TARGET FFR

Physiology-Guided Optimization of PCI

A Randomized Controlled Trial

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on behalf of the TARGET FFR investigators

NHS Golden Jubilee

University of Glasgow

CRF TCT CONNECT

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Consulting Fees/Honoraria	Abbott Medical, MedAlliance

Faculty disclosure information can be found on the app

Background (i)

- Higher post-PCI FFR values are associated with a reduced incidence of adverse clinical events[1]
- A systematic review and meta-analysis of 7470 patients found that post-PCI FFR ≥0.90 is associated with a lower risk of repeat PCI and major adverse cardiovascular events[2]
- In previous studies, the proportion of patients actually achieving final FFR ≥0.90 ranges from 21% to 100%

[1] *Johnson et al. J Am Coll Cardiol 2014;64(16):1641-54.*
[2] *Rimac et al. Am Heart J 2017;183:1-9.*

Background (ii)

- The proportion of patients with post-PCI FFR ≤0.80 ranges from <1% to 36%[3]
- Up to 38% of patients still report angina 1 year after PCI[4]
- Given its apparent frequency, randomized data are required on both the incidence of functionally sub-optimal PCI and the efficacy of strategies to address it

[3] *Uretsky et al. J Am Heart Assoc 2020;9(3):e015073.*
[4] *Stone et al. Lancet 2018;392(10157):1530-40.*

Trial of Angiography versus pressure-Ratio-Guided Enhancement Techniques (TARGET) FFR

- **Design:** Investigator-initiated, single-center RCT
- **Hypothesis:** Application of a physiology-guided incremental optimization strategy (PIOS) can increase the proportion of patients achieving a final post-PCI FFR ≥0.90
- **Power & Sample Size Calculation:** We estimated the PIOS intervention would increase the proportion of patients with final post-PCI FFR ≥0.90 by 20%. A sample size of 130 per group would have 90% power to detect this difference at the 5% significance level

Trial Design

- Informed consent prior to PCI
- *Pre-PCI* coronary physiology assessment
- PCI performed according to local practice
- Patients randomized after operator declares angiographically-guided procedure to be successful and complete
- Control Group: *Blinded post-PCI* coronary physiology assessment
- PIOS Group: Blinded post-PCI coronary physiology assessment; if *FFR <0.90* results disclosed and further *protocol-guided optimization* performed based on the *hyperemic pullback assessment*.
- *Core Lab* coronary physiology analysis (CoreAalst BV, Belgium)

Inclusion & Exclusion Criteria

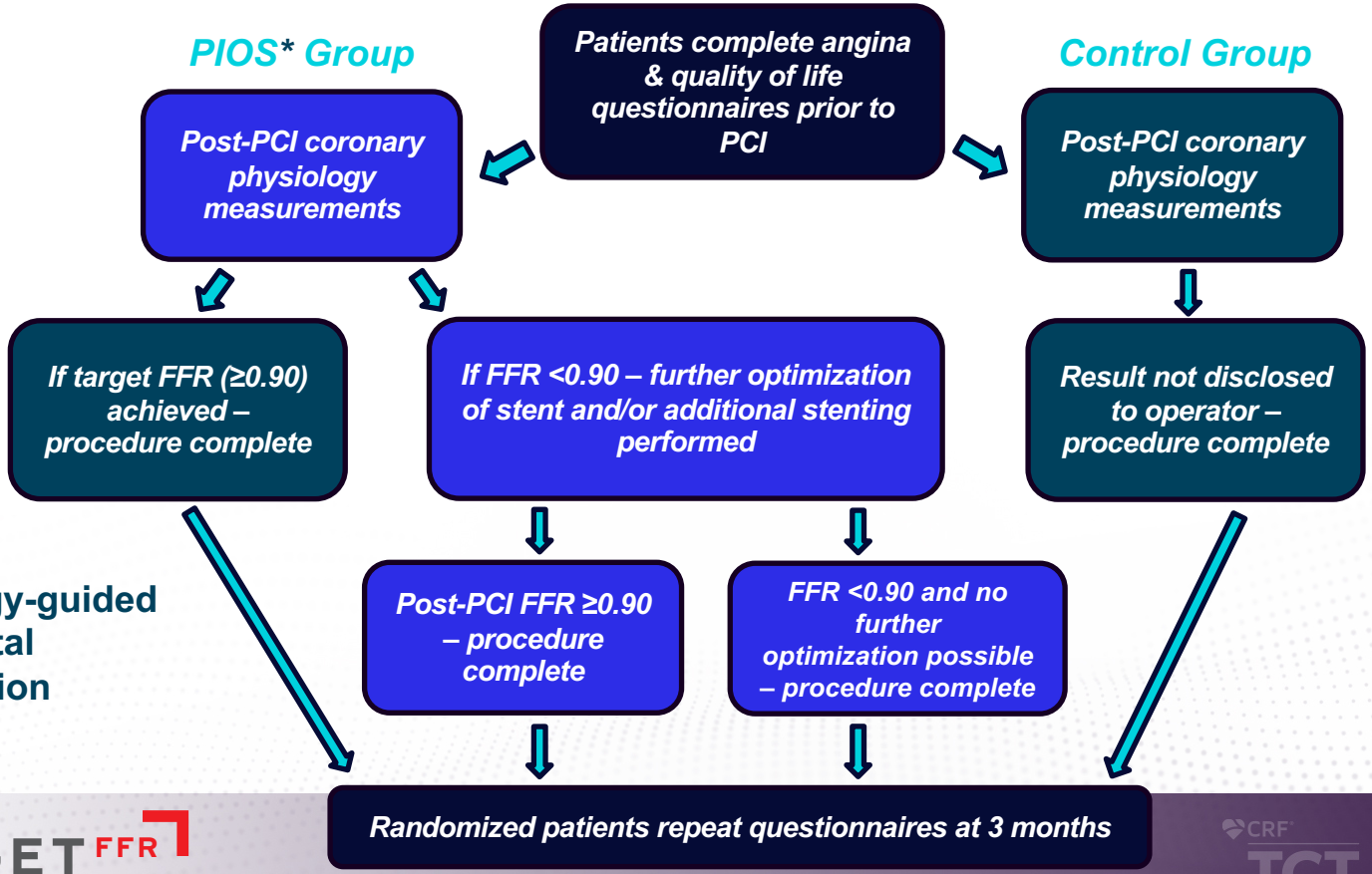
Inclusion Criteria

- Patients >18 years of age with coronary artery disease including stable angina and NSTEMI
- Participants must be able to provide informed consent

Exclusion Criteria

- PCI in a coronary artery bypass graft
- PCI to an In-Stent Restenosis lesion
- PCI to a target artery providing Rentrop Grade 2 or 3 collateral blood supply to another vessel
- Inability to receive adenosine (for example, severe reactive airway disease, marked hypotension, or advanced atrioventricular block without pacemaker).
- Recent (within 1 week prior to cardiac catheterisation) STEMI in any arterial distribution (not specifically target lesion).
- Severe cardiomyopathy (LVEF <30%).
- Renal insufficiency such that an additional 20 to 30 mL of contrast would, in the opinion of the operator, pose unwarranted risk to the patient.

Study Flowchart



* **P**hysiology-guided **I**ncremental **O**ptimization **S**trategy

Physiology-guided Incremental Optimization Strategy

FFR <0.90 and hyperemic pullback shows diffuse atherosclerosis with no focal step-ups: Result accepted, no optimization attempted

Diffuse Gradient

Hyperemic trans-stent gradient (HTG) ≥0.05: Post-dilation with larger NC balloon to 18atm. Intracoronary imaging at operator discretion. Repeat hyperemic pullback

HTG ≥0.05

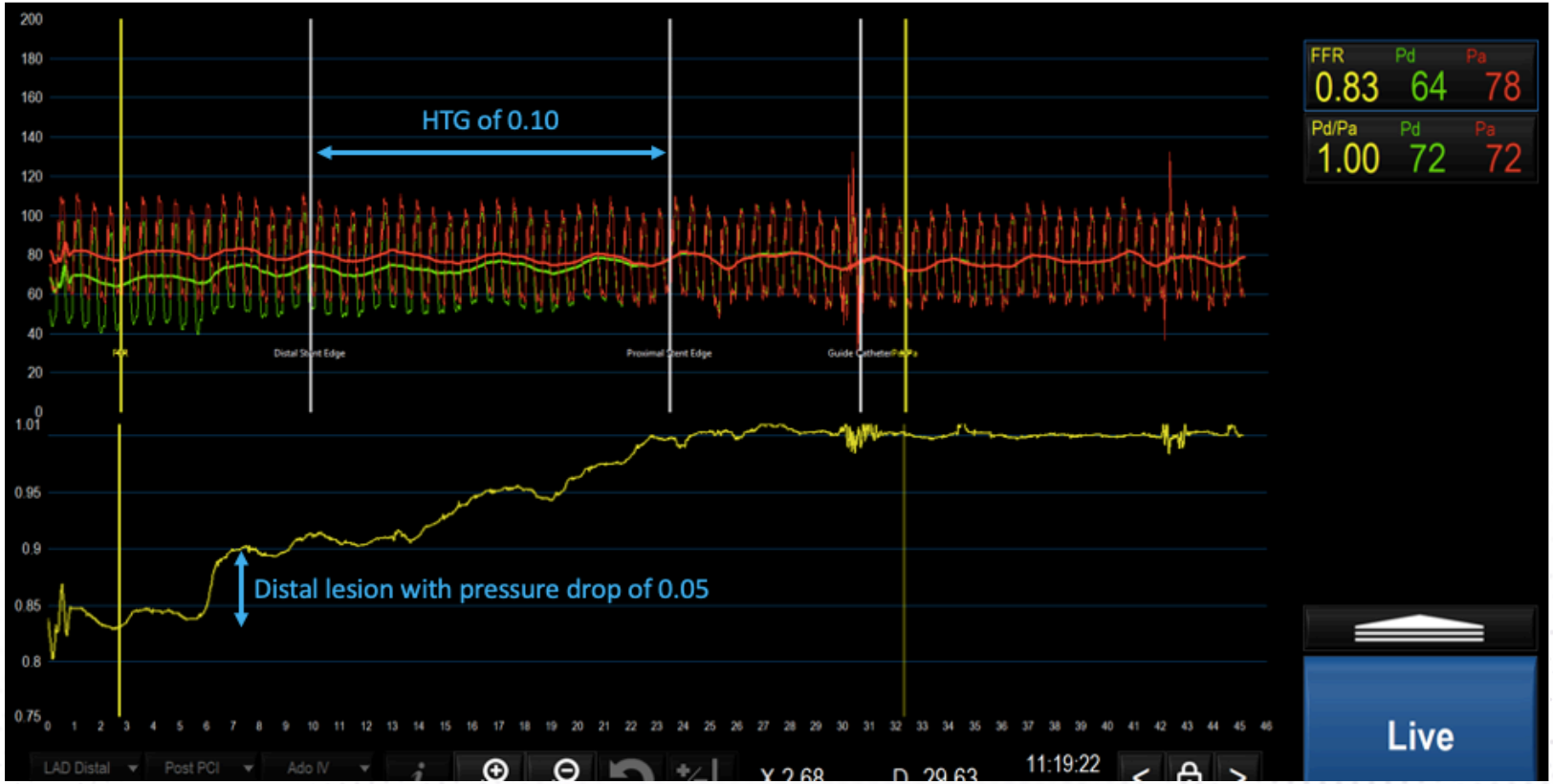
Focal FFR increase ≥0.05 within an unstented segment <20mm: Deploy additional stent. Repeat hyperemic pullback

Focal Step ≥0.05

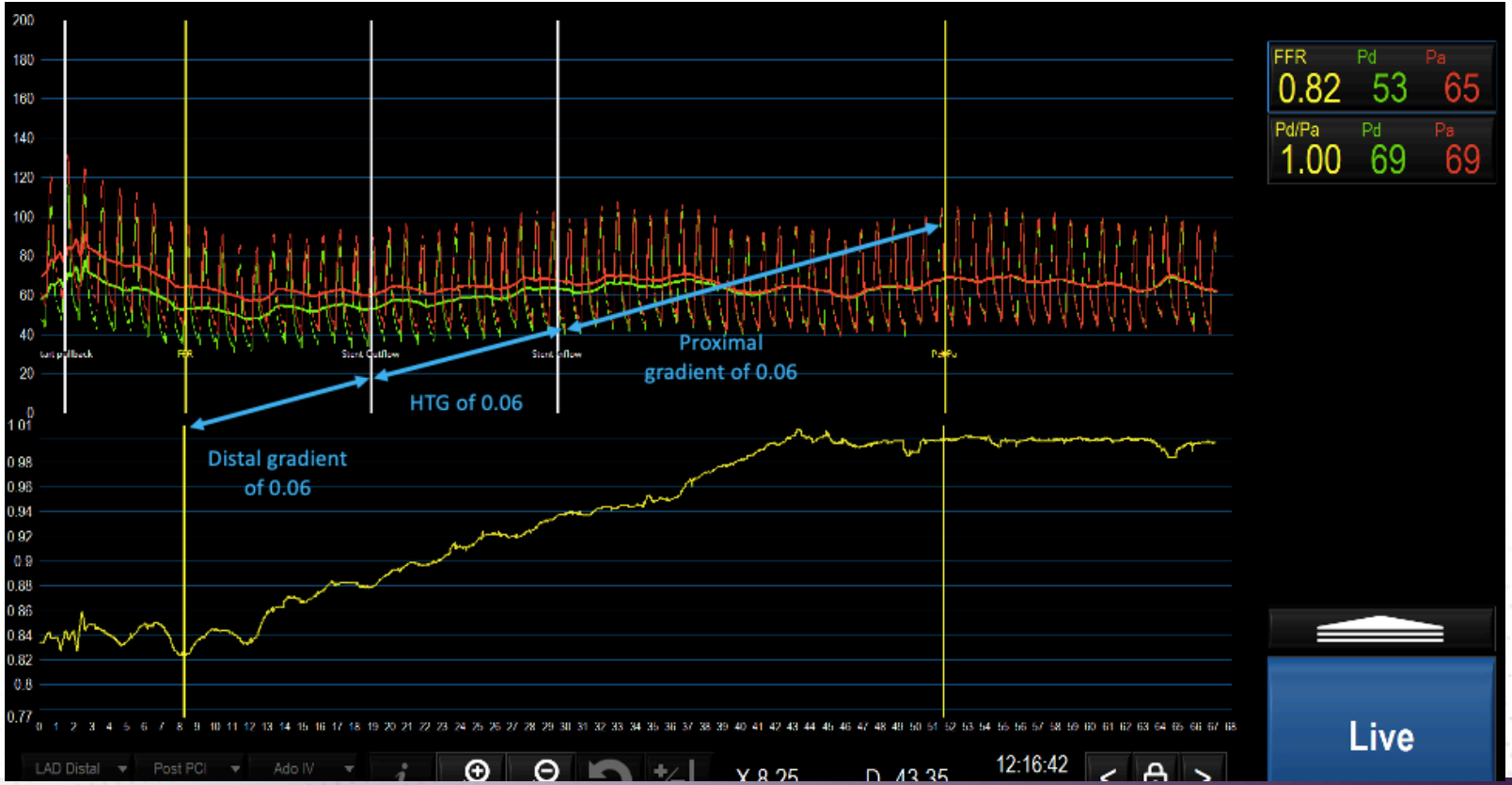
FFR still <0.90: Repeat hyperemic pullback. If either of the above criteria remain, option of further post-dilation or one more additional stent

Final hyperemic pullback

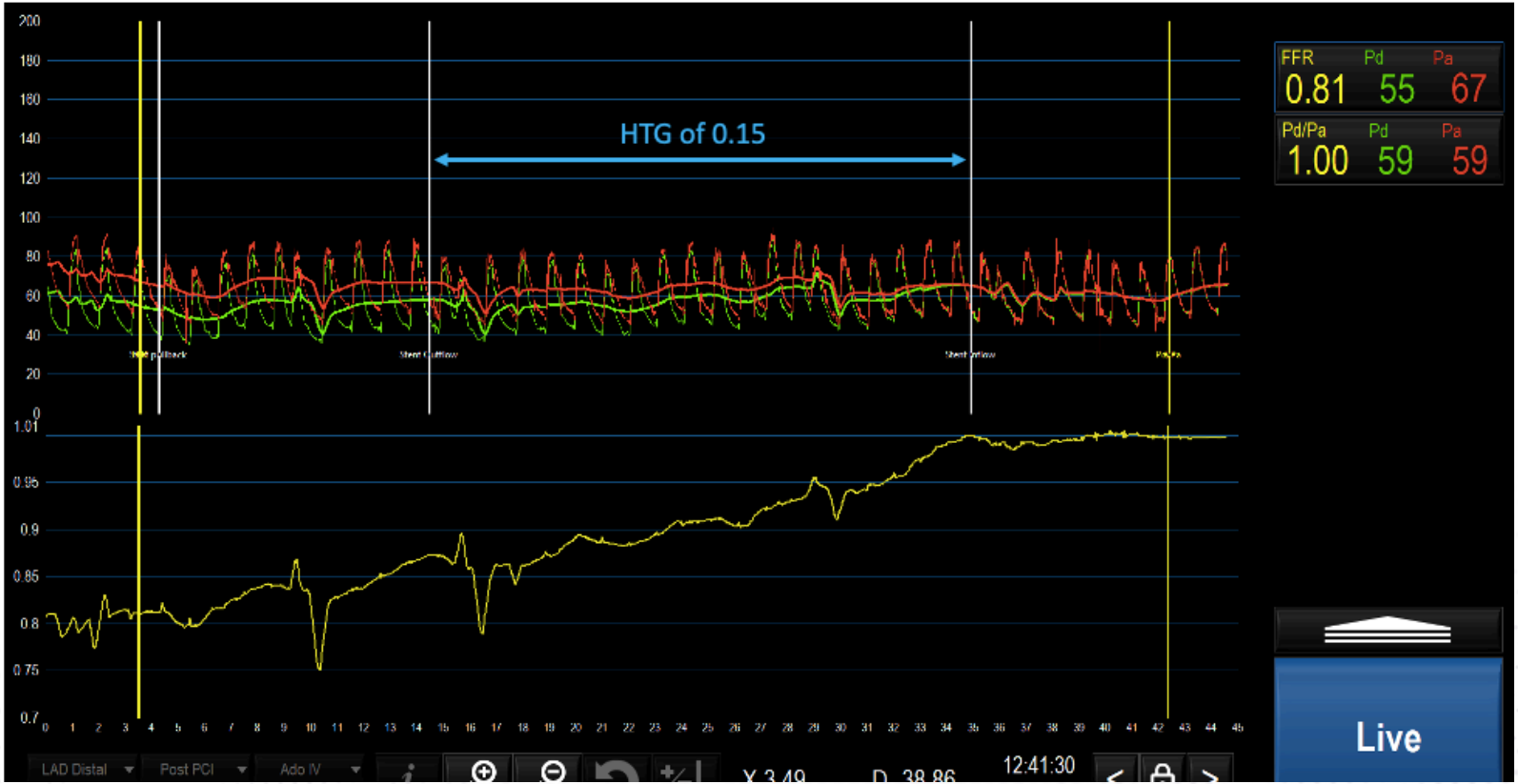
Example 1: Residual Focal Lesion and HTG >0.05



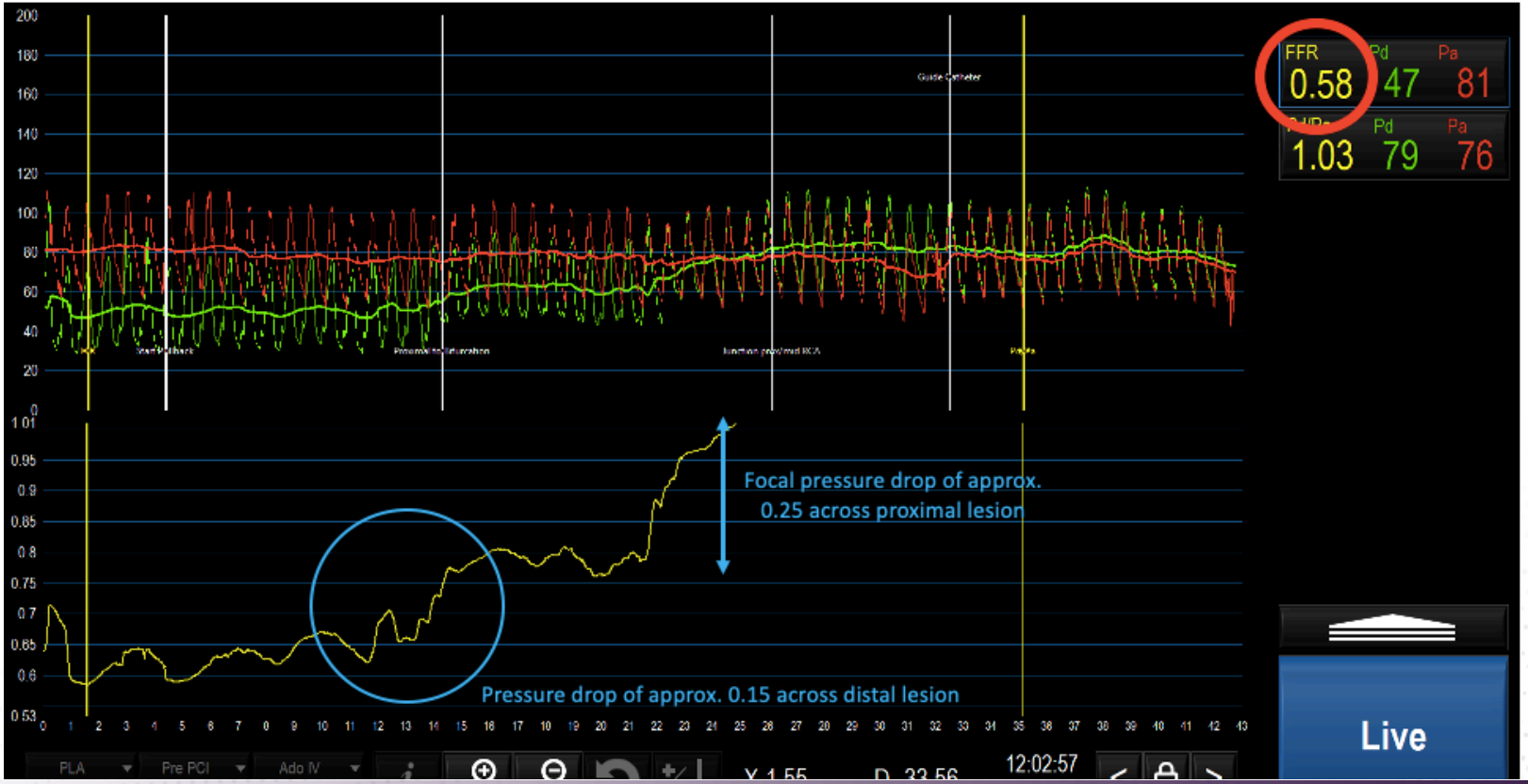
Example 2: HTG ≥0.05 & Diffuse Residual Gradient



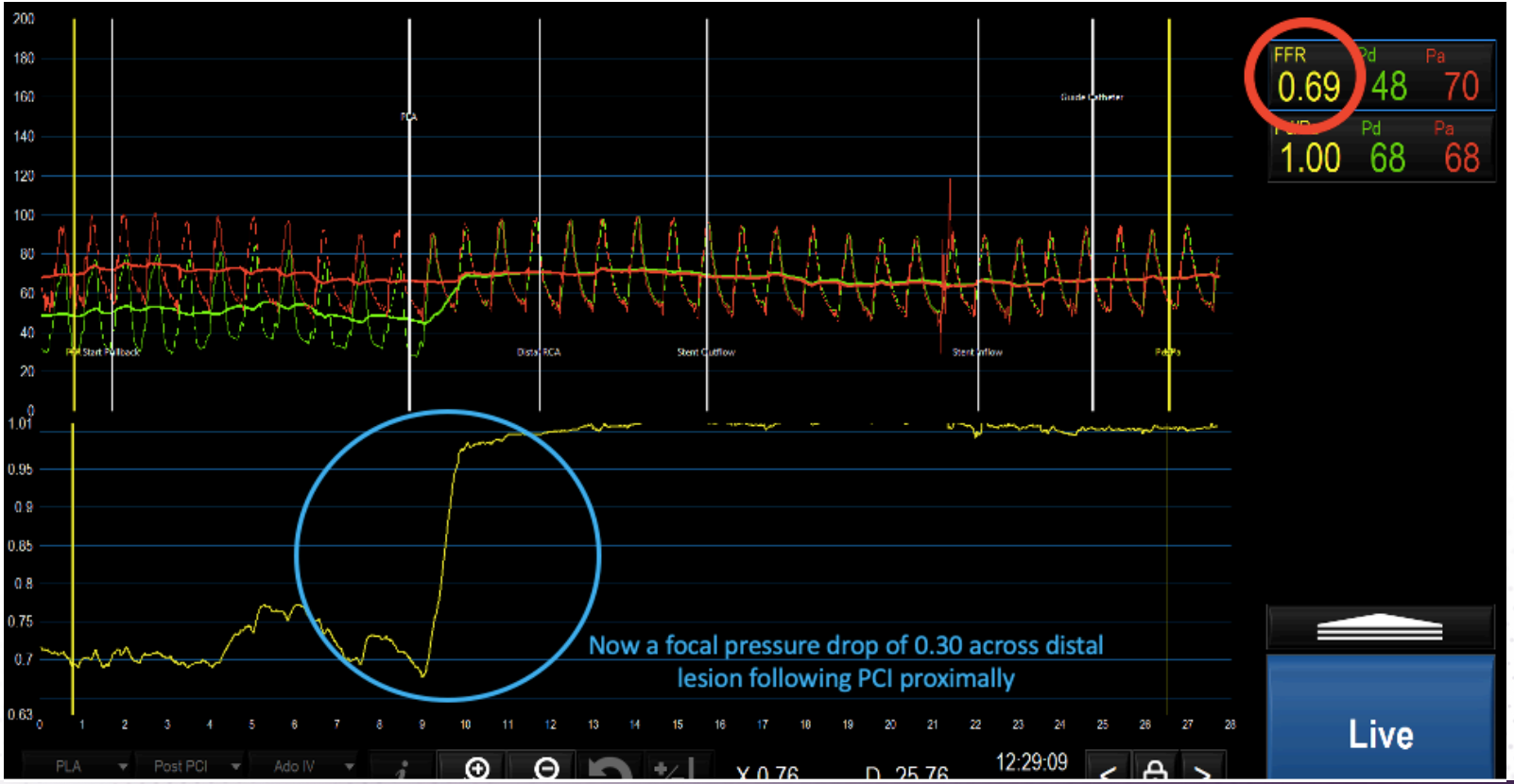
Example 3: Underexpanded Long Stent



Example 4: Unmasked Distal Lesion (Pre-PCI proximally)



Example 4: Unmasked Distal Lesion (Post-PCI proximally)



Consort Diagram

22/02/2018 – 22/11/2019

721 patients consented

- *Angiogram cancelled - 6 (0.8%)*
- *Referred to MDT - 100 (13.9%)*
- *Medical Tx of CAD - 90 (12.5%)*
- *NOCAD on Angiogram - 71 (9.8%)*

- *FFR Negative - 55 (7.6%)*
- *Referred for Surgery - 21 (2.9%)*
- *CTO for staged PCI - 7 (1%)*

371 patients proceeded to PCI

- *STO: no pre-PCI CFR/IMR - 32 (4.4%)*
- *TO: no pre-PCI physiology - 10 (1.4%)*
- *Exclusion Criteria - 17 (2.4%)*
- *Operational Reasons - 15 (2.1%)*
- *Operator Declined - 10 (1.4%)*
- *Iatrogenic Complication - 9 (1.2%)*

- *Unable to pass pressure wire - 3 (0.4%)*
- *Patient withdrew consent - 3 (0.4%)*
- *Balloon Angioplasty only - 2 (0.3%)*
- *Adenosine Intolerance - 1 (0.1%)*
- *Failed PCI - 2 (0.3%)*
- *Miscellaneous - 7 (0.9%)*

260 patients randomized

Results – Baseline Demographics

	PIOS (n=131)	Control (n=129)
Male	117 (89.3%)	109 (84.5%)
Age	58 (54-66)	60 (55-68)
BMI	29 (26-32)	29 (27-32)
Hypertension	58 (44.3%)	58 (45%)
Dyslipidemia	72 (55%)	74 (57.4%)
Diabetes	24 (18.3%)	25 (19.4%)
Atrial Fibrillation	10 (7.6%)	9 (7%)
Previous TIA/Stroke	8 (6.1%)	9 (7%)

	PIOS (n=131)	Control (n=129)
CKD	3 (2.3%)	2 (1.6%)
Family History of CAD	88 (67.2%)	84 (65.1%)
History of Smoking	92 (70.2%)	91 (70.5%)
Heart Failure	27 (20.6%)	15 (11.6%)
Previous MI	37 (28.2%)	40 (31%)
Previous PCI	52 (39.7%)	46 (35.7%)
Previous CABG	1 (0.8%)	0
Valvular Heart Disease	2 (1.5%)	5 (3.9%)

Adapted from Collison et al. Clin Cardiol 2020;43:414–422.

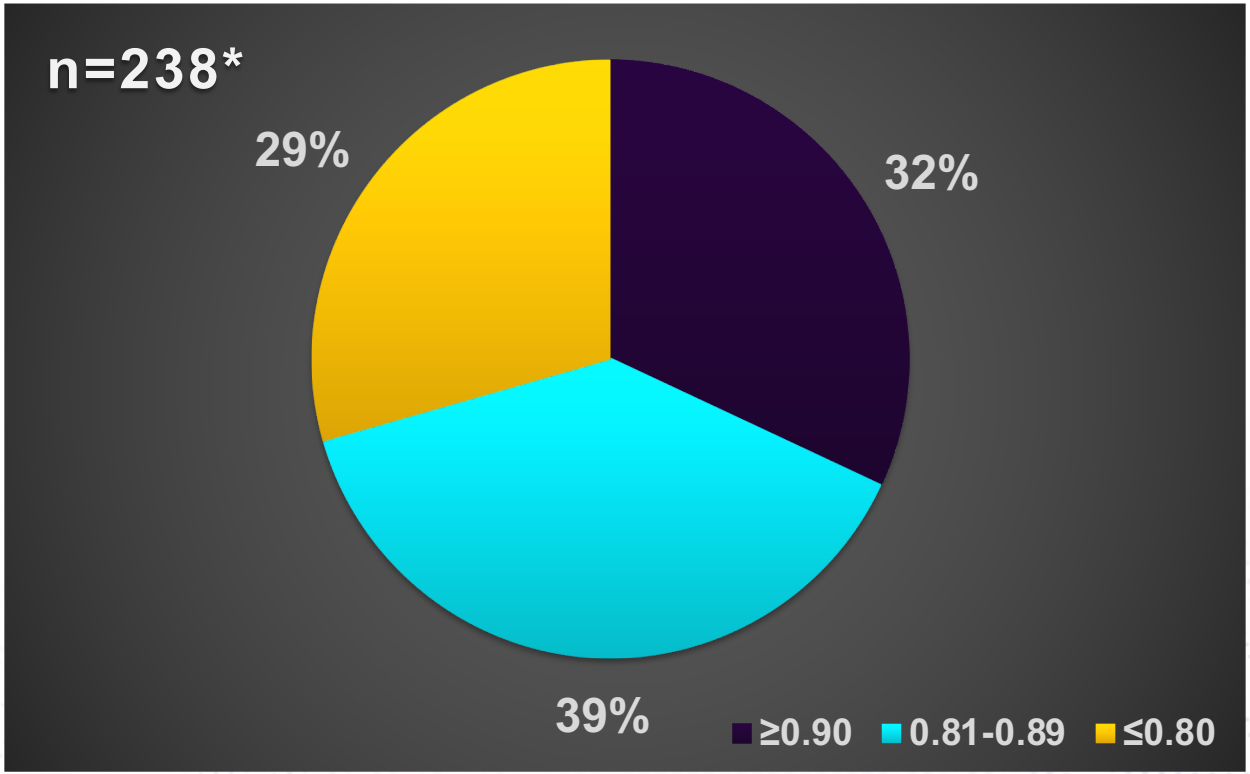
Index PCI - Procedural Details (i)

	PIOS (131)	Control (129)	*P* value
QCA Diameter Stenosis (%)	66±14	66±16	.89
QCA Area Stenosis (%)	86±13	86±12	.96
QCA Lesion Length (mm)	12±5	12±6	.59
Multivessel PCI (%)	13	8.5	.25
PCI performed on PW (%)	24	25	.94
Rotational Atherectomy (%)	1.5	3.9	.24
Pre-dilation (%)	100	100	ns
Post-dilation (%)	99	97	.17
Intravascular Imaging (%)	13.0	19.4	.07

Index PCI - Procedural Details (ii)

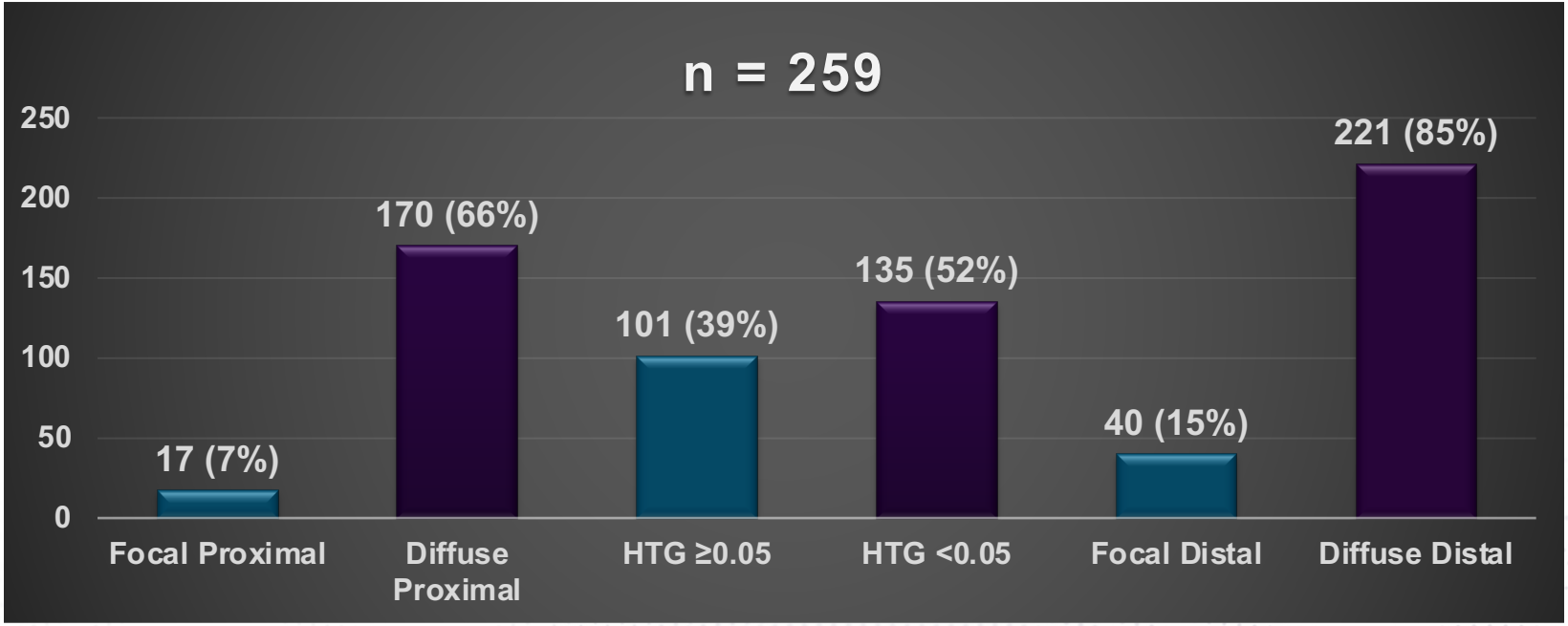
	PIOS (131)	Control (129)	*P* value
Target Lesion Stent Diameter (mm)	3.21±0.43	3.25±0.43	.45
Target Lesion Stent Length (mm)	31±10	31±10	.94
>1 Stent Deployed (%)	26.7	34.1	.20
Total Stent Number in Target Artery (n)	1.5±0.7	1.4±0.6	.49
Total Stent Length in Target Artery (mm)	42±21	41±19	.67
Post-Dilation Balloon Diameter (mm)	3.72±0.58	3.79±0.58	.33
Post-Dilation Pressure (atm)	17±3	17±2	.74
Diameter Difference PD Balloon to Stent	0.5±0.4	0.5±0.4	.63

Angiographically-Guided Post-PCI FFR (pre-randomization)



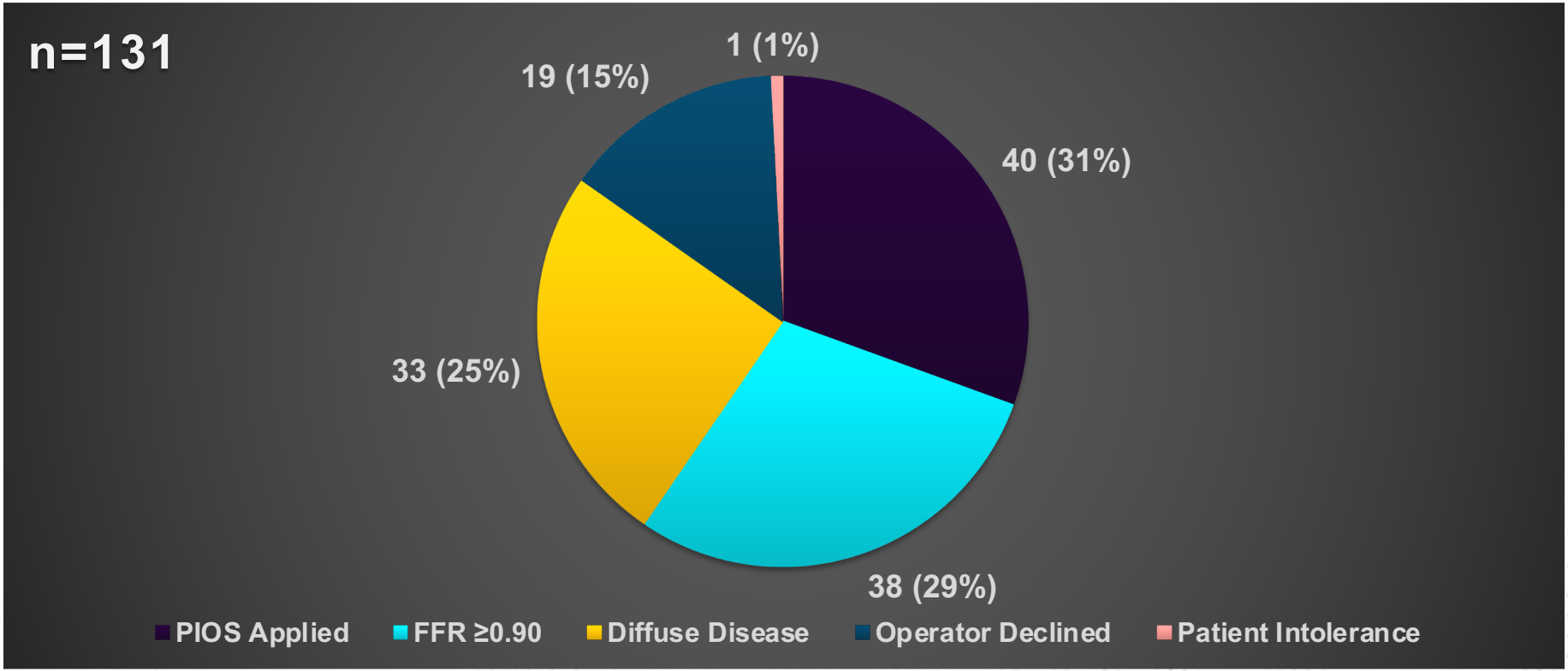
* 238/260 (92%) with Core Lab-adjudicated Post-PCI FFR values for analysis

Post-PCI Hyperemic Pullback Assessment* (pre-randomization)



*: Multiple findings can co-exist in individual vessels
Focal: Abrupt pressure drop ≥0.05 FFR units
HTG: Hyperemic Trans-stent Gradient

Outcomes of Patients Randomized to PIOS

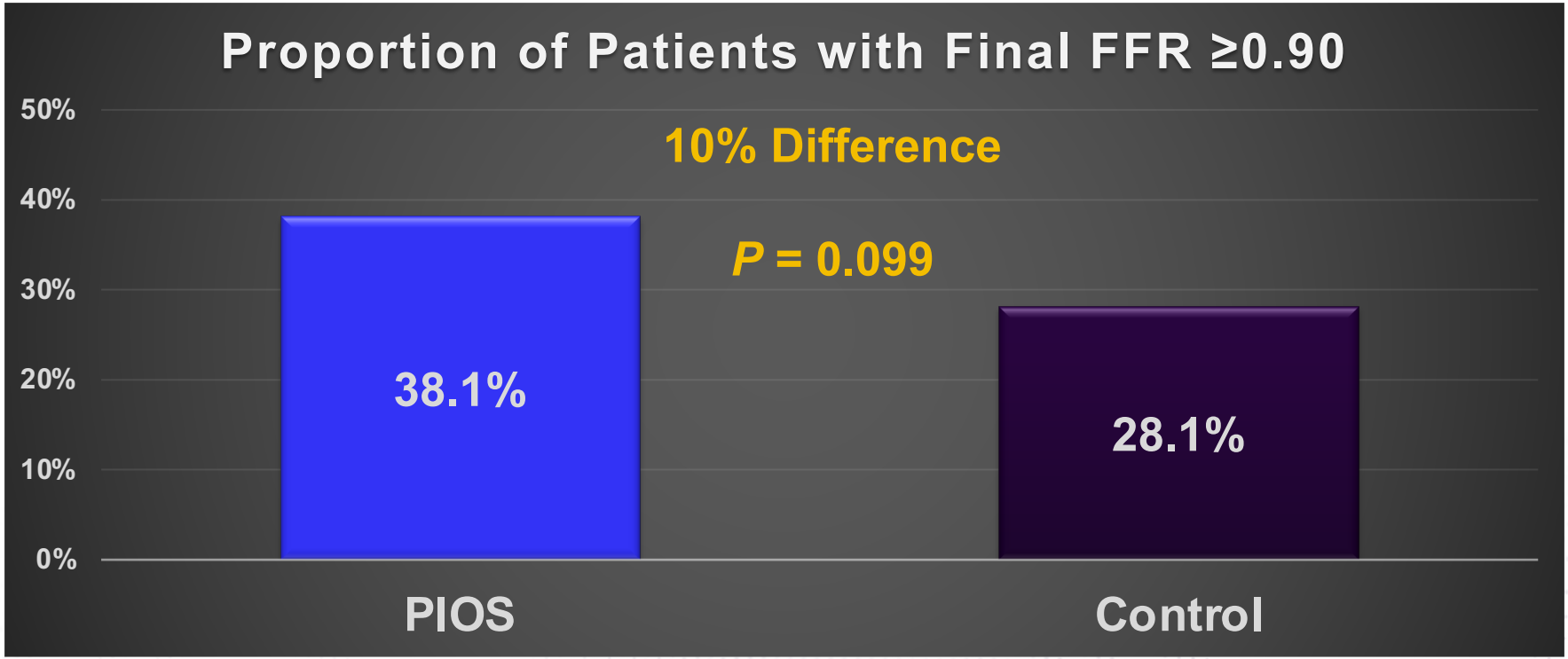


Physiological Effect of PIOS Intervention

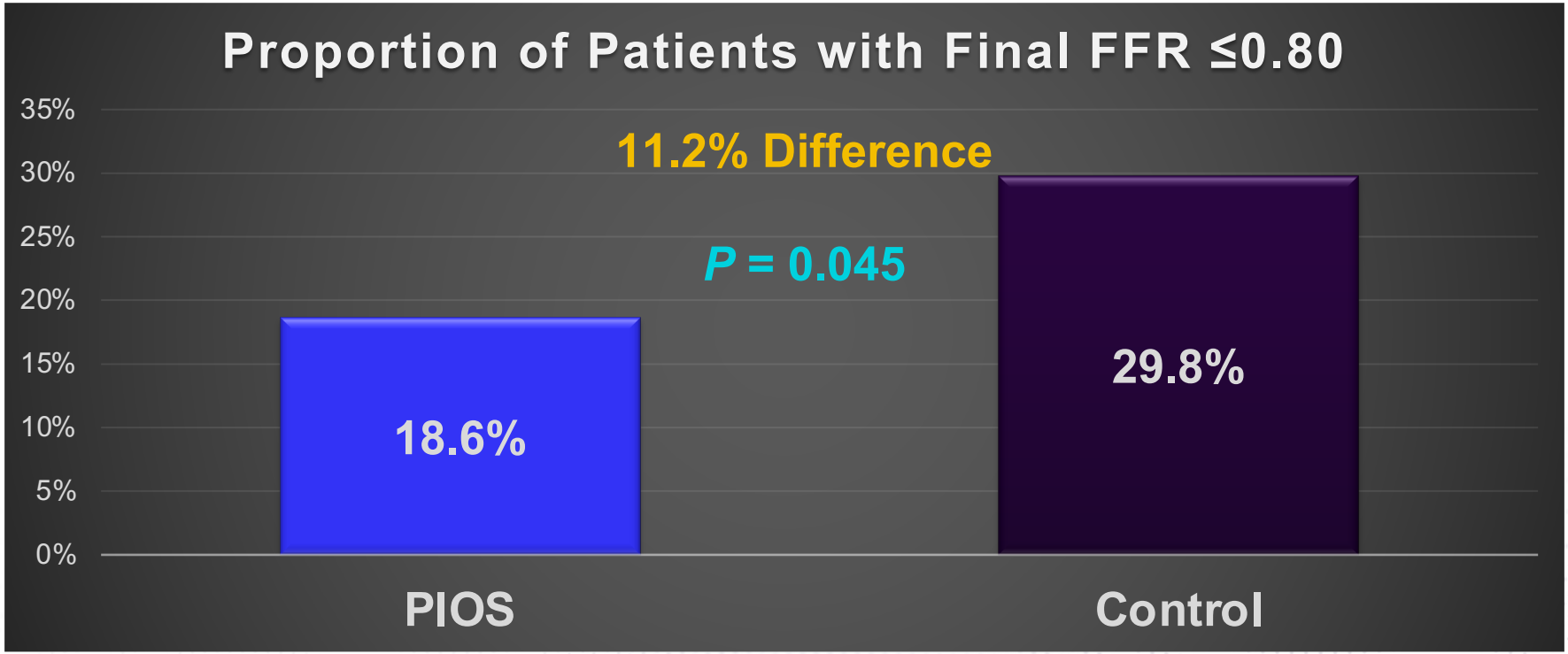
	Initial Post-PCI	Final Post-PCI	Difference	*P* value
FFR	0.76±0.08	0.82±0.06	0.06±0.07	<.001
CFR	3.0±1.6	4.0±2.1	1.0±2.2	.02
IMR	20±8	18±7	-3±8	.08
IMRc	19±7	17±7	-2±8	.17

- 40/131 (31%) had PIOS applied
  - Post-dilation Only – 23/40 (57.5%)
  - Stent Only – 12/40 (30%)
  - Post-dilation & Stent – 5/40 (12.5%)
- 29 paired cases available for analysis after Core Lab adjudication
- Larger increase in FFR observed with Stenting than Post-Dilation

Results – Primary Outcome



Results – Secondary Outcome



Target Vessel Failure

Median (IQR) Follow-Up Time: 1.7 (0.9) years

	PIOS (n=131)	Control (n=129)
Target Vessel Failure, n(%)	1 (0.8)	0
Cardiac Death	1 (0.8)	0
Target Vessel Myocardial Infarction	0	0
Target Vessel Revascularisation	0	0

Additional Procedural Details

	PIOS (n=40)	No PIOS (n=220)	*P* value
Procedure Duration (mins)	94±23	67±24	<.001
Contrast Dose (ml)	225±53	185±51	<.001
Fluoroscopy Time (mins)	23±8	16±8	<.001
Dose Area Product (cGy.cm^2)	5236±2783	3780±2391	<.001
Radiation Dose (mGy)	921±551	686±462	.004
Adenosine Duration (sec)	439±87	290±73	<.001
Adenosine Dose (mg)	93±25	62±32	<.001

Procedural Complications

	PIOS (n=40)	No PIOS (n=220)	*P* value
Procedural Complications (%)	2.5	9.5	.14
Coronary Dissection (%)	0	0.9	.54
Side Branch Occlusion (%)	2.5	3.6	.72
No Flow / Slow Flow (%)	0	0.9	.54
Arm Haematoma >5cm (%)	0	4.5	.17
Type 4a MI (%)	0	2.7	.29

Symptoms - Change in SAQ-7 Scores

Median (IQR) Follow-Up Time: 105 (31) Days

	PIOS (n=114)		Control (n=115)		*P* value
	Value	Change	Value	Change	
Summary Score (SAQ7-SS)					
Baseline	63±25		63±25		.82
Follow-up	82±24	21±25	84±19	22±25	.68

88% of patients completed follow-up questionnaires

Physiology Stratified by Target Vessel

	LAD (n=150)	LCx (n=43)	RCA (n=67)	*P* value
Pre-PCI				
FFR	0.58±0.14	0.61±0.11	0.59±0.16	.52
CFR	2.1±1.0	1.8±0.8	1.8±0.6	.06
IMR	26±10	27±13	32±15	.02
IMRc	19±8	21±10	24±13	.004
Post-PCI				
FFR	0.80±0.07	0.92±0.07	0.91±0.07	<.001
CFR	3.2±1.8	3.3±1.4	3.4±2.1	.82
IMR	22±15	19±11	25±19	.19
IMRc	21±15	19±11	25±19	.14

Physiology Stratified by PCI Indication

	Stable Angina (n=88)	NSTEMI/UA* (n=104)	Staged Non-Culprit PCI (n=68)	*P* value
Pre-PCI				
FFR	0.57±0.14	0.55±0.15	0.67±0.10	<.001
CFR	1.8±0.9	1.8±0.9	2.3±0.9	.005
IMR	29±12	29±13	24±11	.02
IMRc	21±9	21±11	20±10	.99
Post-PCI				
FFR	0.83±0.08	0.86±0.10	0.85±0.09	.11
CFR	3.5±2.1	3.33±1.7	2.9±1.5	.15
IMR	19±11	23±17	24±19	.13
IMRc	19±11	22±17	23±19	.13

*Median of 21 (12-28.5) days post MI

Summary

- In TARGET FFR, after angiographically-guided PCI…
  - *32%* of patients had FFR *≥0.90*
  - *29%* of patients had FFR *≤0.80*
- Based on FFR pullback assessment, a substrate for further optimization was present in 60/131 (46%) patients randomized to PIOS
- Operators considered it appropriate to perform additional post-dilatation +/- stenting in 40/60 (66%) patients
- Among these 40 cases….
  - Mean FFR increased from 0.76 to 0.82, *P*<.001
  - Mean CFR increased from 3.0 to 4.0, *P*=.02

Conclusions

- The majority of patients with angiographically acceptable PCI results have a physiologically suboptimal outcome (post-PCI FFR ≤0.90).
- In an intention-to-treat analysis, randomization of patients with an angiographically acceptable PCI result to an FFR-guided optimization strategy did not achieve a significant (20%) increase in the proportion of patients with final FFR ≥0.90 (38.1% vs. 28.1%, *P=0.099*)
- The PIOS intervention did significantly reduce in the proportion of patients with final FFR ≤0.80 (18.6% vs. 29.8%, *P*=0.045)
- In the subset of patients in whom further intervention was actually performed, final post-PCI FFR and CFR both increased significantly

Acknowledgements

- Patients and staff of the Golden Jubilee National Hospital, Glasgow
- Keith Oldroyd
- Colin Berry
- John McClure
- Carlos Collet & CoreAalst
- Samuel Copt
- Johan Svanerud
- Nils Johnson
- Matthaios Didangelos
- Muhammad Aetesam-ur-Rahman
- Peter McCartney
- Tom Ford
- Novalia Sidik
- David Carrick
- Heerajnarain Bulluck
- Robert McDade
- Ruth McLaren
- Mitchell Lindsay
- Aadil Shaukat
- *Paul Rocchiccioli*
- *Stuart Watkins*
- *Margaret McEntegart*
- *Richard Good*
- *Keith Robertson*
- *Patrick O'Boyle*
- *Andrew Davie*
- *Adnan Khan*
- *Stuart Hood*
- *Hany Eteiba*