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ORIGINAL ARTICLE

Impact of Pullback Pressure Gradient on Clinical Outcomes after Percutaneous Coronary Interventions

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BACKGROUND: Impaired flow following percutaneous coronary intervention (PCI) is a known predictor of adverse outcomes. The pullback pressure gradient (PPG) is a novel physiological metric that differentiates focal from diffuse disease and enables prediction of post-PCI fractional flow reserve (FFR). This post hoc analysis of the PPG Global (NCT04789317) study aimed to evaluate the prognostic performance of a PPG model for predicting post-PCI FFR and to determine whether the predicted physiological outcome is associated with adverse events following PCI.

METHODS: Prospective and multicenter study including patients with hemodynamically significant coronary artery disease undergoing PCI. A prediction model based on FFR and PPG was used to estimate post-PCI FFR. Based on the predicted values, vessels were classified as having either optimal or suboptimal post-PCI physiology. The primary end point was target vessel failure at 1 year. Target vessel failure was defined as a composite of cardiac death, target-vessel myocardial infarction, and ischemia-driven target vessel revascularization.

RESULTS: A total of 855 patients (890 vessels) were analyzed. The mean difference between predicted and measured post-PCI FFR was 0.001 (limits of agreement, −0.10 to 0.10). There was a strong correlation between predicted and measured delta FFR (r=0.92 [95% CI, 0.91–0.93]; P<0.001). Vessels with predicted suboptimal post-PCI physiology had a significantly higher incidence of target vessel failure (adjusted hazard ratio,1.97 [95% CI, 1.24–3.15]; P=0.004). Predicted suboptimal physiology was independently associated with adverse clinical outcomes.

CONCLUSIONS: PPG-predicted post-PCI physiology was associated with target vessel failure at 1 year. These findings extend the role of coronary physiology beyond diagnostic assessment to include risk stratification and outcome prediction following PCI.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: coronary artery disease ■ fractional flow reserve, myocardial ■ myocardial infarction ■ percutaneous coronary intervention ■ prognosis

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WHAT IS KNOWN

- Lower fractional flow reserve after percutaneous coronary intervention is associated with worse clinical outcomes.
- The pullback pressure gradient predicts flow improvement after percutaneous coronary intervention.

WHAT THE STUDY ADDS

- A physiology-based prediction model integrating fractional flow reserve, pullback pressure gradient, and vessel type, which accurately forecasts post-percutaneous coronary intervention fractional flow reserve.
- Patients with predicted suboptimal postpercutaneous coronary intervention physiological outcomes experienced higher rates of target vessel failure, target-vessel myocardial infarction, and ischemia-driven target vessel revascularization.
- Predicted suboptimal physiology after percutaneous coronary intervention was independently associated with a higher risk of target vessel failure at 1 year.

Nonstandard Abbreviations and Acronyms

CAD	coronary artery disease
FFR	fractional flow reserve
HR	hazard ratio
LAD	left anterior descending
MI	myocardial infarction
PCI	percutaneous coronary intervention
PPG	pullback pressure gradient
TVF	target vessel failure

The use of fractional flow reserve (FFR) to guide revascularization decisions is well established and supported by multiple randomized trials and guidelines.[1,2] More recently, growing evidence has highlighted the prognostic importance of FFR measured immediately after percutaneous coronary intervention (PCI).[3–6] Patients with suboptimal coronary physiology following angiographic successful PCI—as reflected by low post-PCI FFR values—have a higher risk of adverse clinical outcomes.[7]

The pullback pressure gradient (PPG) is a novel metric derived from pressure pullback curves that quantitatively characterizes the pattern of coronary artery disease (CAD) on a scale from 0 (diffuse disease) to 1 (focal disease).[8] The effectiveness of PCI has been shown to differ according to the underlying CAD pattern, with patients exhibiting a more focal disease phenotype (high PPG) achieving higher post-PCI FFR values and a lower rate of residual angina compared with those with diffuse disease (low PPG).[8–10]

By integrating the information in the pressure pullback curve, PPG has also been shown to predict post-PCI FFR.[8–10] However, whether this prediction of physiological outcomes using PPG translates into differences in long-term clinical outcomes remains uncertain. In this study, we aim to evaluate the prognostic value of a PPG-based prediction model for coronary flow improvement on clinical outcomes in patients undergoing PCI.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Population and Procedures

This is a post hoc analysis of the PPG Global (URL: https://www.clinicaltrials.gov; Unique identifier: NCT04789317) study, a prospective, investigator-initiated, multicenter, international, single-arm study. The design and primary results of the trial have been reported previously.[9,11] In brief, patients with hemodynamically significant CAD based on FFR ≤0.80 intended to be treated with PCI were eligible for inclusion. A full list of inclusion and exclusion criteria is provided in Table S1. The study met its prespecified primary objective, demonstrating that PPG accurately predicts optimal post-PCI FFR.[9] In the present study, we included patients who underwent PCI to assess the prognostic performance of the PPG prediction model for post-PCI FFR on target vessel failure (TVF) at 1-year follow-up. Every participant gave written informed consent, and every site received approval from its local institutional review board.

Invasive Assessment

Patients underwent a standardized invasive physiological assessment using a coronary pressure wire (PressureWire X, Abbott Vascular, Santa Clara, CA). The pressure wire was positioned in the distal coronary artery in a segment ≥2 mm in diameter and at least 15 mm beyond the most distal stenosis by visual estimation.[12] A pullback manoeuvre in hyperemic conditions was performed manually at a constant speed during 20 to 30 seconds. When the pressure sensor reached the catheter tip, the pullback recording was stopped, and PPG was calculated onsite using CoroFlow software (Coroventis Research AB, Uppsala, Sweden). PPG results in a numerical value ranging from 0 to 1; PPG values nearing 1 are indicative of focal disease, while values approaching 0 identify diffuse CAD.[8] The PCI procedure, including the use of intracoronary imaging, was left at the operator's discretion. Following PCI, FFR was remeasured at the exact anatomic location as before PCI. Delta FFR was defined as the measured (or predicted) post-PCI FFR minus pre-PCI FFR.

Core Laboratory Analysis

All angiographic and physiological data underwent centralized, independent review at the CoreAalst core laboratory (Aalst, Belgium). A 2- or 3-dimensional quantitative coronary angiography was performed with CAAS 8.2 software (Pie

Medical Imaging, Maastricht, the Netherlands). Offline evaluation of physiology tracings was conducted using CoroFlow software (Coroventis Research AB, Uppsala, Sweden). The physiology core laboratory assessed each recording for quality following predefined criteria, including an examination of the aortic and coronary pressure tracings for any signs of waveform distortion or loss and aortic pressure ventricularization.

Clinical Outcomes

TVF was defined as a composite of cardiac death, target-vessel myocardial infarction (MI), and ischemia-driven target vessel revascularization. Peri-procedural MI was defined according to the Fourth Universal Definition of Myocardial Infarction.[13] Clinical outcomes were adjudicated by an independent committee blinded to the procedural and physiological data.

Prediction Model and Statistical Analysis

We previously developed and internally validated a PPG model to predict post-PCI FFR.[9] The model was derived from a random sample of 524 patients and internally validated in an independent cohort of 367 patients, all enrolled in the PPG Global study.[9] The predictive model incorporates 3 variables: (1) pre-PCI FFR, (2) PPG, and (3) vessel type (left anterior descending [LAD] artery or non-LAD). The resulting regression equation for estimating post-PCI FFR is as follows:

$$Predicted post\text{-}PCI FFR = 0.67 + 0.15 \times (pre\text{-}PCI FFR) + 0.20 \times (PPG) - 0.05 \times (LAD = 1, non\text{-}LAD = 0)$$

For the present analysis, we applied the previously developed prediction model to the entire PPG Global cohort to evaluate its association with clinical outcomes. Vessel-specific thresholds for optimal versus suboptimal physiological outcomes were applied based on values derived from a large patient-level meta-analysis. Specifically, post-PCI FFR cutoffs of 0.83 for the LAD and 0.93 for non-LAD vessels were used to classify predicted physiological outcomes as optimal or suboptimal.[14]

Categorical variables are presented as counts and percentages, while continuous variables are summarized as mean±SD or median with interquartile range, depending on their distribution. Comparisons between categorical variables were performed using the χ^2 test. Continuous variables were compared between groups using the independent (2-sample) Student *t* test or the Wilcoxon rank-sum test, as appropriate according to data distribution. The Pearson correlation coefficient was used to assess relationships between continuous variables. Agreement between predicted and measured post-PCI FFR values was evaluated using the Bland-Altman method. The cumulative incidence of clinical events was estimated using Kaplan-Meier curves and compared with the log-rank test. Cox

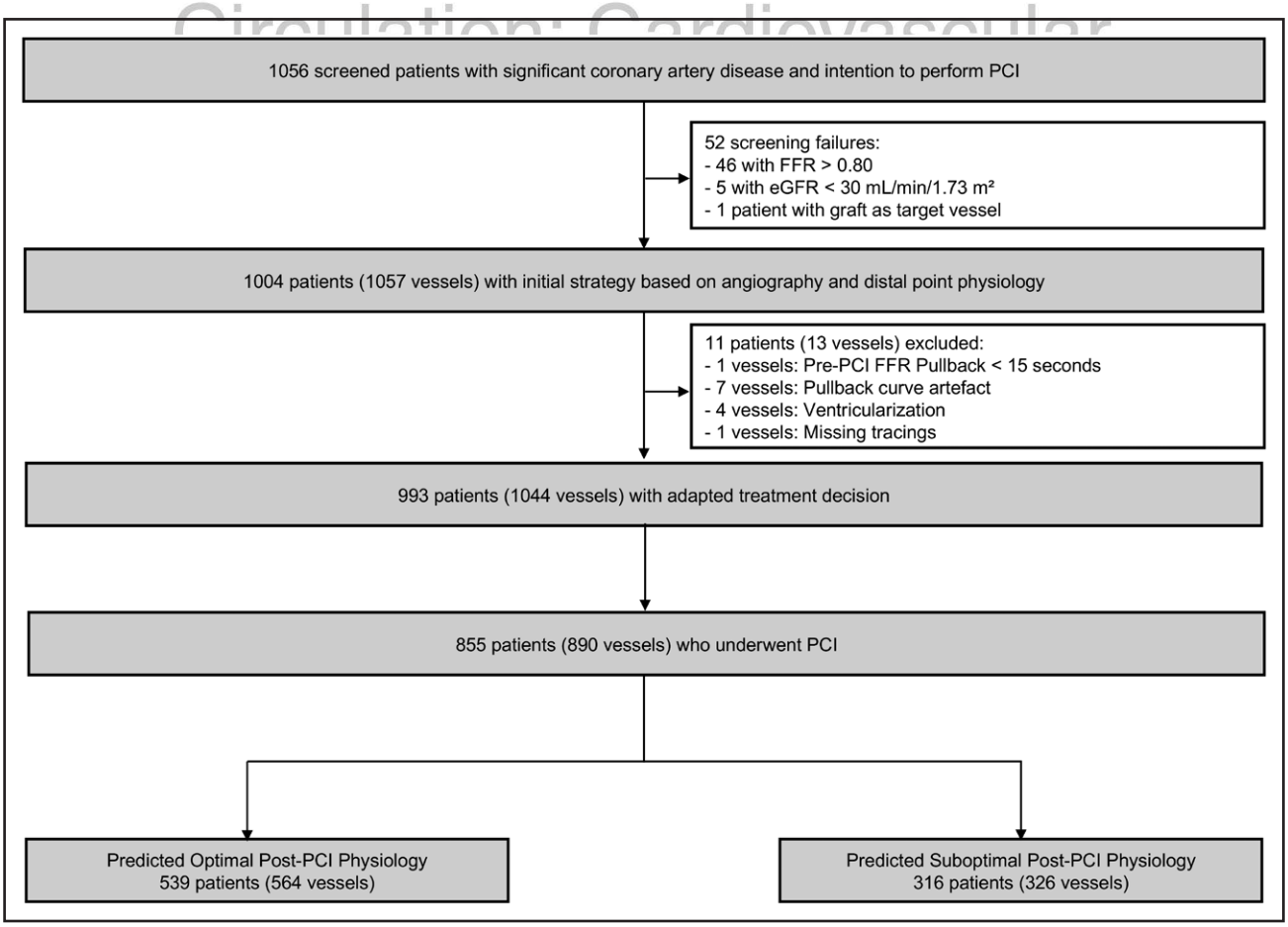

Figure 1. Study flow chart.
eGFR indicates estimated glomerular filtration rate; FFR, fractional flow reserve; and PCI, percutaneous coronary intervention.

proportional hazards regression models were used to calculate hazard ratios (HR) and 95% CIs for the comparison of clinical event risk between groups, stratified according to optimal versus suboptimal predicted post-PCI physiology. Adjusted HR was calculated using age, sex, arterial hypertension, diabetes, renal function, prior history of PCI, angiographic lesion severity, lesion length, and the use of intravascular imaging during PCI. Regression analyses were performed using random-intercept models to account for clustering of patients within centers. The proportional hazards assumption was assessed using the Schoenfeld residuals test. A 2-sided $P<0.05$ was considered statistically significant. All statistical analyses were conducted using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Baseline characteristics

A total of 855 patients (890 vessels) who underwent physiology-guided PCI were included in the analysis. The study flowchart is presented in Figure 1. In 539 patients (63%), the PPG model predicted an optimal post-PCI physiological outcome. Baseline clinical characteristics were comparable between patients with predicted optimal and suboptimal physiology after PCI (Table 1).

Table 2 shows the procedural, angiography, and physiological characteristics stratified by predicted optimal and suboptimal physiology after PCI. Vessels classified as having predicted suboptimal post-PCI physiological outcomes exhibited significantly lower baseline FFR (0.63±0.13 versus 0.69±0.10; $P<0.001$), lower PPG values (0.58±0.16 versus 0.69±0.13; $P<0.001$), and lower measured post-PCI FFR (0.86±0.08 versus 0.88±0.06; $P<0.001$) compared with those in the predicted optimal post-PCI physiology. Vessels with predicted suboptimal physiological outcomes required more, longer, and smaller stents. The rates of intravascular imaging use did not differ between patients with predicted optimal and suboptimal physiology after PCI (43.1% versus 46.6%; $P=0.340$).

Validation of Predicted Post-PCI FFR

The correlation coefficient between predicted and measured post-PCI FFR was 0.65 (95% CI, 0.61–0.68; $P<0.001$). The mean difference between predicted and measured post-PCI FFR was 0.001, with limits of

Table 1. Patient Characteristics Stratified by Predicted Post-PCI Physiology

Variable	Predicted optimal post-PCI physiology	Predicted suboptimal post-PCI physiology	*P* value
Number of patients	539	316	
Age, y, median (IQR)	69 (61–76)	70 (61–75)	0.830
Sex (men), n (%)	395 (73.3)	249 (78.8)	0.085
BMI, kg/m², median (IQR)	25.9 (23.1–29.6)	26.1 (23.4–29.3)	0.891
Dyslipidemia, n (%)	396 (73.5)	219 (69.3)	0.219
Hypertension, n (%)	377 (69.9)	214 (67.7)	0.547
Diabetes, n (%)	150 (27.8)	98 (31.0)	0.362
Current smoking, n (%)	98 (18.2)	48 (15.2)	0.304
Creatinine clearance, mL/min/1.73 m², median (IQR)	71.5 (54.9–90.4)	69.7 (54.8–87.2)	0.541
Prior PCI for target vessel, n (%)	50 (9.3)	45 (14.3)	0.033
Prior MI, n (%)	94 (17.4)	78 (24.7)	0.014
Peripheral artery disease, n (%)	29 (5.4)	25 (7.9)	0.186
Clinical presentation, n (%)			0.143
NSTEMI	27 (5.0)	20 (6.3)	
Unstable angina	22 (4.1)	17 (5.4)	
Asymptomatic	67 (12.4)	32 (10.1)	
Silent ischemia*	68 (12.6)	55 (17.4)	
CCS I	170 (31.5)	97 (30.7)	
CCS II	125 (23.2)	69 (21.8)	
CCS III	44 (8.2)	24 (7.6)	
CCS IV	16 (3.0)	2 (0.6)	

Thresholds of 0.83 for the LAD and 0.93 for non-LAD vessels were applied to stratify patients into optimal or suboptimal post-PCI physiology. BMI indicates body mass index; CCS, Canadian Cardiovascular Society Angina Score; IQR, interquartile range; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; and PCI, percutaneous coronary intervention.

*Define as a positive functional noninvasive test in an asymptomatic patient.

Table 2. Procedural, Angiography, and Physiological Characteristics Stratified by Predicted Post-PCI Physiology

Variable	Predicted optimal post-PCI physiology	Predicted suboptimal post-PCI physiology	*P* value
Number of vessels	564	326	
Vessel, n (%)			<0.001
LAD	453 (80.3)	164 (50.3)	
LCX	58 (10.3)	59 (18.1)	
RCA	53 (9.4)	103 (31.6)	
Minimal lumen diameter, mm, median (IQR)	1.42 (1.02–1.77)	1.48 (1.12–1.86)	0.026
Diameter stenosis (%), median (IQR)	53 (43–63)	51 (39–60)	0.006
Reference vessel diameter, mm, median (IQR)	2.63 (2.31–3.01)	2.54 (2.22–2.98)	0.097
Lesion length, mm, median (IQR)	17.20 (11.65–24.56)	17.10 (11.25–25.81)	0.700
FFR, mean (SD)	0.69±0.10	0.63±0.13	<0.001
PPG, mean (SD)	0.69±0.13	0.58±0.16	<0.001
Minimal lumen diameter (post-PCI; mm), median (IQR)	2.74 (2.44–3.06)	2.75 (2.48–3.06)	0.775
Reference vessel diameter (post-PCI; mm), median (IQR)	2.74 (2.34–3.05)	2.66 (2.32–3.07)	0.355
Number of stents, median (IQR)	1 (1–1)	1 (1–2)	<0.001
Total stent length, mm, median (IQR)	28 (20–38)	30 (20.5–48)	<0.001
Stent diameter, mm, mean (SD)	3.06±0.44	3.00±0.44	0.037
Acute gain, mm, median (IQR)	1.30 (0.96–1.66)	1.23 (0.92–1.58)	0.188
Intracoronary imaging pre-PCI, n (%)	243 (43.1)	152 (46.6)	0.340
Intracoronary imaging post-PCI, n (%)	228 (40.5)	148 (45.5)	0.163
Measured post-PCI FFR, mean (SD)	0.88±0.06	0.86±0.08	<0.001
Measured delta FFR, mean (SD)*	0.19±0.11	0.23±0.16	<0.001
Predicted post-PCI FFR, mean (SD)	0.88±0.04	0.86±0.05	<0.001
Predicted delta FFR, mean (SD)†	0.18±0.10	0.23±0.15	<0.001

Thresholds of 0.83 for the LAD and 0.93 for non-LAD vessels were applied to stratify patients into PPG-predicted optimal or suboptimal physiology. FFR indicates fractional flow reserve; IQR, interquartile range; LAD, left anterior descending artery; LCX, left circumflex artery; PCI, percutaneous coronary intervention; PPG, pullback pressure gradient; and RCA, right coronary artery.

*Measured delta FFR was calculated as post-PCI FFR–FFR.

†Predicted delta FFR was calculated as predicted post-PCI FFR–FFR.

agreement ranging from −0.10 to 0.10. The correlation coefficient between predicted and measured delta FFR was 0.92 (95% CI, 0.91–0.93; *P*<0.001). The mean difference in delta FFR was 0.001, with limits of agreement from −0.10 to 0.10 (Figure 2). The agreement between predicted and measured delta FFR did not differ between vessels (Figure S1).

Clinical Outcomes

Clinical follow-up at 1 year was available for 849 patients (99%). The overall incidence of TVF was 9.1% (Table 3). Vessels with predicted suboptimal post-PCI physiology experienced a significantly higher rate of TVF compared with those with predicted optimal physiology (adjusted HR, 1.97 [95% CI, 1.24–3.15]; *P*=0.004; Figure 3). This association remained significant after exclusion of peri-procedural MI, with a higher risk of TVF in the predicted suboptimal physiology group (adjusted HR, 3.31 [95% CI, 1.11–9.86]; *P*=0.031). Additionally, vessels with predicted suboptimal physiology had a higher incidence of MI (adjusted HR, 1.88 [95% CI, 1.14–3.11]; *P*=0.014) and a 5-fold increase in risk of ischemia-driven target vessel revascularization (adjusted HR, 5.56 [95% CI, 1.12–27.6]; *P*=0.036). The composite end point of cardiac death and MI was also significantly more frequent in the predicted suboptimal physiology group (adjusted HR, 1.81 [95% CI, 1.11–2.94]; *P*=0.018). Kaplan-Meier curves for clinical outcomes are presented in Figure 4. Notably, predicted suboptimal post-PCI physiology by the PPG model remained independently associated with 1-year TVF in multivariable analysis (Table 4). Importantly, after removing peri-procedural MI, predicted post-PCI FFR remained associated with TVF (Table S2).

To further explore the angiographic, procedural, and physiological variables associated with TVF, we constructed a series of multivariable regression models (Table S3). The PPG prediction model was consistently associated with TVF. In addition, predicted post-PCI FFR as a continuous metric was significantly associated with TVF in LAD (Table S4). Event rates according to measured post-PCI FFR did not differ between optimal and

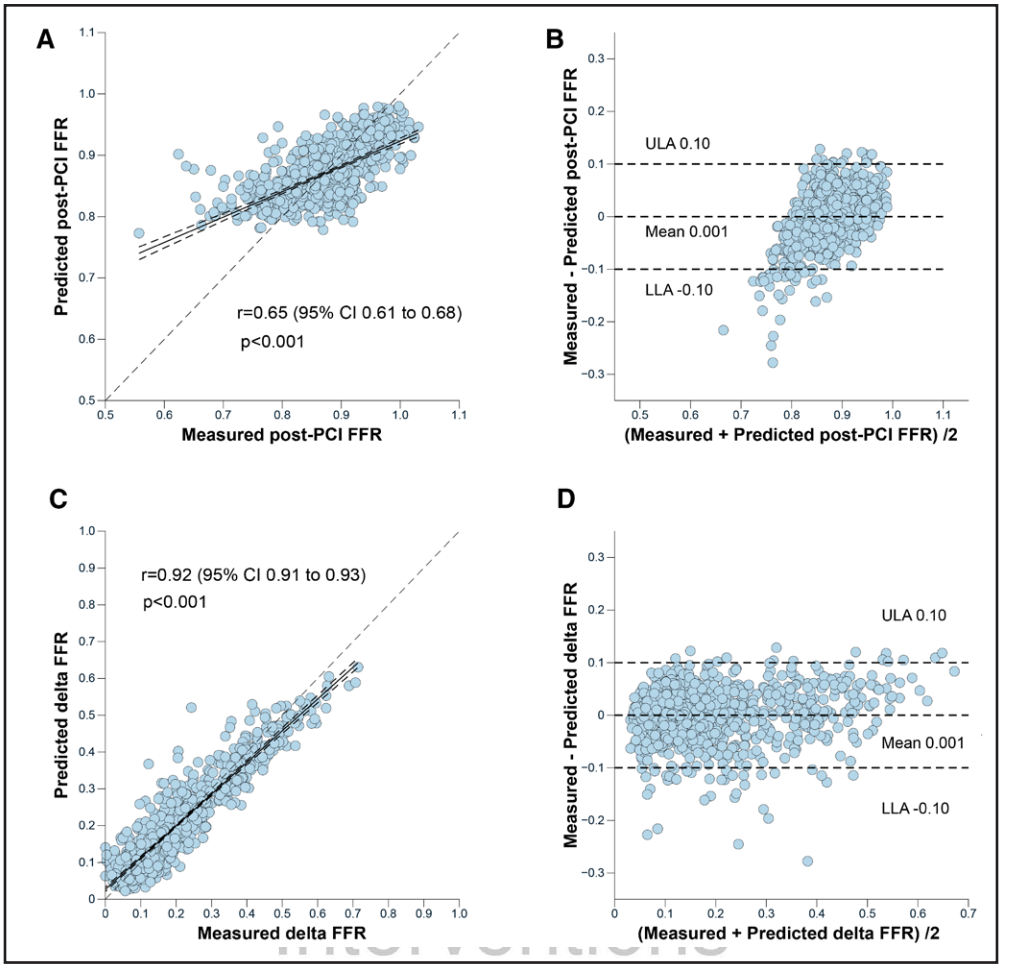

Figure 2. Agreement between predicted and measured postpercutaneous coronary intervention (PCI) fractional flow reserve (FFR) and delta FFR.

A, Correlation between predicted and measured FFR. **B**, Mean difference between predicted and measured FFR. **C**, Correlation between predicted and measured delta FFR. **D**, Mean difference between predicted and measured delta FFR. LLA indicates the lower limit of agreement; and ULA, upper limit of agreement.

suboptimal physiology (Table S5). Clinical outcomes stratified by agreement between predicted and measured post-PCI physiological outcomes is shown inTable S6). The difference between predcited and measured post-PCI FFR values in patients with and without periprocedural MI in shown in Table S7.

DISCUSSION

This study leveraged the predictive capability of the PPG to estimate physiological improvement following PCI. Using a previously validated model that integrates baseline disease severity (pre-PCI FFR), disease distribution (PPG), and vessel type, we assessed the prognostic value of predicted post-PCI FFR. The key findings of the study are as follows: first, the predicted post-PCI FFR (and delta FFR) showed good agreement with the invasively measured post-PCI FFR. Second, patients with predicted suboptimal post-PCI physiology experienced significantly higher rates of TVF, target-vessel MI, and ischemia-driven target vessel revascularization. Third, predicted suboptimal physiological outcomes were independently associated with TVF at 1 year.

Several studies have demonstrated that post-PCI FFR is a significant determinant of clinical outcomes. In stable patients, impaired flow after PCI is primarily caused by the presence of diffuse disease. Diffuse functional disease—characterized by gradual pressure losses in the pullback curve—is present in approximately one-third of patients considered for PCI.[9] Previous studies have shown that in these cases without focal trans-lesional pressure gradients, PCI fails to significantly increase coronary flow.[3] Furthermore, patients with diffuse disease (low PPG) treated with PCI require the implantation of more, smaller, and longer stents, and PCI results in smaller minimal stent areas.[15] In addition, the underlying plaque in cases with diffuse disease is predominantly calcified,[16] which is a known predictor of stent under-expansion and adverse event after PCI.[17,18] As a result, the worse clinical outcomes observed in

Table 3. Adverse Event Rates at 1 Year Stratified by Predicted Post-PCI Physiology

Variable	Overall	Predicted optimal post-PCI physiology	Predicted suboptimal post-PCI physiology	Adjusted HR (95% CI)	*P* value*
Number of vessels	890	564	326		
TVF	81 (9.1)	39 (6.9)	42 (12.9)	1.97 (1.24–3.15)	0.004
TVF without periprocedural MI	17 (1.9)	5 (0.9)	12 (3.7)	3.31 (1.11–9.86)	0.031
All-cause death	13 (1.5)	9 (1.6)	4 (1.2)	0.32 (0.07–1.42)	0.134
Cardiac death	6 (0.7)	3 (0.5)	3 (0.9)	1.04 (0.16–6.86)	0.967
All MI	70 (7.9)	36 (6.4)	34 (10.4)	1.88 (1.14–3.11)	0.014
Periprocedural MI	66 (7.4)	35 (6.2)	31 (9.5)	1.76 (1.05–2.95)	0.032
Spontaneous MI	2 (0.2)	0 (0)	2 (0.6)	NA	NA
Stent thrombosis	2 (0.2)	1 (0.2)	1 (0.3)	6.28 (0.05–724)	0.448
Cardiac death and all MI	74 (8.3)	38 (6.7)	36 (11.0)	1.81 (1.11–2.94)	0.018
Ischemia-driven TVR	10 (1.1)	2 (0.4)	8 (2.5)	5.56 (1.12–27.6)	0.036
Ischemia-driven TLR	10 (1.1)	2 (0.4)	8 (2.5)	5.56 (1.12–27.6)	0.036

Thresholds of 0.83 for the LAD and 0.93 for non-LAD vessels were applied to stratify patients into optimal or suboptimal post-PCI physiology. HR indicates hazard ratio; MI, myocardial infarction; PCI, percutaneous coronary intervention; TLR, target lesion revascularization; TVF, target vessel failure; and TVR, target vessel revascularization.

**P* values derived from Cox regression analysis adjusted by clinical characteristics, quantitative coronary angiography, and use of intravascular imaging.

patients with PPG prediction of suboptimal post-PCI physiological results likely stem from both increased procedural risk—reflected in a higher incidence of periprocedural MI in vessels with low PPG—and a greater likelihood of stent failure, shown by the higher rates of spontaneous MI and target vessel revascularization. These findings are consistent with those reported by Patel et al,[19] who also found that patients with suboptimal post-PCI physiology are at increased risk of subsequent TVF, cardiac death, MI, and target vessel revascularization.

The regression formula used to estimate post-PCI FFR offers mechanistic insight into the factors influencing physiological outcomes after coronary intervention. The positive coefficients for both pre-PCI FFR and PPG indicate that a higher hyperemic coronary flow at baseline (ie, higher pre-PCI FFR) and a more focal pattern of CAD (ie, higher PPG) are associated with a more favorable physiological result after PCI. Conversely, patients with low FFR and low PPG are more likely to remain with impaired flow after PCI; this supports the clinical notion that more severe and diffuse disease portends a worse

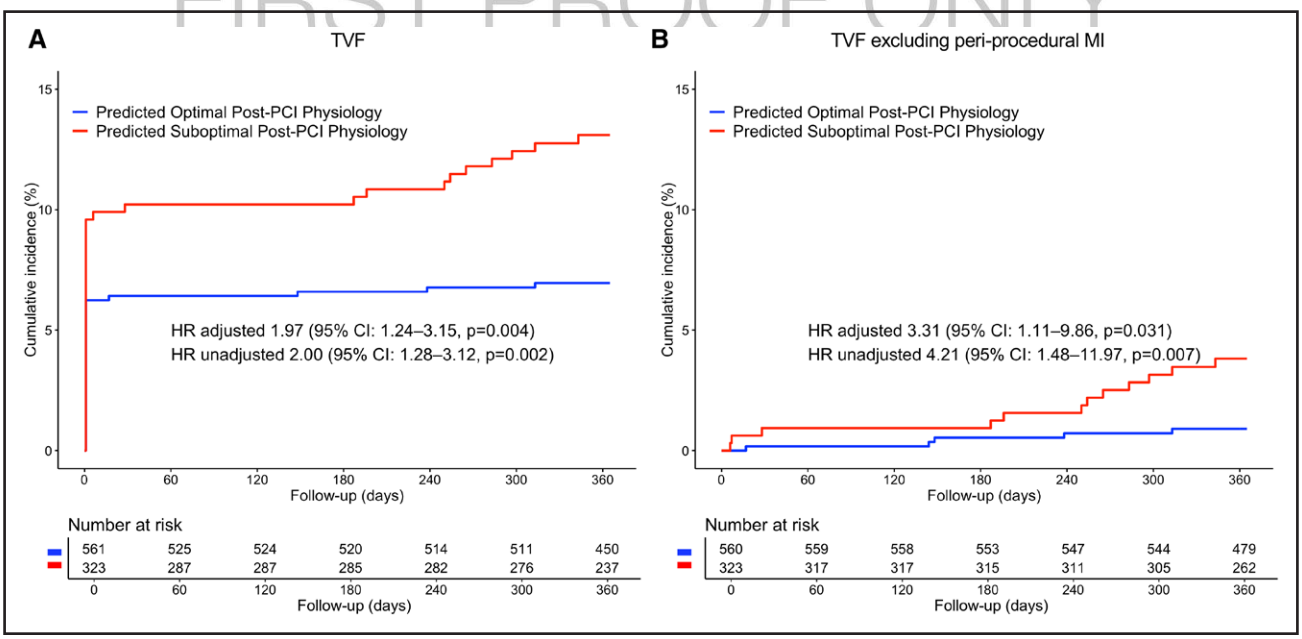

Figure 3. The rate of target vessel failure (TVF) stratified by predicted postpercutaneous coronary intervention (PCI) physiology. **A**, The rate of TVF (cardiac death, target-vessel myocardial infarction, and ischemia-driven target vessel revascularization). **B**, The rate of TVF, excluding peri-procedural myocardial infarction (MI).

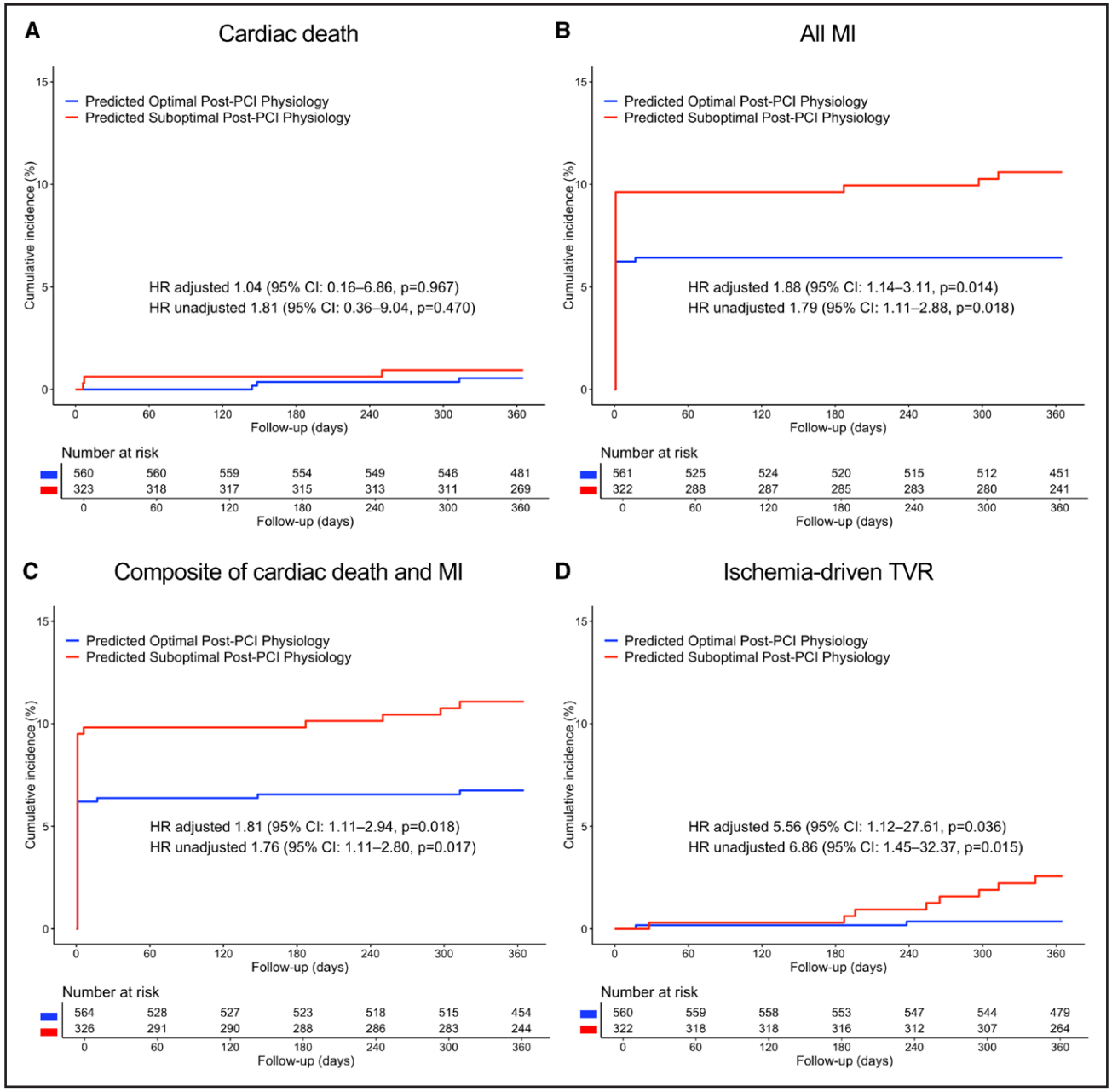

Figure 4. Clinical outcomes stratified by predicted postpercutaneous coronary intervention (PCI) physiology.
Each Kaplan-Meier curve shows the incidence of (**A**) cardiac death, (**B**) all myocardial infarction (MI), (**C**) composite of cardiac death and all myocardial infarction, and (**D**) ischemia-driven target vessel revascularization (TVR), respectively.

prognosis. In addition, the model assigns a negative coefficient to LAD vessels, meaning that interventions in the LAD are associated with slightly lower (≈0.05 FFR units) predicted post-PCI FFR. This reflects the intrinsic properties of LAD, where achieving optimal FFR restoration is more challenging due to myocardial territory, higher prevalence of diffuse disease, and the hydrostatic effect affecting measurements with pressure wires. This differentiation is key as the prediction of outcomes using post-PCI physiology requires a vessel-specific approach.

There is no consensus on what represents an optimal post-PCI FFR. We previously showed that post-PCI FFR should be interpreted as a vessel-specific metric. In a large individual patient-level meta-analysis including 3336 vessels (2760 patients), we showed that vessels with low post-PCI FFR had twice the risk of TVF compared with high post-PCI FFR. Consequently, we applied the same vessel-specific post-PCI FFR cutoffs of 0.83 for the LAD and 0.93 for non-LAD, and we observed that vessels with a prediction of suboptimal post-PCI physiological results had a significantly higher incidence of TVF (HR, 1.97 [95% CI, 1.24–3.15];*P*=0.004). Importantly, the higher TVF risk in patients with predicted suboptimal physiological results

Table 4. Univariable and Multivariable Predictors of Target Vessel Failure at 1 Year

	Univariate		Multivariable	
Variables	Estimate (95% CI)	*P* value	Estimate (95% CI)	*P* value
Age	1.03 (1.00–1.05)	0.035	1.04 (1.01–1.07)	0.005
Sex (men)	1.69 (0.91–3.11)	0.094	1.86 (0.94–3.69)	0.074
Dyslipidemia	0.83 (0.49–1.41)	0.492	0.96 (0.54–1.69)	0.877
Hypertension	0.67 (0.40–1.12)	0.127	0.61 (0.34–1.09)	0.094
Diabetes	0.91 (0.53–1.54)	0.723	1.04 (0.59–1.85)	0.891
Prior PCI	0.71 (0.31–1.61)	0.409	0.49 (0.20–1.20)	0.118
Prior MI	2.15 (1.27–3.66)	0.005	2.81 (1.56–5.06)	<0.001
Percent diameter stenosis	0.99 (0.97–1.01)	0.188	0.99 (0.97–1.01)	0.315
Lesion length	1.00 (0.98–1.02)	0.978	1.00 (0.98–1.02)	0.936
Intracoronary imaging	1.34 (0.67–2.69)	0.408	1.29 (0.60–2.79)	0.514
Predicted suboptimal post-PCI Physiology	2.04 (1.26–3.31)	0.004	1.87 (1.12–3.14)	0.017

MI indicates myocardial infarction; and PCI, percutaneous coronary intervention.
*In the prediction model, the group with suboptimal physiological outcome was used as the reference category.

remained after the exclusion of peri-procedural MI. The clinical usefulness of these findings lies in the fact that the PPG prediction is available before stenting, potentially allowing for a more refined decision-making process based on the prognosis after PCI. Therefore, the use of pressure pullbacks with PPG opens up a novel application of physiology, evolving from a diagnostic to a prognostic tool.

Accurately predicting post-PCI FFR is challenging, given that it is influenced by numerous factors, including the ability to induce maximal hyperemia after vessel instrumentation and variability in the PCI technique (eg, use of intravascular imaging).[20] Nevertheless, the model incorporating just 3 variables (pre-PCI FFR, PPG, and vessel type) was able to predict measured post-PCI FFR with good performance. In addition, predicted delta FFR showed a strong correlation with measured delta FFR.[10,21,22] The stronger performance of predicted delta FFR compared with absolute post-PCI FFR results can be attributed to the adjustment with baseline FFR values. Unexpectedly, measured post-PCI FFR did not associate with clinical outcomes in this cohort, whereas the PPG prediction model did. This finding highlights the prognostic value of pre-PCI predictors—such as PPG, vessel type, and baseline FFR— and the anticipated physiological benefit compared with post-PCI measurements, which are susceptible to technical and procedural variation.

The present findings underscore the evolving role of coronary physiology in optimizing PCI strategy. By showing that pre-PCI indices such as FFR and PPG can forecast both physiological gain and the likelihood of adverse events, this study reinforces the shift to predictive revascularization strategies. The prognostic stratification derived from this approach can further enhance shared decision-making. The favorable outcomes observed in patients with predicted optimal physiology (<1% TVF after excluding periprocedural MI) also suggest that not all hemodynamically significant lesions carry the same risk profile, underscoring the need to consider disease pattern—not just ischemic burden—when selecting revascularization strategies and investigating clinical outcomes in patients undergoing PCI. Future studies assessing the impact of therapies in patients with CAD should account for the pathophysiological pattern of disease, as the response to treatment may differ according to the disease phenotype.

Study Limitations

This study should be interpreted in the context of several limitations. First, although the PPGprediction model was internally validated, both the model derivation and clinical outcome analysis were performed within the same data set (PPG Global), which may introduce bias and limit the generalizability of the results. External validation in an independent cohort is needed to confirm the accuracy of the model for post-PCI FFR and outcomes prediction. Second, the follow-up duration was limited to one year. Although this was sufficient to capture a substantial number of adverse events, it may underestimate the long-term prognostic implications of post-PCI physiology and disease pattern. Patients in PPG Global will be followed up for 3 years, and longer-term follow-up will be available.

Conclusions

In this multicenter study, we demonstrated that a physiology-based prediction model integrating FFR, PPG, and vessel type can accurately predict post-PCI physiological outcomes and identify patients at higher risk of TVF. Given the potential of PPG-based stratification to personalize PCI strategies, a prospective randomized trial

is warranted to determine whether PPG-guided revascularization improves clinical outcomes.

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Supplemental Material

Tables S1–S7
Figure S1

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