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ORIGINAL RESEARCH

Changes in absolute coronary blood flow and myocardial resistance after percutaneous coronary intervention

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ABSTRACT

BACKGROUND: Treating a coronary stenosis by percutaneous coronary intervention (PCI) aims to relieve myocardial ischaemia by improving coronary blood flow. The evolution of coronary flow and resistance post-PCI is not fully understood.

AIMS: This study aimed to investigate the immediate impact of PCI on absolute coronary flow (Q), and epicardial and microvascular resistance (R_{epi} and R_{μ}).

METHODS: In a two-centre cohort including 52 patients, pre- and post-PCI physiological assessments were performed using continuous thermodilution, via a combination of a pressure-temperature sensor wire and a dedicated infusion microcatheter.

RESULTS: Resting Q remained similar before and after PCI (Δ +2 [interquartile range {IQR} −9 to 21] mL/min; p=0.21), as a 193 Wood unit (WU) reduction in resting R_{epi} (Δ −193 [IQR −400 to −59] WU; p<0.001) was offset by a 267 WU increase in resting R_{μ} (Δ +267 [IQR −20 to 474] WU; p=0.002). Conversely, hyperaemic Q rose significantly (Δ +44 [IQR 16 to 92] mL/min; p<0.001), reflecting a 195 WU reduction in hyperaemic R_{epi} (Δ −195 [IQR −379 to −82] WU; p<0.001), while hyperaemic R_{μ} remained stable (Δ +3 [IQR −96 to 75] WU; p=0.87). The median microvascular resistance reserve (MRR) did not change significantly after PCI (Δ −0.2 [IQR −0.7 to 0.6]; p=0.301). Pre- and post-PCI fractional flow reserve (FFR) were strongly and inversely associated with R_{epi} and predicted the improvement of hyperaemic Q.

CONCLUSIONS: PCI significantly reduces epicardial resistance, leading to a pronounced increase in hyperaemic flow, which can be predicted by FFR. Resting Q remained unchanged because of compensatory increases in microvascular resistance, providing direct evidence of coronary flow autoregulation in humans. The MRR was unaffected by PCI, confirming its specificity as an index of microvascular function.

KEYWORDS: absolute coronary flow; coronary physiology; ischaemic heart disease; myocardial resistance; percutaneous coronary intervention

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The progression of the atherosclerotic process within the coronary arteries results in the development of coronary stenoses, which can significantly reduce coronary blood flow during exercise, resulting in angina as a result of myocardial ischaemia and subsequent functional, metabolic, and structural changes of the myocardium[1].

Percutaneous coronary intervention (PCI) aims to address epicardial coronary narrowing to improve coronary blood flow and relieve angina symptoms associated with myocardial ischaemia[2].

Over the years, several coronary flow-surrogate indices (fractional flow reserve [FFR], bolus thermodilution, and Doppler-based indices) have been developed and validated, but more recently, the introduction of the continuous thermodilution method has represented a step forward in facilitating a direct and highly reproducible assessment of absolute coronary flow (Q) and resistance[3] both at rest and during maximal hyperaemia[4].

The aim of the present work was to investigate, for the first time, the impact of PCI on myocardial blood flow and coronary resistance (assessed by continuous intracoronary thermodilution) across the spectrum of patients with ischaemic heart disease.

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Methods

Patients admitted to the Oxford Heart Centre and the Essex Cardiothoracic Centre from December 2021 until October 2022 for a clinically indicated coronary angiogram were enrolled into the Oxford Acute Myocardial Infarction (OxAMI) study and the Essex Stable Angina and Acute Myocardial Infarction study, respectively (REC number 10/H0408/24 and REC reference 22/EE/0016). Both studies were conducted in accordance with the Declaration of Helsinki, and all patients provided informed, written consent for participation in the study. A list of the OxAMI study investigators is provided in **Supplementary Appendix 1**.

The inclusion criteria were the presence of a significant coronary stenosis in a proximal or mid-segment of an epicardial vessel with a diameter of >3.0 mm, with confirmed presence of ischaemia in the respective myocardial territory and suitability for percutaneous revascularisation. Patients presenting with either acute coronary syndrome (non-ST-segment elevation myocardial infarction or unstable angina) or chronic coronary syndrome were included in the present study. Patients were excluded if they presented with ST-segment elevation myocardial infarction, haemodynamic or electrical instability, or out-of-hospital cardiac arrest. Further exclusion criteria were age <18 years, pregnant status, renal impairment (defined as a glomerular filtration rate below 30 mL/min), contraindication to the administration of adenosine, significant valvular disease, and previous coronary artery bypass grafting.

Impact on daily practice

This study demonstrated that percutaneous coronary intervention (PCI) markedly reduces epicardial resistance, resulting in a significant flow increase that is strongly predicted by pre-PCI fractional flow reserve (FFR). The improvement in FFR after PCI closely reflects the gain in flow, supporting the measurement of post-PCI FFR not only as a prognostic index but also as an indicator of effective flow restoration. Furthermore, the finding that resting flow remains unchanged underscores the compensatory role of the coronary microcirculation, with important implications for patient management.

STUDY PROTOCOL

Enrolled patients underwent a coronary physiology assessment using the continuous thermodilution technique before proceeding to intervention. It was left to the operator's discretion whether to predilate with an undersized balloon (≤2.0 mm for vessels with a diameter ≤3.5 mm and ≤2.5 mm for vessels with a diameter >3.5 mm) in the presence of a subtotal occlusion (diameter stenosis >90%). PCI was performed by default with a drug-eluting stent. Upon completion of PCI, the physiological assessment was repeated, ensuring that the location of the pressure-wire sensor and the continuous thermodilution microcatheter tip matched their locations during the preprocedural assessment.

QUANTITATIVE CORONARY ANGIOGRAPHY

Two-dimensional quantitative coronary angiography (QCA) was performed offline using the integrated analysis software of the Philips console (Philips). Measurements were obtained in end-diastolic frames, minimising vessel foreshortening and overlap. The reference vessel diameter, minimal lumen diameter (MLD), lesion length, and percentage diameter stenosis (DS%) were automatically computed and manually adjusted when required.

CORONARY PHYSIOLOGY ASSESSMENT

The index vessel was instrumented with a combined pressure/thermistor guidewire (PressureWire X [Abbott Vascular]). After pressure-waveform equalisation of the wire, aortic pressure (P_a) was measured via the guide catheter, and distal coronary pressure (P_d) was measured via the pressure wire (CoroFlow v3.01 [Abbott]). The resting P_d/P_a ratio and FFR were computed as the ratio of P_d and P_a at rest and during maximal hyperaemia induced by continuous intracoronary

Abbreviations

CFR	coronary flow reserve	**P_d**	distal pressure
FFR	fractional flow reserve	**Q**	absolute coronary flow
hyper	hyperaemia	**R_{epi}**	epicardial resistance
MRR	microvascular resistance reserve	**rest**	resting
P_a	aortic pressure	**R_μ**	microvascular resistance

infusion of saline at room temperature through the RayFlow microcatheter (Hexacath) as described below.

Continuous thermodilution was used to measure Q during resting and hyperaemic conditions as previously described[5]. A thermo-pressure coronary wire (PressureWire X) was placed distally in the artery under assessment, and the dedicated RayFlow microcatheter was positioned just beyond the vessel ostium. Room-temperature saline was infused through the microcatheter via a mechanical pump (MEDRAD Mark 7 Arterion [Bayer]). After zeroing the temperature, infusion was started, and the temperature of the blood-saline mixture (T_{mix}), P_a, and P_d were all recorded (CoroFlow). Resting measurements were obtained with saline infusion at 10 mL/min, annotating resting T_{mix} ($T_{mix,rest}$) and P_d ($P_{d,rest}$) values after a steady state was reached (e.g., at least 1 minute after infusion)[6]. Hyperaemic measurements were then acquired with an infusion rate of 20 mL/min for the left anterior descending artery (or 15 mL/min for other vessels), annotating hyperaemic T_{mix} ($T_{mix,hyp}$) and P_d ($P_{d,hyper}$) values after a steady state was reached (e.g., at least 1 minute after infusion). Finally, the wire was retracted into the microcatheter to record the infusion temperature (T_{inf}) at rest ($T_{inf,rest}$) and during hyperaemia ($T_{inf,hyp}$).

Resting absolute coronary flow (Q_{rest}) was calculated during a low saline infusion rate (10 mL/min) as follows:

$$Q_{rest} = 10\text{mL/min} \times \frac{T_{\text{inf},rest}}{T_{\text{mix},rest}} \times 1.08$$

Hyperaemic absolute coronary flow (Q_{hyper}) was calculated during a high saline infusion rate (20 mL/min or 15 mL/min) as follows:

$$Q_{hyper} = high\ infusion\ rate \times \frac{T_{inf,hyper}}{T_{\text{mix},hyper}} \times 1.08$$

Resting absolute microvascular resistance ($R_{\mu,rest}$) was calculated as follows:

$$R_{\mu,rest} = \frac{P_{d,rest}}{Q_{rest}}$$

Hyperaemic absolute microvascular resistance ($R_{\mu,hyper}$) was calculated as follows:

$$R_{\mu,hyper} = \frac{P_{d,hyper}}{Q_{hyper}}$$

Resting epicardial resistance ($R_{epi,rest}$) was calculated as follows:

$$R_{epi,rest} = \frac{P_{a,rest} - P_{d,rest}}{Q_{rest}}$$

Hyperaemic epicardial resistance ($R_{epi,hyper}$) was calculated as follows:

$$R_{epi,hyper} = \frac{P_{a,hyper} - P_{d,hyper}}{Q_{hyper}}$$

The total resting and hyperaemic absolute resistance ($R_{total,rest}$ and $R_{total,hyper}$) was calculated as the sum of the respective epicardial and microvascular resistances as follows:

$$R_{total,rest} = R_{epi,rest} + R_{\mu,rest}$$

and

$$R_{total,hyper} = R_{epi,hyper} + R_{\mu,hyper}$$

The coronary flow reserve (CFR) was calculated as follows:

$$CFR_{continuous} = \frac{Q_{hyper}}{Q_{rest}}$$

The microvascular resistance reserve (MRR) was calculated as follows[7]:

$$MRR = \frac{CFR}{FFR} x \frac{P_{a,rest}}{P_{a,hyper}}$$

STATISTICAL ANALYSIS

After normality assessment (Shapiro-Wilk), data are expressed as mean±standard deviation (SD) or median (interquartile range [IQR]). Categorical variables are expressed as n (%). For the paired comparison of absolute values before and after PCI, we calculated the absolute difference (post-PCI–pre-PCI) for each parameter. The statistical significance of these paired absolute differences was assessed using a one-sample t-test when normally distributed or a Wilcoxon signed-rank test when not normally distributed. Two-sided p-values<0.05 were considered statistically significant. Paired differences are expressed as a percentage (Δ%) of the pre-PCI value, and their significance versus zero was assessed on paired data by a one-sample t-test or Wilcoxon signed-rank test for non-normally distributed differences. Correlations between variables are expressed using Spearman coefficients. The relative change of Q_{hyper} was defined as the primary outcome. Because data exhibited marked skewness even after Yeo-Johnson transformation (Shapiro-Wilk p<0.05), and to minimise the influence of outliers, we modelled the median response using univariable quantile generalised additive models (qGAMs) at τ=0.5. Each smooth term was specified as a cubic regression spline (k=4) and fitted via the extended log-F likelihood, with smoothing parameters selected by restricted maximum likelihood. Model performance is reported as effective degrees of freedom (EDF), Wald χ^2, p-values, deviance explained, and adjusted pseudo-R^2. All predictions were back-transformed for the display of partial-effect curves. Pre-PCI Q_{hyper} was intentionally excluded from the predictive models, because its presence in both the numerator and the denominator of the percentage-change outcome would introduce mathematical coupling and regression to the mean, yielding a spurious, non-biological association. Statistical analysis was performed with RStudio 2021.09.0 (Build 351 [R Foundation for Statistical Computing]). All tests were 2-sided, and a p-value<0.05 was considered significant.

Results

A total of 52 patients were included in the present study, of whom 41 enrolled at the Oxford Heart Centre and 11 at the Essex Heart Centre. Invasive physiology data were successfully measured before and after PCI in all 52 treated vessels, but two vessels were excluded from the final analysis because of technical issues (significant temperature [≥0.05°C] and/or pressure ratio drift [≥0.03 FFR]). Baseline and angiographic characteristics are summarised in **Table 1**. All patients underwent successful PCI without any procedural complications, and only one patient was treated with a drug-eluting balloon.

CORONARY PHYSIOLOGY CHANGES ASSOCIATED WITH PCI

Physiological measurements before and after PCI are presented in **Table 2** and in **Supplementary Table 1**. In 15 (29%) cases, pre-PCI assessment had to be performed after predilation with an undersized balloon. After PCI,

Table 1. Baseline, angiographic, and procedural characteristics.

Population	n=52
Baseline characteristics	
Age, years	64±10
Male	41 (79)
Body mass index, kg/m^2	28 (26-32)
Hypertension	28 (54)
Diabetes mellitus	10 (19)
Hypercholesterolaemia	20 (39)
Acute coronary syndrome	30 (58)
Previous coronary intervention	11 (21)
Smoking habit	22 (42)
Angiographic characteristics	
Vessel	
Left anterior descending	34 (65)
Left circumflex	6 (12)
Right coronary	12 (23)
Diameter stenosis, %	67±14
Minimal lumen diameter, mm	0.95±0.42
Lesion length, mm	22.1 (17.5-37.1)
Reference vessel diameter, mm	2.81±0.49
Procedural characteristics	
Contrast, mL	213±67
Stent volume, mm^3	114 (69-162)
Stent length, mm	32 (24-48)

Values are presented as mean±standard deviation, median (interquartile range), or n (%).

we observed a significant improvement in the resting P_d/P_a ratio from 0.83 (IQR 0.71-0.90) to 0.95 (IQR 0.93–0.99; Δ +0.13 [IQR 0.04-0.25]; p<0.001), FFR from 0.59±0.15 to 0.86±0.09 (Δ +0.27±0.17; p<0.001) and CFR from 1.7 (IQR 1.4-1.9) to 2.2 (IQR 1.9-2.6; Δ +0.5 [IQR 0.1-1.1]; p<0.001). The median Q_{rest} did not significantly increase after PCI (76 [IQR 52-94] mL/min vs 80 [IQR 56-102] mL/min; Δ +2 [IQR −9 to 21] mL/min; p=0.210) **(Figure 1A)**, nor did $R_{total,rest}$ (1,226 [IQR 909-1,843] WU vs 1,130 [IQR 958-1,716] WU; Δ −2 [IQR −293 to 297] WU; p=0.819). This was the result of a significant decrease in the $R_{epi,rest}$ post-PCI from 235 (IQR 144-502) WU to 76 (IQR 33-152) WU (Δ −193 [IQR −400 to −59] WU; p<0.001) coupled with a concomitant increase in the $R_{\mu,rest}$ from 899 (IQR 625-1,381) WU to 1,097 (IQR 907-1,567) WU (Δ +267 [IQR −20 to 474] WU; p=0.002) **(Figure 1B-Figure 1C)**. In contrast, the median Q_{hyper} significantly increased after PCI from 122 (IQR 89-154)±57 mL/min to 190 (IQR 124-230) mL/min (Δ +44 [IQR 16-92] mL/min; p<0.001) **(Figure 1D)**, while the $R_{total,hyper}$ decreased from 724 (IQR 558-935) WU to 512 (IQR 411-708) WU (Δ −164 [IQR −328 to −38] WU; p<0.001). This was driven by a significant decrease in $R_{epi,hyper}$ post-PCI from 275 (IQR 168-454) WU to 72 (IQR 29-122) WU (Δ −195 [IQR −379 to −82] WU; p<0.001) **(Figure 1E)**, whereas $R_{\mu,hyper}$ remained unchanged (from 429 [IQR 343-538] WU to 452 [IQR 325-581] WU; Δ +3 [IQR −96 to 75] WU; p=0.866) **(Figure 1F)**. The median MRR did not significantly change after PCI (from 2.7 [IQR 2.4-3.4] to 2.6 [IQR 2.2-3.4]; Δ −0.2 [IQR −0.7 to 0.6]; p=0.301). A sensitivity analysis excluding patients who required gentle predilation before the

Table 2. Pre-PCI and post-PCI invasive physiology measurements.

Variable	Pre-PCI	Post-PCI	Δ absolute change	*p*-value
$P_{a,rest}$, mmHg	91 (83-101)	96 (87-104)	+5 (–3 to 10)	0.018
$P_{d,rest}$, mmHg	68±20	89±13	+21±19	<0.001
$P_{a,hyper}$, mmHg	88 (80-99)	91 (83-105)	+3 (–3 to 9)	0.136
$P_{d,hyper}$, mmHg	53±15	78±15	+24±16	<0.001
P_d/P_a	0.83 (0.71-0.90)	0.95 (0.93-0.99)	+0.13 (0.04 to 0.25)	<0.001
FFR	0.59±0.15	0.86±0.09	+0.27±0.17	<0.001
P_a ratio	1.02 (0.98-1.08)	1.02 (0.98-1.07)	+0.01 (–0.06 to 0.09)	0.518
Q_{rest}, mL/min	76 (52-94)	80 (56-102)	+2 (–9 to 21)	0.210
Q_{hyper}, mL/min	122 (89-154)	190 (124-230)	+44 (16 to 92)	<0.001
$R_{\mu,rest}$, WU	899 (625-1,381)	1,097 (907-1,567)	+267 (–20 to 474)	0.002
$R_{epi,rest}$, WU	235 (144-502)	76 (33-152)	–193 (–400 to –59)	<0.001
$R_{total,rest}$, WU	1,226 (909-1,843)	1,130 (958-1,716)	–2 (–293 to 297)	0.819
$R_{\mu,hyper}$, WU	429 (343-538)	452 (325-581)	+3 (–96 to 75)	0.866
$R_{epi,hyper}$, WU	275 (168-454)	72 (29-122)	–195 (–379 to –82)	<0.001
$R_{total,hyper}$, WU	724 (558-935)	512 (411-708)	–164 (–328 to –38)	<0.001
CFR	1.7 (1.4-1.9)	2.2 (1.9-2.6)	+0.5 (0.1 to 1.1)	<0.001
MRR	2.7 (2.4-3.4)	2.6 (2.2-3.4)	–0.2 (–0.7 to 0.6)	0.301
CFR/FFR ratio	2.9±1.0	2.7±1.1	–0.2±1.2	0.329

Values are presented as mean±SD or median (interquartile range). CFR: coronary flow reserve; FFR: fractional flow reserve; hyper: hyperaemic; MRR: microvascular resistance reserve; P_a: aortic pressure; $P_{a,hyper}$: hyperaemic aortic pressure; P_a ratio: resting to hyperaemic aortic pressure; $P_{a,rest}$: resting aortic pressure; PCI: percutaneous coronary intervention; P_d: distal pressure; $P_{d,hyper}$: hyperaemic distal pressure; $P_{d,rest}$: resting distal pressure; Q: absolute coronary flow; R_{epi}: epicardial resistance; rest: resting; R_{total}: total myocardial resistance; R_μ: microvascular resistance; SD: standard deviation; WU: Wood units; Δ: delta

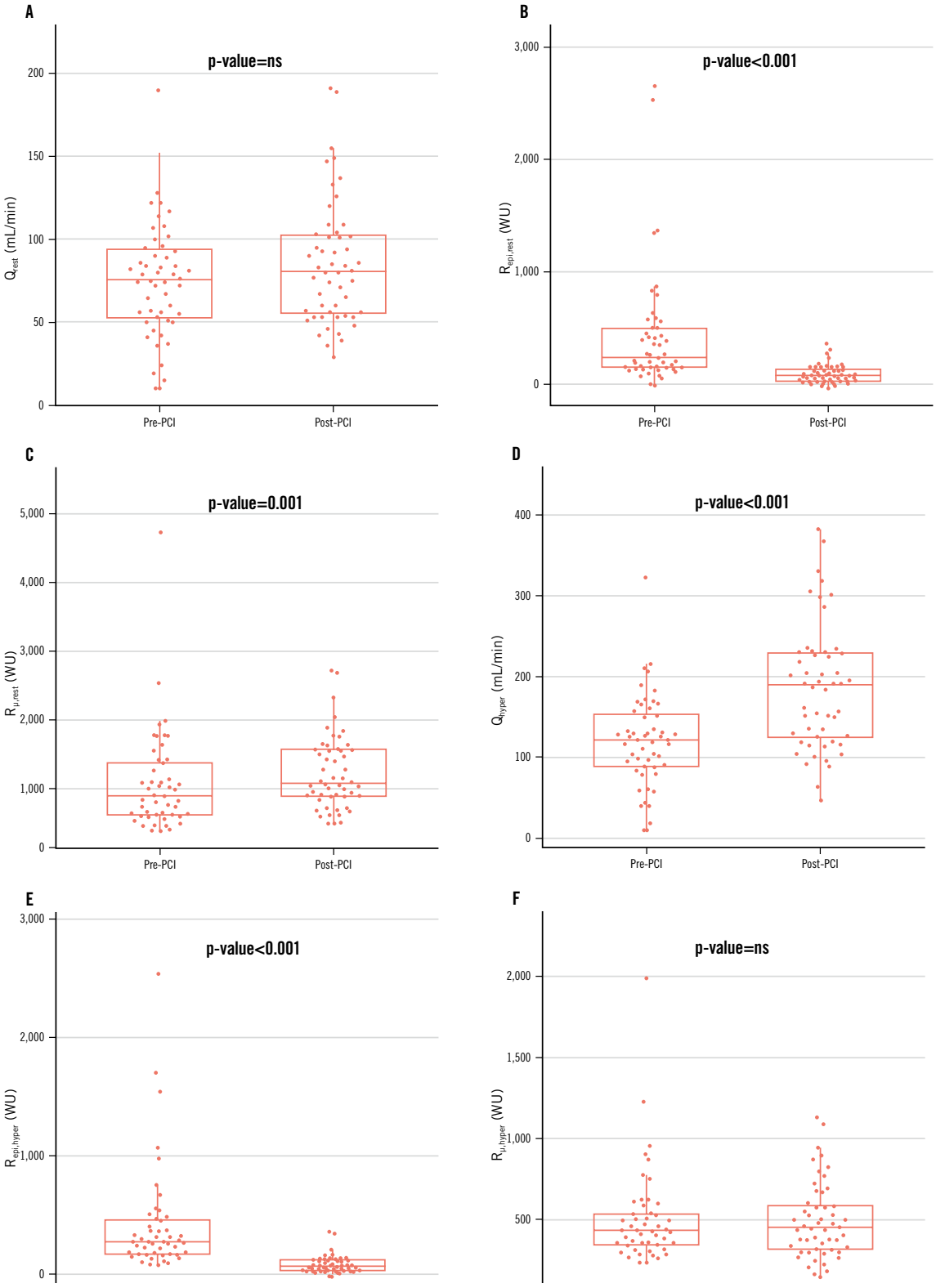


Figure 1. *Pre- and post-PCI changes in coronary flow and resistance (absolute changes). Six paired box plots (A-F) compare baseline (pre-PCI) with post-intervention (post-PCI) values for each physiological variable: (A) Q_{rest}; (B) $R_{epi,rest}$; (C) $R_{\mu,rest}$; (D) Q_{hyper}; (E) $R_{epi,hyper}$; (F) $R_{\mu,hyper}$. Centre lines show the medians, boxes the IQR, and whiskers 1.5×IQR. Above each panel the Wilcoxon signed-rank p-value is reported as "p-value=ns" when p≥0.05, "p-value<0.001" when p<0.001, otherwise the exact value to 3 decimal places. ns: not significant; PCI: percutaneous coronary intervention; Q_{hyper}: hyperaemic absolute coronary flow; Q_{rest}: resting absolute coronary flow; $R_{epi,hyper}$: hyperaemic epicardial resistance; $R_{epi,rest}$: resting epicardial resistance; $R_{\mu,hyper}$: hyperaemic microvascular resistance; $R_{\mu,rest}$: resting microvascular resistance; WU: Wood units*

physiological measurements yielded results consistent with the overall findings **(Supplementary Table 2)**.

Of note, a decrease in Q_{rest} and Q_{hyper} after PCI was observed in 23 (46%) and in 4 (8%) cases, respectively, despite an improvement in both the P_d/P_a ratio and FFR post-PCI **(Supplementary Table 3)**. Neither Q_{rest} nor Q_{hyper} changes were statistically different across the types of coronary syndrome presentation or vessel treated **(Supplementary Figure 1)**.

QUANTITATIVE CORONARY ANGIOGRAPHY

QCA was available in 32 out of 52 vessels. Four vessels were excluded because of poor image quality, and in 15 vessels, QCA could not be performed because calibration data were missing. The mean DS% was 67±14%, with a reference vessel diameter of 2.81±0.49 mm, an MLD of 0.95±0.42 mm, and a median lesion length of 22.1 mm (IQR 17.5-37.1). DS% correlated inversely with FFR (ρ=–0.40; p=0.030) and P_d/P_a (ρ=–0.39; p=0.037), whereas MLD correlated positively with FFR (ρ=0.48; p=0.009) and P_d/P_a (ρ=0.46; p=0.012). MLD also showed a moderate inverse correlation with hyperaemic epicardial resistance ($R_{epi,hyper}$; ρ=–0.40; p=0.035). None of the QCA-derived parameters showed a significant correlation with microcirculatory resistance, either at rest or during hyperaemia. When assessing changes after PCI, the relative change of $R_{epi,hyper}$ correlated inversely with DS% (ρ=–0.39; p=0.042) and positively with MLD (ρ=0.42; p=0.024), indicating that more severe anatomical stenoses were associated with greater reductions in epicardial resistance following stenting. No significant correlations were observed between any QCA parameter and the relative increase in resting or hyperaemic absolute coronary flow after PCI **(Supplementary Figure 2)**.

PRE-PCI PREDICTORS OF CHANGE IN HYPERAEMIC CORONARY FLOW

The relative change in Q_{hyper} (ΔQ_{hyper}) was significantly associated with a lower pre-PCI FFR (ρ=–0.53; p<0.001), and higher $R_{epi,hyper}$ (ρ=0.51; p<0.001) **(Supplementary Figure 3)**. Notably, FFR demonstrated a strong inverse correlation with $R_{epi,hyper}$ (ρ=–0.83; p-value <0.001) **(Figure 2)**. CFR, $R_{\mu,hyper}$ and MRR pre-PCI were not significantly correlated with ΔQ_{hyper}.

In univariate qGAMs (τ=0.50) on Yeo-Johnson-transformed ΔQ_{hyper}, baseline FFR demonstrated a hyperbolic association (EDF=1.94, χ^2=5.61; p=0.074), with the steepest increases in median ΔQ_{hyper} occurring at lower FFR values and a plateau ($\Delta Q_{hyper} \rightarrow 0$) as FFR exceeded ~0.8 **(Figure 3A)**. This model explained 19.4% of the deviance (adjusted pseudo-R^2=0.23). In contrast, baseline epicardial resistance ($R_{epi,hyper}$) exhibited a highly significant linear association (EDF=1.00, χ^2=214.4; $p<2\times10^{-16}$), accounting for 28.6% of the deviance (adjusted pseudo-R^2=0.45) **(Figure 3B)**. These fin+dings indicate that, although both pre-PCI FFR and $R_{epi,hyper}$ predict median hyperaemic flow gain, epicardial resistance offers the stronger univariate signal.

IMPACT OF PCI ON EPICARDIAL AND MICROVASCULAR HYPERAEMIC MYOCARDIAL RESISTANCE

ΔQ_{hyper} was strongly related to the reduction in total hyperaemic resistance ($\Delta R_{total,hyper}$; ρ=–0.84; p<0.001) and to its epicardial and microvascular components after PCI

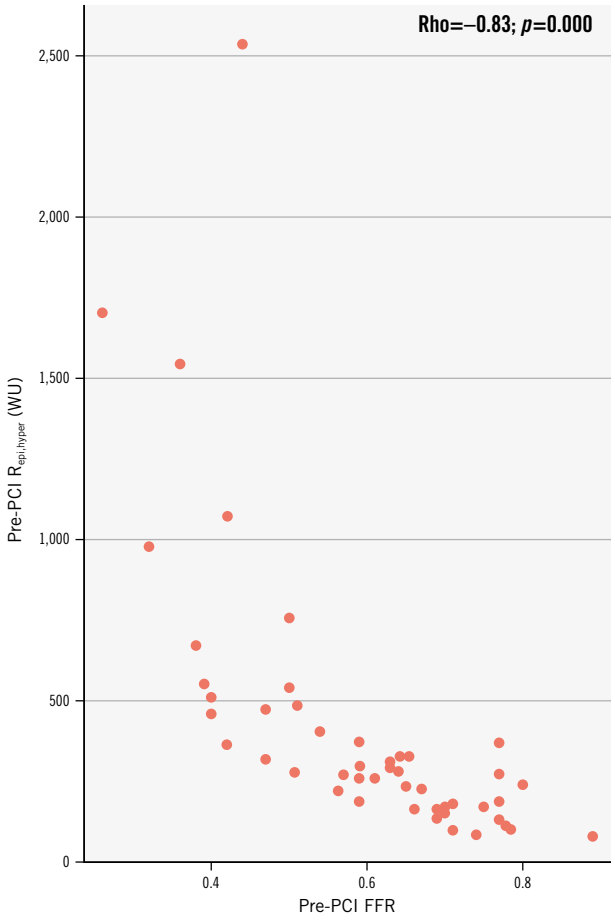


Figure 2. *Relationship between fractional flow reserve and epicardial resistance. FFR: fractional flow reserve; PCI: percutaneous coronary intervention; $R_{epi,hyper}$: epicardial resistance during hyperaemia; Rho: Spearman's rho; WU: Wood units*

($\Delta R_{epi,hyper}$; ρ=–0.47; p<0.001 and $\Delta R_{\mu,hyper}$; ρ=–0.68; p<0.001, respectively).

Epicardial resistance decreased in 95% of vessels after PCI, and the reduction of $R_{epi,hyper}$ was strongly associated with the improvement of FFR (ρ=–0.84; p-value <0.001) **(Figure 4A)**, which in turn was related to the improvement of ΔQ_{hyper} (ρ=0.52; p-value<0.001) as shown in **Figure 4B**.

Microvascular resistance showed a bimodal pattern, decreasing in 48% of vessels and increasing in the remainder. Accordingly, the increase in ΔQ_{hyper} was significantly larger in vessels with a reduction in $R_{\mu,hyper}$ post-PCI compared with those with an increase (+58.4 mL/min [132] vs +15.4 mL/min [34.7]; p-value <0.001), despite a similar reduction in $R_{epi,hyper}$ in the two subgroups (–78.9 WU [33.6] vs –67.2 WU [38.6]; p-value=0.62).

To further assess the joint contribution of epicardial and microvascular resistance changes to the flow response, we fitted univariable and multivariable models. Both $\Delta R_{epi,hyper}$ and $\Delta R_{\mu,hyper}$ were independently associated with the median increase in hyperaemic flow ($\Delta R_{epi,hyper}$: EDF 1.00, χ^2=11.8; p=0.0006; $\Delta R_{\mu,hyper}$: EDF 2.82, χ^2=124.6; p<0.001). **Figure 5**

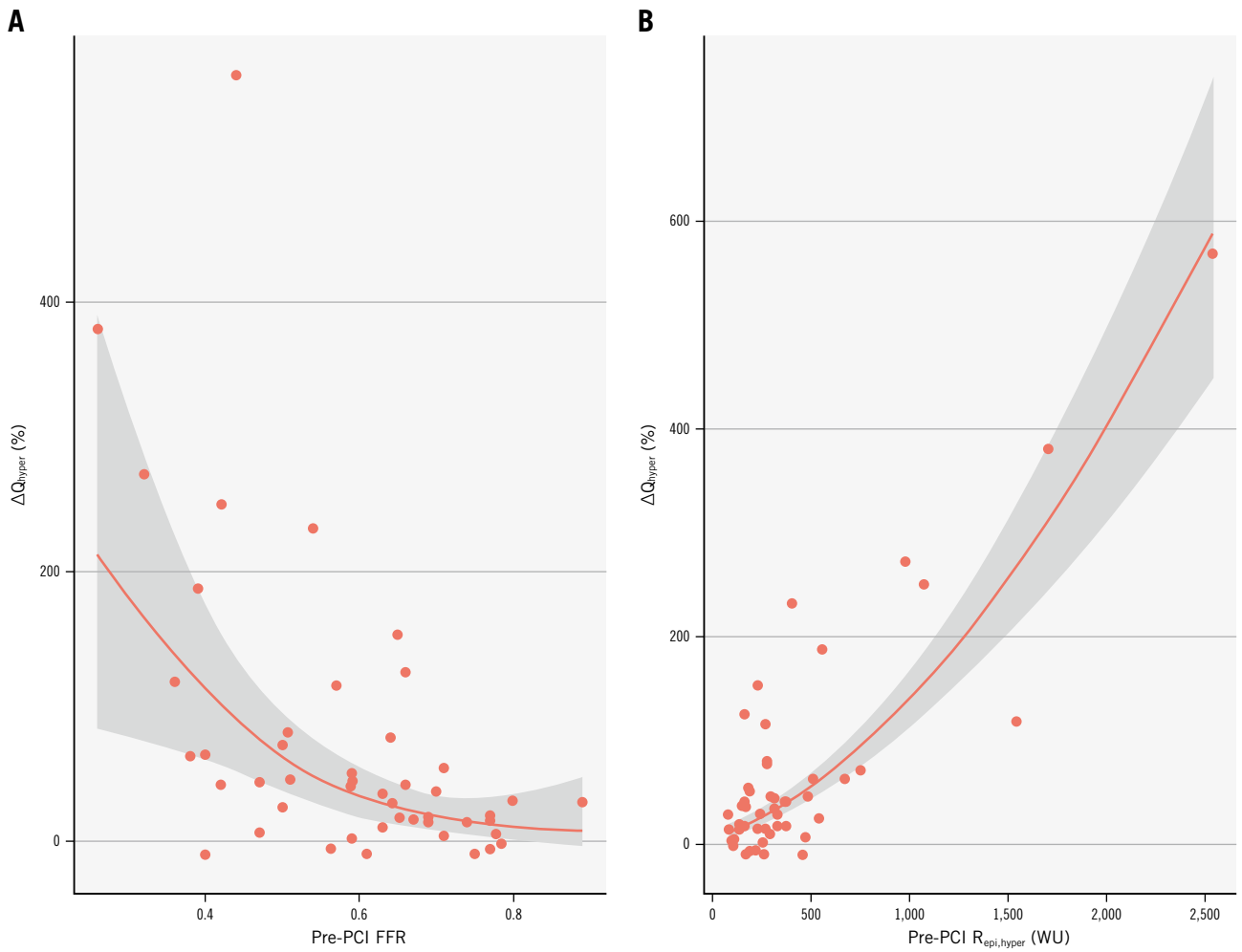


Figure 3. *Pre-PCI predictors of hyperaemic flow change. Partial-effect curves from univariate qGAMs (τ=0.5) showing the median ΔQ_{hyper} (%) plotted against baseline (pre-PCI) FFR and hyperaemic epicardial resistance ($R_{epi,hyper}$): a hyperbolic increase in flow gain is seen at low FFR values, which plateaus as FFR approaches unity (A), and an approximately linear rise in flow gain is observed with higher $R_{epi,hyper}$ (B); shaded ribbons indicate 95% confidence intervals. FFR: fractional flow reserve; PCI: percutaneous coronary intervention; qGAM: quantile generalised additive model; Q_{hyper}: hyperaemic absolute coronary flow*

displays the back-transformed partial-effect curves from the multivariable model. In **Figure 5A**, progressive reductions in epicardial resistance are associated with an almost linear increase in the median ΔQ_{hyper} across the observed range. In **Figure 5B**, the relationship between $\Delta R_{\mu,hyper}$ and ΔQ_{hyper} is non-linear: when microvascular resistance decreases post-PCI, the median ΔQ_{hyper} rises steeply, whereas the increase in microvascular resistance progressively offsets the beneficial effect of epicardial resistance relief, so that the net flow gain is largely neutralised.

Discussion

The present study investigated, for the first time, the impact of PCI on absolute coronary blood flow and myocardial resistance measured with continuous intracoronary thermodilution. The main findings of the study are the following **(Central illustration)**: (1) PCI improves Q_{hyper} with no significant impact on Q_{rest}; (2) both resting and hyperaemic R_{epi} decrease post-PCI; (3) $R_{\mu,rest}$ increases after PCI, whilst $R_{\mu,hyper}$ remains constant; (4) the main pre-PCI determinants of flow changes are FFR and epicardial resistance. Post-PCI flow is influenced by the relative changes in both epicardial and microvascular resistances.

THE RELATION BETWEEN FLOW AND RESISTANCE AT REST

In accordance with Ohm's law, absolute coronary flow is inversely related to the total myocardial resistance, which is the sum of the epicardial and microvascular resistances. In our work, we demonstrated, using the continuous thermodilution technique, that despite PCI significantly reducing $R_{epi,rest}$, Q_{rest} remained unchanged. This is the result of a concomitant increase in $R_{\mu,rest}$ post-PCI, buffering the reduction in $R_{epi,restt}$ and keeping the $R_{total,rest}$ unchanged. Of note, Q_{rest} remained stationary, despite the fact that the resting aortic pressure showed a modest but statistically significant increase after PCI, further supporting the role

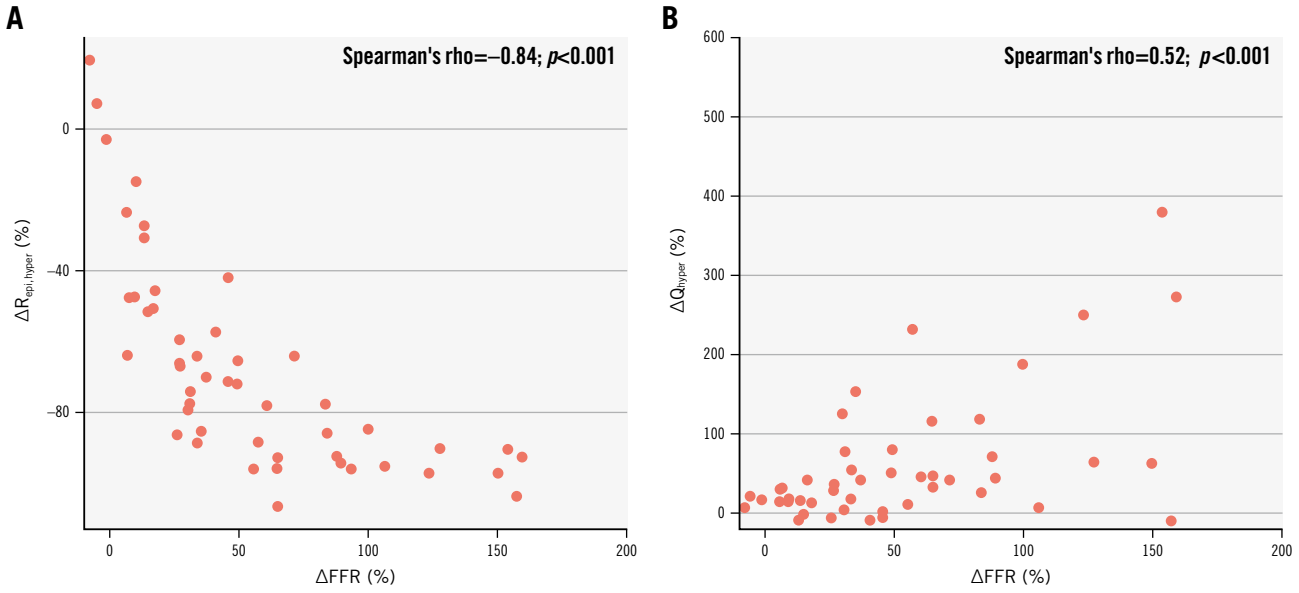


Figure 4. *Correlation between the relative change in FFR and epicardial resistance and the relative hyperaemic flow change after PCI. A) The relative change (Δ) in FFR and $R_{epi,hyper}$ post-PCI; (B) the relative change in FFR and Q_{hyper} post-PCI. FFR: fractional flow reserve; PCI: percutaneous coronary intervention; Q_{hyper}: hyperaemic absolute coronary flow; $R_{epi,hyper}$: hyperaemic epicardial resistance*

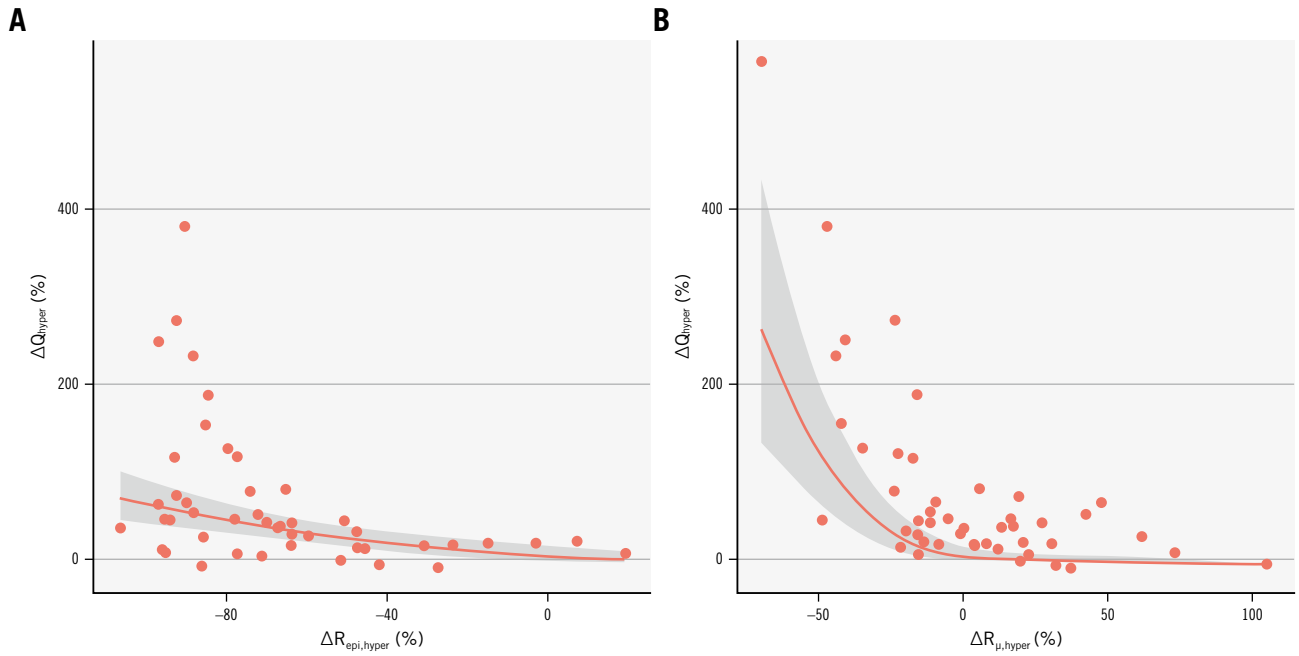
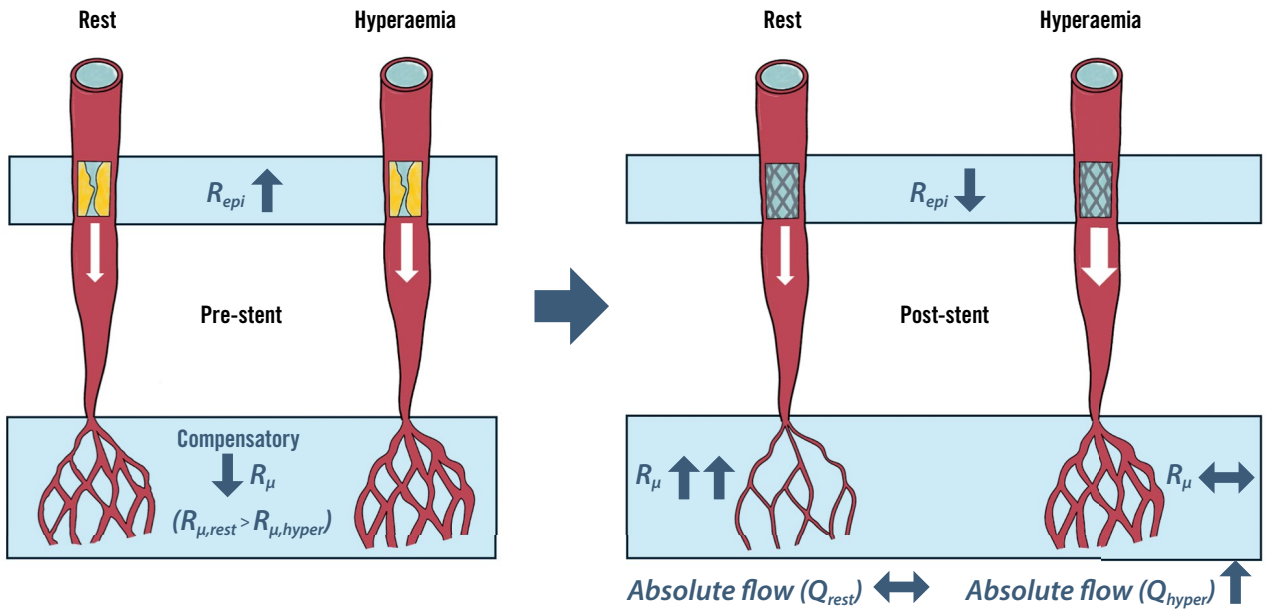


Figure 5. *Impact of epicardial and microvascular resistance changes after PCI on hyperaemic flow. Partial-effect plots relating $\Delta R_{epi,hyper}$ (A) and $\Delta R_{\mu,hyper}$ (B) to the relative hyperaemic flow increase (ΔQ_{hyper}). PCI: percutaneous coronary intervention; ΔQ_{hyper}: change in hyperaemic absolute coronary flow; $\Delta R_{epi,hyper}$: change in hyperaemic epicardial resistance; $\Delta R_{\mu,hyper}$: change in hyperaemic microvascular resistance*

of microcirculation in regulating flow. The behaviour of microvascular resistance at rest provides direct proof of coronary autoregulation as the mechanism maintaining consistency of blood flow across different degrees of coronary stenosis through a compensatory drop in microcirculatory resistances. Ischaemia is the result of the exhaustion of autoregulation that PCI aims to restore[8,9]. Our observations are consistent with those by Nijjer et al, who – by measuring flow velocity with a Doppler wire system – showed that there was a significant increase in

EuroIntervention — Central Illustration

Immediate physiological effects of percutaneous coronary intervention on coronary flow and resistance.



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Q_{hyper}: hyperaemic absolute coronary flow; Q_{rest}: resting absolute coronary flow; R_{epi}: epicardial resistance; R_μ: microvascular resistance; $R_{\mu,hyper}$: hyperaemic microvascular resistance; $R_{\mu,rest}$: resting microvascular resistance

resting flow velocity after intervention only in stenoses with an FFR ≤0.60[10].

THE RELATION BETWEEN FLOW AND RESISTANCE DURING HYPERAEMIA

Contrary to Q_{rest}, Q_{hyper} was shown to significantly improve after PCI in our work (relative change: +39% [IQR 14.7-88.8]), as $R_{epi,hyper}$ decreased and $R_{\mu,hyper}$ remained stationary. It should be highlighted that the hyperaemic aortic pressure ($P_{a,hyper}$) did not change significantly before or after PCI, supporting the hypothesis that the improvement in flow is driven by the reduction in total resistance. These findings are again aligned with what was shown by Nijjer et al, who reported an increase in hyperaemic flow velocity, measured with a Doppler wire system, across all stenoses, with a relative change that was higher for the most significant stenoses (FFR <0.80). Equally, Kanaji et al[11] showed that Q_{hyper} significantly increased after PCI and that R_μ remained unchanged, though their findings were limited by the application of the continuous thermodilution technique using a non-dedicated single lumen microcatheter. The improvement of Q_{hyper} resulted in a significant increase in the CFR, while MRR remained unchanged after PCI. These data prove that MRR, unlike CFR, is minimally influenced by R_{epi}, as shown by Mahendiran et al, who, using a human model of controlled graded epicardial stenosis, demonstrated that regardless of the epicardial resistance, MRR exhibited a negligible decrease while CFR significantly decreased[12,13].

THE VALUE OF FFR PRE- AND POST-PCI

Pre-PCI FFR is a well-established marker of lesion severity; our data confirmed a significant correlation between FFR and epicardial resistance, as well as between angiographic indices (MLD and DS%). We observed a continuous relationship between pre-PCI FFR values and the magnitude of coronary flow improvement after PCI. In contrast, no significant correlations were observed between any QCA parameter and the relative increase in resting or hyperaemic absolute coronary flow after PCI. Aligning with this finding, the Placebo-controlled Trial of Percutaneous Coronary Intervention for the Relief of Stable Angina (ORBITA-2) trial by Foley et al demonstrated that physiological stenosis severity, as measured by FFR and the instantaneous wave-free ratio, predicts placebo-controlled angina relief from PCI[14]. Additionally, Johnson et al showed that lower pre-PCI FFR values are associated with a higher risk, thereby conferring larger absolute benefits from revascularisation[15]. We reinforce the value of physiology-guided revascularisation in predicting coronary flow improvement post-PCI, symptom relief, and the prognostic benefits of myocardial revascularisation.

The correlation observed between a change in FFR and hyperaemic flow change after intervention supports the value of pre- and post-PCI FFR (FFR_{pre} and FFR_{post},

respectively) assessment as a potential surrogate of coronary flow improvement. FFR is theoretically defined as the maximum achievable blood flow in the presence of a stenosis divided by the maximum flow (Q_{max}) if there is no obstructive epicardial coronary disease at all[16] **(Equation 1)**. It follows that the ratio of pre- and post-PCI FFR equals the ratio of pre- and post-PCI hyperaemic flow (Q_{pre} and Q_{post}, respectively) **(Equation 2)**.

$$FFR = \frac{Q_{hyper}}{Q_{max}}$$

(Equation 1)

$$\frac{FFR_{pre}}{FFR_{post}} = \frac{\frac{Q_{pre}}{Q_{max}}}{\frac{Q_{post}}{Q_{max}}} = \frac{Q_{pre}}{Q_{post}}$$

(Equation 2)

As hypothesised, we found a strong relation between the pre- and post-PCI ratios of FFR and hyperaemic flow (ρ=0.63; p<0.001) **(Figure 6)**, supporting the expected coupling between the change in FFR and the change in hyperaemic flow. This is in agreement with previous findings from Aarnoudse et al who found good agreement between the increase in thermodilution-derived volumetric blood flow after PCI and the increase in FFR[5]. In contrast, Kanaji et al[11] found no relationship between the change in FFR and the increase in hyperaemic flow. This discrepancy may stem from different equipment and hyperaemia-induction methods. In our study, saline was infused using a dedicated microcatheter with four side holes (RayFlow), which is the demonstrated gold standard for continuous thermodilution[4]. Kanaji et al measured flow using a microcatheter with a single distal end-hole (3.9 Fr, KIWAMI [Terumo]). The microcatheter used in our study has a larger outer diameter (0.84 mm vs 1.3 mm for KIWAMI), which might translate into greater haemodynamic impact on the FFR measurement, especially in diseased vessels. The haemodynamic effect of the microcatheter is indeed a well-established cause of discordance when FFR is measured conventionally or with continuous thermodilution, with a mean difference of ~0.03 FFR[3,17]. In this regard, in our cohort, we found a broadly similar difference in FFR values measured with the two approaches (0.05 FFR)[3,17]. Another difference between our study and that of Kanaji et al lies in the method for induction of maximal hyperaemia. Kanaji et al reached maximal hyperaemia with a continuous intracoronary infusion of saline at 20 mL/min on top of peripheral adenosine infusion, postulating that adenosine infusion can further increase Q when compared with saline infusion only. In our study, maximal hyperaemia was reached only with a continuous infusion of saline through the RayFlow microcatheter, as previous studies have shown that it guarantees maximal hyperaemia[18-21].

THE IMPACT OF MICROVASCULAR RESISTANCE CHANGE AFTER PCI

Despite the strong relation between pre- and post-PCI ratios of FFR and hyperaemic flow as shown in **Figure 6**, in our study we observed a reduction in Q_{hyper} following PCI in 4 out of 52 cases (8%), despite an improvement in FFR post-PCI and stationary haemodynamic conditions compared with pre-PCI. This pattern is compatible with previous literature.

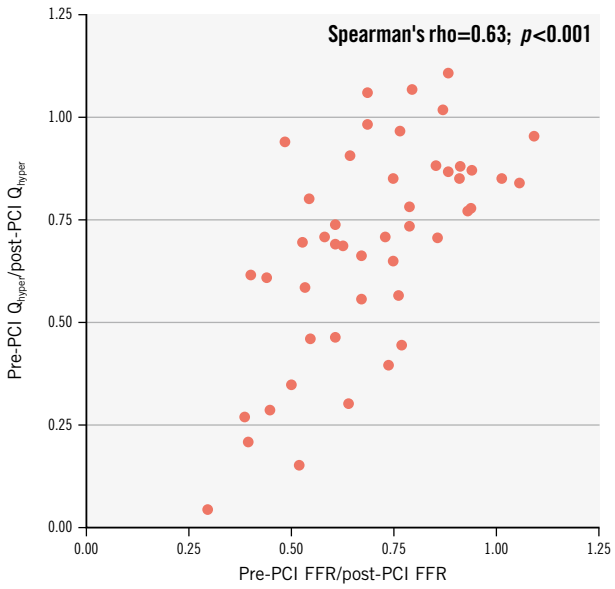

Figure 6. *Correlation between the pre- and post-PCI ratio of FFR and the pre- and post-PCI ratio of hyperaemic coronary flow. FFR: fractional flow reserve; PCI: percutaneous coronary intervention; Q_{hyper}: hyperaemic absolute coronary flow*

Matsuda et al showed a 14% discordance rate between FFR and flow velocity following successful PCI[22]. Similarly, Kanaji et al observed a reduction in coronary sinus flow, as measured by phase-contrast cine-magnetic resonance, in 24% of patients with successful PCI despite positive FFR changes[11]. In our study, cases with a discordance between a drop in Q_{hyper} and improvement in FFR were all associated with increased R_{μ} post-PCI. The relative changes of $R_{\mu,hyper}$ after PCI could explain the potential discordance between FFR and Q changes after PCI. The equivalence between FFR and Q ratio **(Equation 2)** is based on the assumption that microvascular resistance is minimal and constant after PCI, a condition not often met, as evidenced in our cohort. Indeed, we observed that after PCI, $R_{\mu,rest}$ increased in 35 vessels (71%) and decreased in 14 (29%), leading to a significant cohort-level increase. Conversely, $R_{\mu,hyper}$ increased in 25 vessels (51%) and decreased in 24 (49%), resulting in a neutral overall effect.

Several mechanisms may explain the observed changes in R_{μ} after PCI. As discussed above, the increase in $R_{\mu,rest}$ after PCI, paired with the modestly changed $R_{\mu,hyper}$ is a hallmark of the autoregulation mechanism that occurred in 13 (27%) cases. However, in 22 cases (45%), we observed a simultaneous increase in $R_{\mu,rest}$ and $R_{\mu,hyper}$; this phenomenon can be interpreted as the result of distal embolisation after PCI[23-25]. On the other hand, a combined decrease in $R_{\mu,rest}$ and $R_{\mu,hyper}$ after PCI (observed in our cohort in 11 cases [22%]) can be the result of an intrinsic vasodilatory response of the microcirculation immediately after the procedure. This would fit with what has been reported by Verhoeff et al, who showed a decrease of $R_{\mu,hyper}$ to a level below that of the corresponding non-treated reference vessel in the immediate post-PCI period[26]. Equally, in a larger cohort of 245 vessels,

Murai et al showed that the index of microvascular resistance significantly decreased after PCI (median 1.9 [IQR −4.9 to 10.1])[27]. The reduction of hyperaemic resistance after PCI is supposed to be related to an increase in distal pressure after the intervention, which leads to an increase in the diameter (flow-mediated dilation) of the microvasculature, according to a mechanism often referred to as "pressure dependence of hyperaemic microvascular resistance"[28-30].

This is the first study investigating the relative changes of Q, R_{epi}, and R_{μ} at rest and during maximal hyperaemia in a real-world cohort of patients undergoing PCI. Our data reveal that flow results from a complex interaction between epicardial and microvascular resistances, both of which can be directly and indirectly affected by PCI. Despite advancements in PCI techniques, residual angina persists in up to 60% of patients undergoing PCI, as recently demonstrated in the ORBITA-2 study[31]. While various hypotheses have been proposed to explain this phenomenon, it would seem that a better understanding of the behaviour of coronary flow and resistance after PCI might play a role, underscoring the need for further research in the field.

Limitations

Several limitations of our study should be acknowledged. First, an *a priori* sample size calculation was not possible because of the lack of preliminary data. This may affect the statistical power of our findings and their generalisability, which should therefore be considered hypothesis-generating and useful for the design of future studies. The relatively small sample size also limits our ability to draw firm conclusions for different subgroups. Coronary flow is influenced by haemodynamic variables, such as heart rate and driving pressure. Additionally, flow was not indexed for the subtended myocardial mass. However, we believe that the paired data analysis adopted in our study effectively addresses this limitation, enhancing the robustness and reliability of our conclusions. Flow and resistance were measured 5 to 10 minutes after PCI, and our results may be influenced by the presence of acute and reversible mechanisms. Wedge pressure and central venous pressure measurements were largely unavailable, precluding quantification of collateral flow; therefore, we cannot exclude a contribution of collateral dynamics to the observed changes in absolute coronary flow after PCI. In this study, maximal hyperaemia was induced by intravenous adenosine infusion, which should be regarded as a surrogate of exercise-induced hyperaemia and not an equivalent stimulus. The physiological and haemodynamic responses to adenosine hyperaemia cannot be considered directly comparable to those observed during exercise. An invasive follow-up was not part of our protocol.

Conclusions

This study demonstrated that PCI significantly reduces epicardial resistance, leading to a pronounced increase in hyperaemic flow, which can be predicted by FFR. Resting flow remained unchanged because of compensatory increases in microvascular resistance, providing direct evidence of coronary flow autoregulation in humans. MRR was unaffected by PCI, confirming its specificity as an index of microvascular function.

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Conflict of interest statement

The authors have no conflicts of interest to declare related to the present manuscript.

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Supplementary data

Supplementary Appendix 1. The Oxford Acute Myocardial Infarction (OxAMI) Study investigators list.

Supplementary Table 1. Pre-PCI and post-PCI invasive physiology measurement with relative changes.

Supplementary Table 2. Pre-PCI and post-PCI invasive physiology measurement, excluding patients who underwent predilation of the lesion.

Supplementary Table 3. Physiological data of the 4 cases with negative change of hyperaemic coronary flow despite an improvement in FFR.

Supplementary Figure 1. Resting and hyperaemic flow changes across different clinical presentations and vessel treated.

Supplementary Figure 2. Relationship between anatomical stenosis severity and physiological indices.

Supplementary Figure 3. Relationship between the relative change in hyperaemic flow (ΔQ_{hyper}) and pre-PCI FFR and $R_{epi,hyper}$.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-25-00784

Supplementary data

Supplementary Appendix 1. The Oxford Acute Myocardial Infarction (OxAMI) Study investigators list.

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Supplementary Table 1. Pre-PCI and post-PCI invasive physiology measurement with relative changes.

Variable	Pre-PCI	Post-PCI	Δ%	Δ % [95% CI]	p-value
Pa rest (mmHg)	91 [83–101]	95±13	5.9% [-3.0–11.1]	0.8% to 8.0%	0.015
Pd rest (mmHg)	68±20	89±13	24.7% [9.0–69.4]	21.8% to 51.5%	<0.001
Pa hyper (mmHg)	90±15	91 [83–105]	3.1% [-3.1–10.0]	-0.8% to 7.6%	0.107
Pd hyper (mmHg)	53±15	78±15	45.2% [24.0–84.8]	37.3% to 65.0%	<0.001
Pd/Pa	0.83 [0.71–0.90]	0.96±0.04	15.2% [4.8–35.7]	13.8% to 38.1%	<0.001
FFR	0.59±0.15	0.86±0.09	43.4% [19.5–83.8]	37.1% to 66.8%	<0.001
Pa ratio	1.02 [0.98–1.08]	1.02 [0.98–1.07]	0.5% [-5.7–8.7]	-2.0% to 5.0%	0.432
Qrest (mL/min)	75±35	80 [56–102]	2.2% [-12.1–36.8]	-1.3% to 32.8%	0.088
Qhyper (mL/min)	120±57	186±78	39.0% [14.7–88.8]	30.8% to 89.2%	<0.001
Rμ.rest (WU)	899 [625–1381]	1097 [907–1567]	28.9% [-2.2–51.6]	14.6% to 44.0%	<0.001
Repi.rest (WU)	235 [144–502]	76 [33–152]	-77.0% [-92.2–-48.3]	-80.8% to -55.6%	<0.001
Rtotal.rest (WU)	1226 [909–1843]	1130 [958–1716]	3.0±41.4	-8.9% to 14.9%	0.617
Rμ.hyper (WU)	429 [343–538]	452 [325–581]	4.6±36.5%	-5.9% to 15.1%	0.381
Repi.hyper (WU)	275 [168–454]	72 [29–122]	-74.3% [-90.4–-51.6]	-79.5% to -61.9%	<0.001
Rtotal.hyper (WU)	724 [558–935]	512 [411–708]	-27.0±27.9	-35.0% to -19.0%	<0.001
CFR	1.7 [1.4–1.9]	2.2 [1.9–2.6]	34.4% [7.8–57.7]	23.5% to 53.1%	<0.001
MRR	2.7 [2.4–3.4]	2.6 [2.2–3.4]	-7.9% [-21.7–18.6]	-13.5% to 8.7%	0.468
CFR/FFR ratio	2.6 [2.3–3.3]	2.6 [2.1–3.4]	-8.7% [-28.3–15.7]	-14.8% to 7.3%	0.462

Values are presented as mean ± SD, median [Inter quartile range].
Abbreviations: Δ %: relative change expressed in percentage; Δ % [95% CI]: 95% confidence interval of the relative change expressed in percentage CFR: coronary flow reserve; FFR: fractional flow reserve; MRR: microvascular resistance reserve; Pa rest: resting aortic pressure; Pd rest: resting distal pressure; Pa hyper: hyperemic aortic pressure; Pd hyper: hyperemic distal pressure; Pa ratio: resting to hyperemic aortic pressure; Q: flow; Rμ: microvascular resistance.; Repi: epicardial resistance; Rtotal: total myocardial resistance; Hyper: hyperemic; Rest: resting.

Supplementary Table 2. Pre-PCI and post-PCI invasive physiology measurement, excluding patients who underwent predilation of the lesion.

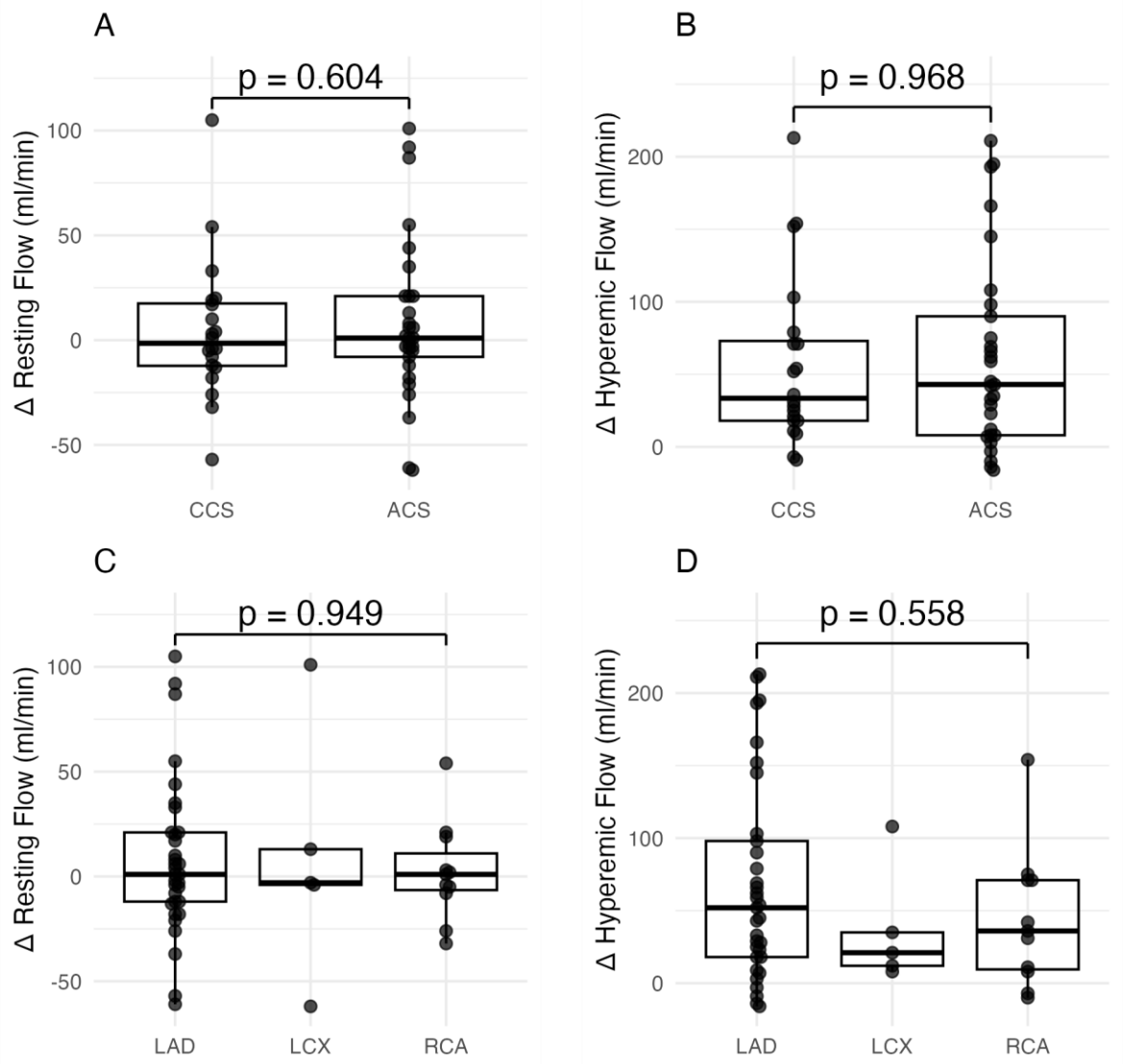
Variable	Pre	Post	Δ absolute	Δ absolute 95% CI	p-value (Δ absolute)
Pa rest (mmHg)	91 [83–100]	96 [87–103]	5 [-1–11]	1 to 8	**0.010**
Pd rest (mmHg)	76 [54–83]	91 [81–97]	16 [7–32]	12 to 25	**<0.001**
Pa hyper (mmHg)	89 [81–98]	91 [84–106]	3 [-3–9]	-2 to 6	0.235
Pd hyper (mmHg)	56 ± 15	78 ± 16	22 ± 16	17 to 28	**<0.001**
Pd/Pa	0.84 [0.73–0.90]	0.95 [0.93–0.99]	0.11 [0.04–0.22]	0.09 to 0.22	**<0.001**
FFR	0.61 ± 0.14	0.86 ± 0.09	0.25 ± 0.16	0.20 to 0.30	**<0.001**
Pa ratio	1.01 [0.97–1.07]	1.01 [0.98–1.07]	0.01 [-0.04–0.09]	-0.02 to 0.07	0.314
Qrest (mL/min)	78 [55–96]	78 [54–100]	-2 [-13–18]	-8 to 13	0.879
Qhyper (mL/min)	130 [96–167]	195 [135–231]	50 [18–96]	35 to 88	**<0.001**
Rμ,rest (WU)	960 ± 440	1233 ± 489	273 ± 344	155 to 391	**<0.001**
Repi,rest (WU)	198 [131–392]	75 [23–153]	-129 [-288–-42]	-248 to -97	**<0.001**
Rtotal,rest (WU)	1153 [884–1628]	1261 [989–1708]	119 [-260–320]	-79 to 234	0.276
Rμ,hyper (WU)	439 ± 157	447 ± 186	8 ± 149	-43 to 59	0.757
Repi,hyper (WU)	256 [165–320]	73 [31–119]	-180 [-269–-87]	-241 to -136	**<0.001**
Rtotal,hyper (WU)	660 [497–871]	481 [402–618]	-161 [-316–-35]	-246 to -93	**<0.001**
CFR	1.7 [1.4–2.0]	2.4 [2.0–2.7]	0.5 [0.3–1.1]	0.4 to 0.9	**<0.001**
MRR	2.7 [2.5–3.2]	3.0 [2.3–3.7]	-0.0 [-0.5–0.8]	-0.3 to 0.5	0.572
CFR/FFR ratio	2.9 ± 1.0	3.0 ± 1.1	0.1 ± 1.2	-0.3 to 0.5	0.644

Values are presented as mean ± SD, median [Inter quartile range].
Abbreviations: Δ absolute: delta; CFR: coronary flow reserve; FFR: fractional flow reserve; MRR: microvascular resistance reserve; Pa rest: resting aortic pressure; Pd rest: resting distal pressure; Pa hyper: hyperemic aortic pressure; Pd hyper: hyperemic distal pressure; Pa ratio: resting to hyperemic aortic pressure; Q: flow; Rμ: microvascular resistance.; Repi: epicardial resistance; Rtotal: total myocardial resistance; Hyper: hyperemic; Rest: resting.

Supplementary Table 3. Physiological data of the 4 cases with negative change of hyperaemic coronary flow despite an improvement in FFR.

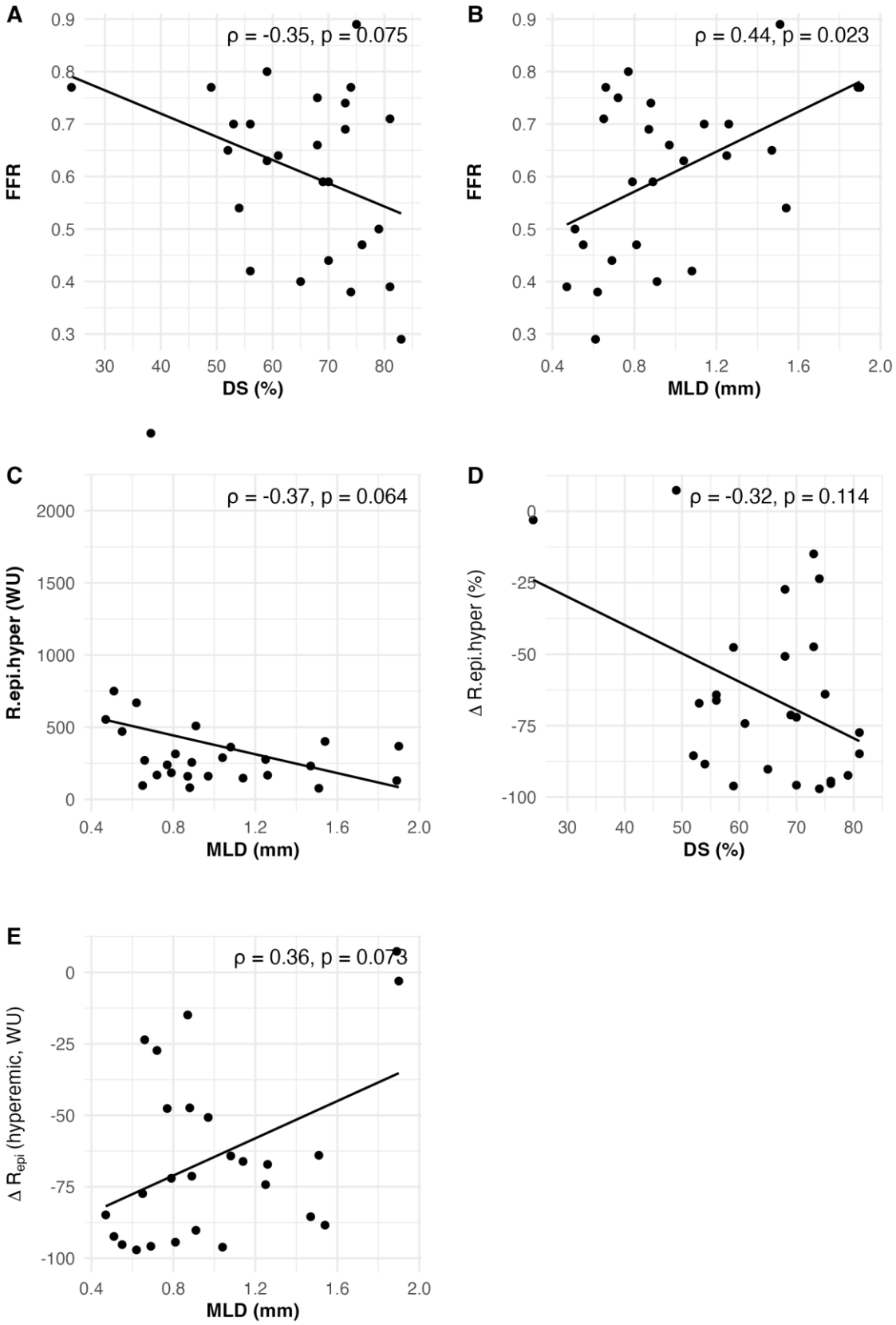
ID	Vessel	Pre-PCI			Post-PCI			ΔQ_{hyper} (mL/min)	ΔR_{hyper} (WU)
		Pa.hyper	Q_{hyper} (ml/min)	FFR	Pa.hyper	Q_{hyper} (ml/min)	FFR		
Case 1	LAD	87	190	0.78	90	187	0.90	-3	72
Case 2	LAD	112	166	0.75	122	150	0.85	-16	188
Case 3	RCA	90	111	0.77	88	104	0.97	-7	201
Case 4	LAD	80	161	0.56	107	152	0.82	-9	296

Abbreviations: FFR: fractional flow reserve; Pa.hyper: hyperemic aortic pressure; ΔQ_{hyper}: absolute difference of hyperemic coronary flow post PCI and hyperemic coronary flow pre-PCI; ΔR_{hyper} : absolute difference of hyperemic coronary resistance post PCI and hyperemic coronary resistance pre PCI; Q_{hyper}: hyperemic coronary flow.



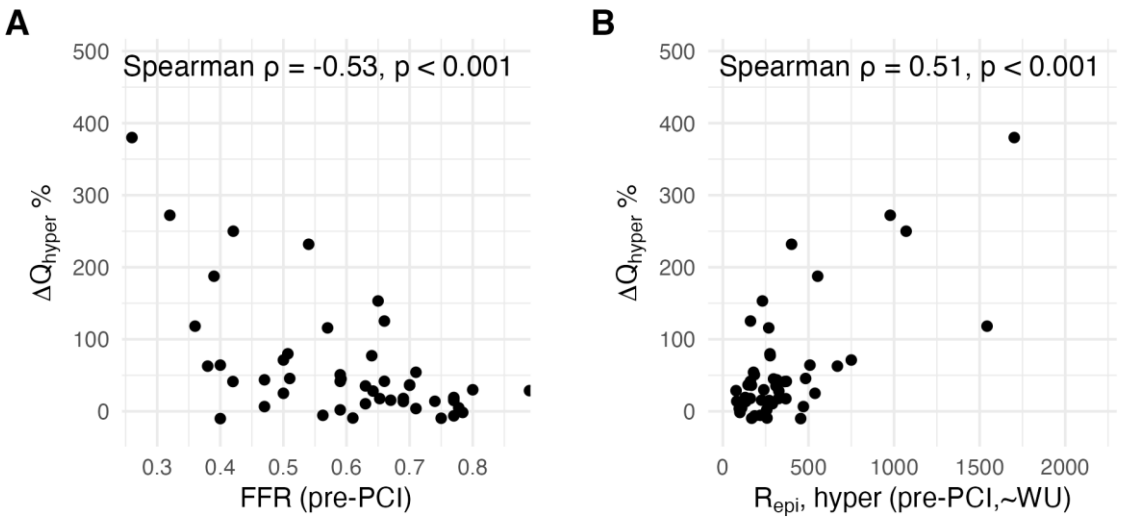
Supplementary Figure 1. Resting and hyperaemic flow changes across different clinical presentations (A and B) and vessel treated (C, D).

Abbreviations: ACS: acute coronary syndrome, CCS: chronic coronary syndrome, LAD left anterior descending artery, LCX: left circumflex artery, RCA: right coronary artery.



Supplementary Figure 2. Relationship between anatomical stenosis severity and physiological indices.

(A) Percent diameter stenosis (DS %) versus fractional flow reserve (FFR); (B) minimal lumen diameter (MLD) versus FFR; (C) MLD versus hyperemic epicardial resistance (R_epi, WU); (D) DS % versus ΔR_epi. hyperemic, WU); (E) MLD versus ΔR_epi (hyperemic, WU). Spearman correlation coefficients (ρ) and p values are reported in each panel.



Supplementary Figure 3. Relationship between the relative change in hyperaemic flow (ΔQ_{hyper}) and pre-PCI FFR (A) and $R_{epi.hyper}$ (B).