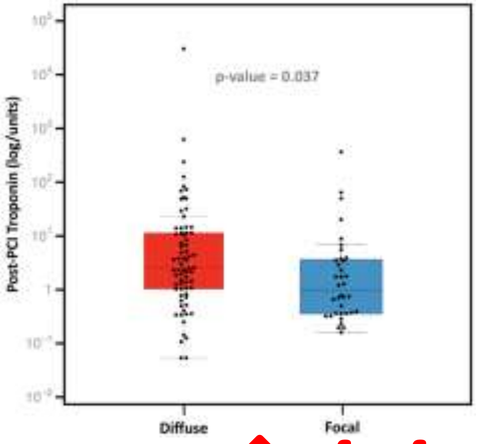
↑ TVF



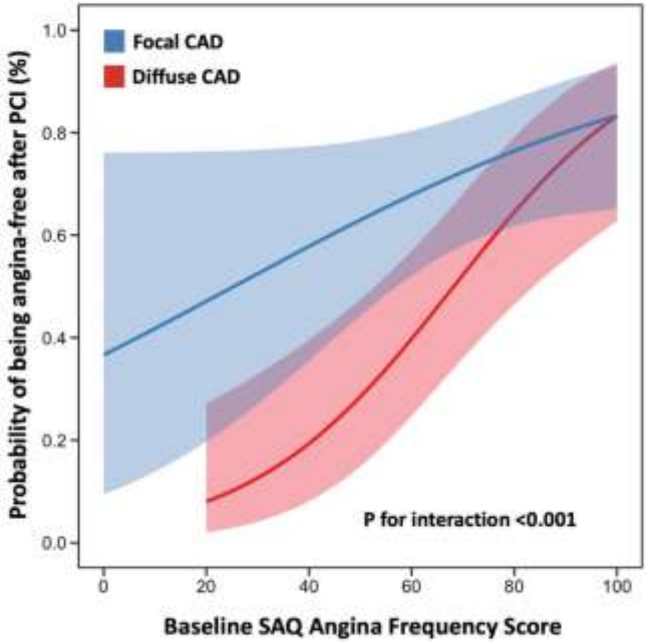
↓ echo



↑ angina

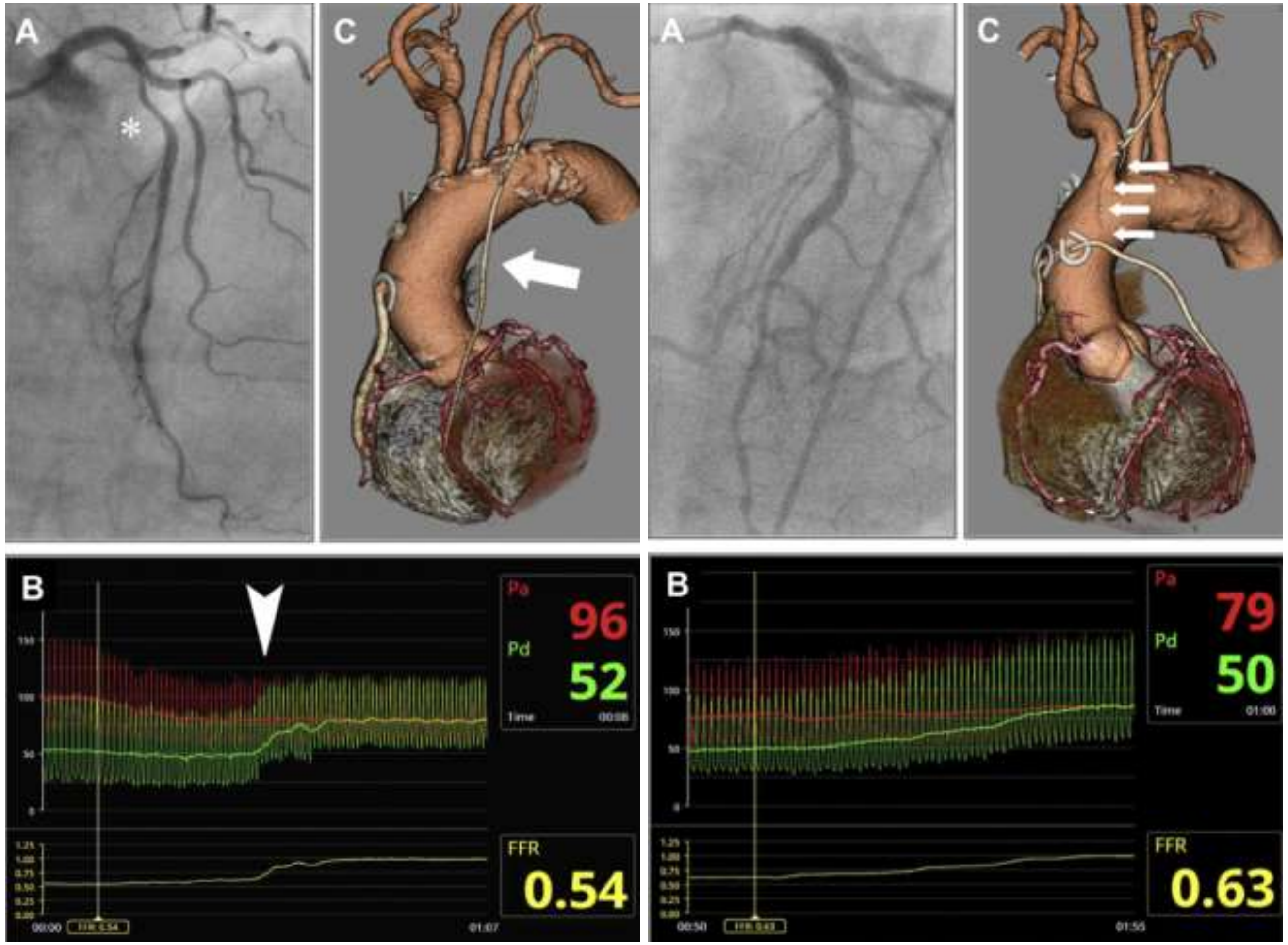


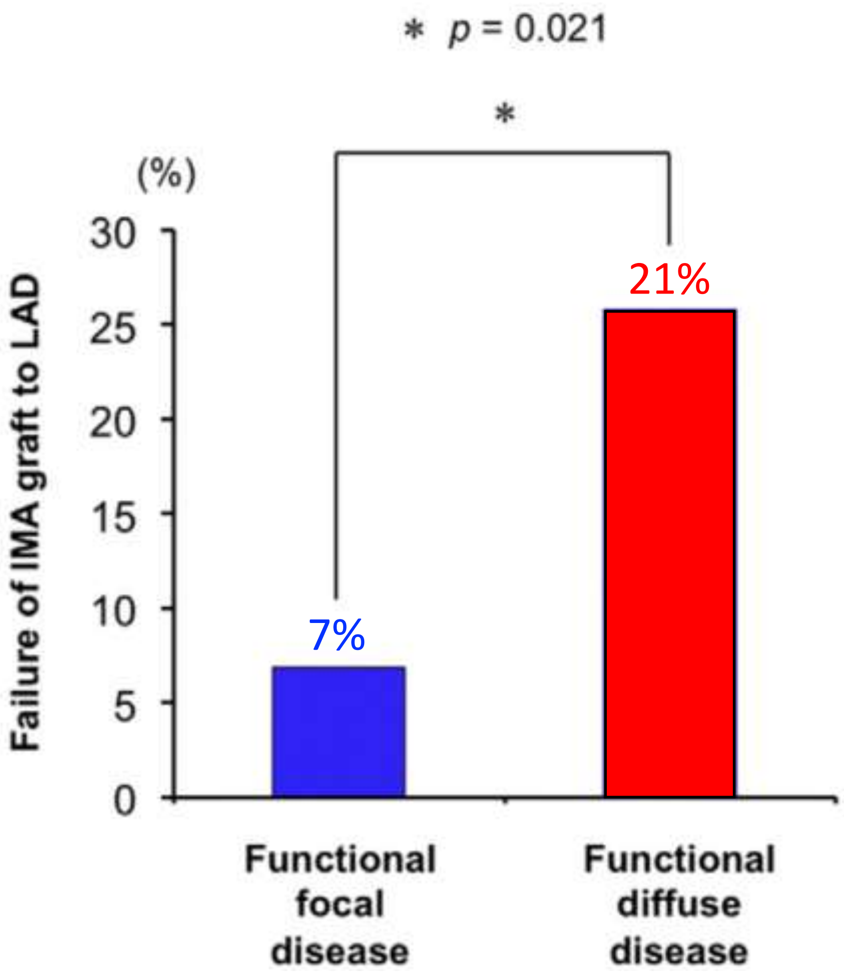
↑ injury



injury = Mizukami T, *J Am Heart Assoc*. 2022 Dec 6;11(23):e026960. (Figure S4)
outcomes = Shin D, *JACC Cardiovasc Interv*. 2021 Aug 23;14(16):1771-1785. (Figure 6A)
echo = Rajkumar CA, *Circ Cardiovasc Interv*. 2021 Aug;14(8):e009891. (Figure 1 B(ii))
angina = Collet C, *JACC Cardiovasc Interv*. 2022 Dec 26;15(24):2506-2518. (Figure 4 part and Figure 5)

Treat diffusely diseased LAD with LIMA?





Focal disease
Patent LIMA
@ 3 months

Diffuse disease
Atretic LIMA
@ 4 months

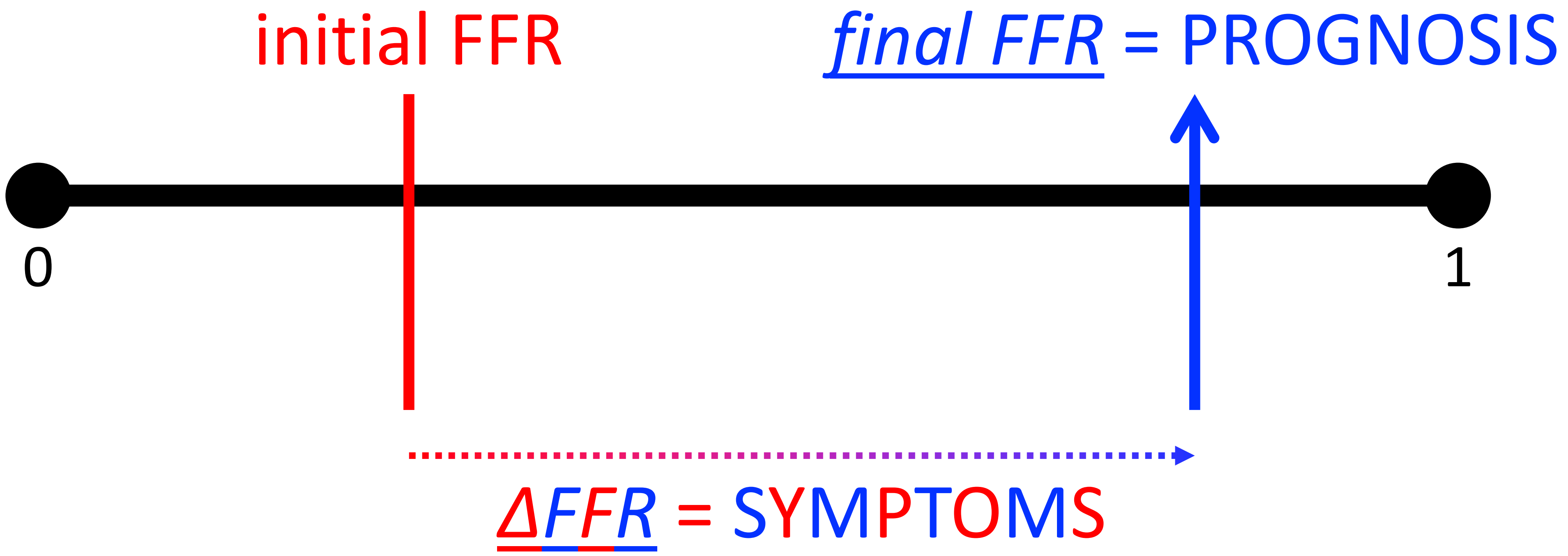
7% versus 21%

Shiono Y, *Int J Cardiol*. 2016 Nov 1;222:16-21. (Figures 1-3 with *colored annotations*)

final FFR

surprised?

Key concept

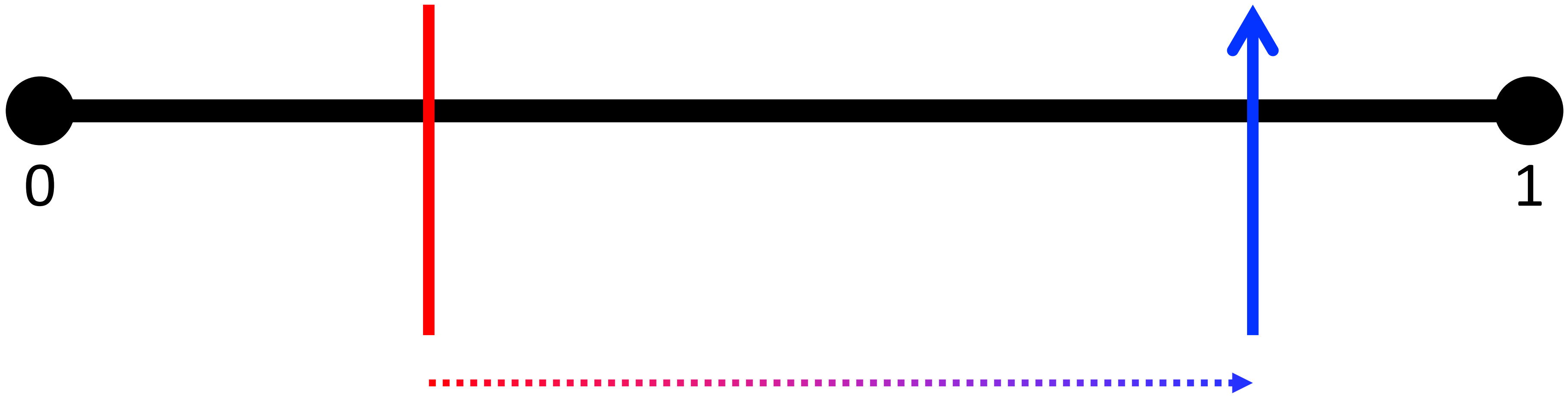


Final FFR should not be a *surprise*

final FFR = PROGNOSIS

- DIFFUSE DISEASE
- poor PCI
- LAD = lower (mass, hydrostatics)

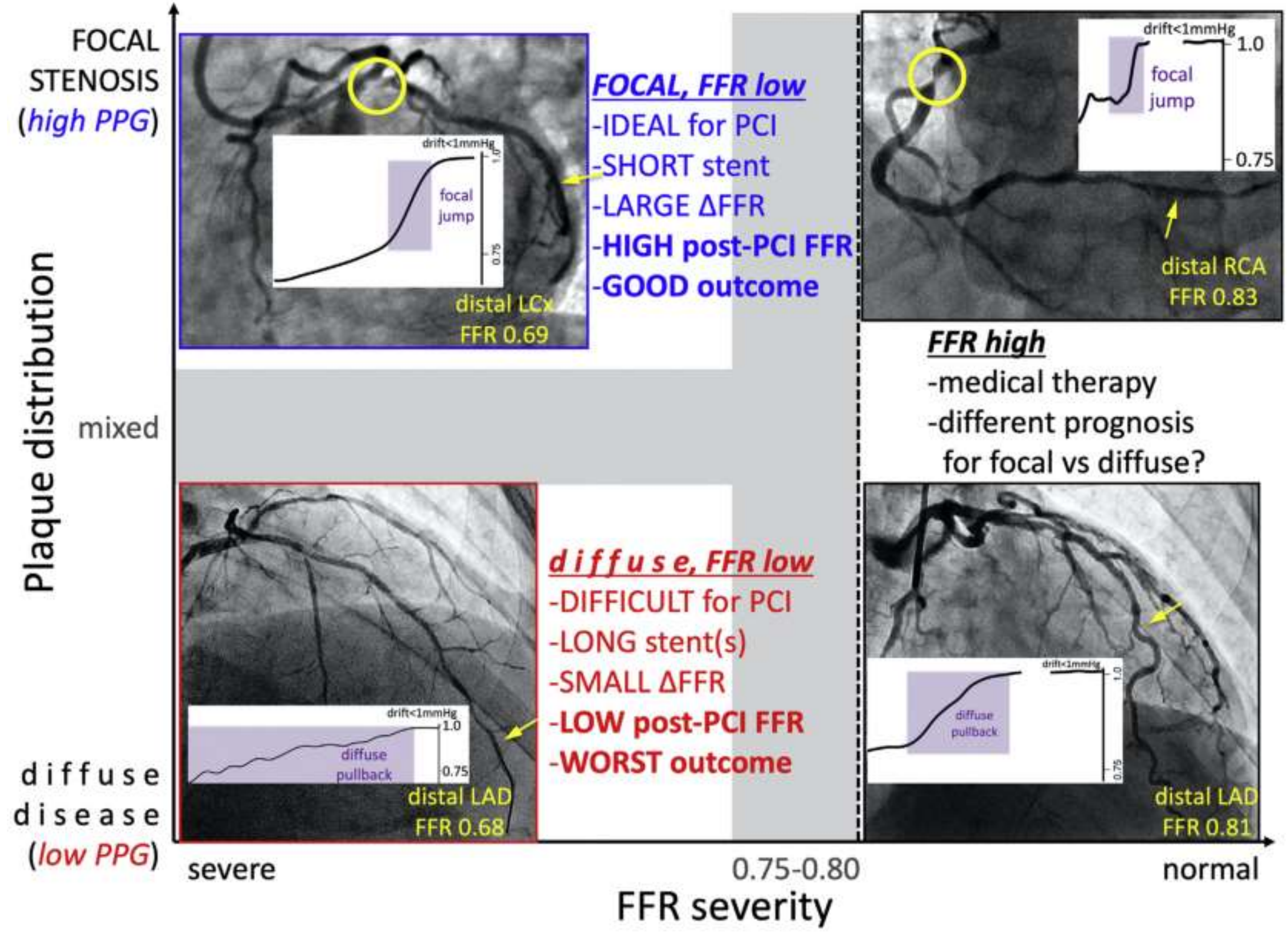
initial FFR



ΔFFR = SYMPTOMS

- diffuse = small Δ
- focal = large Δ

2D-physiology = depth + distribution



Johnson NP, *JACC Cardiovasc Interv*. 2020 Jul 27;13(14):1651-1654. (Figure 1)