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ABSTRACT

Background: Microvascular resistance (MR) has prognostic value in acute and chronic coronary syndromes following percutaneous coronary intervention (PCI), however anatomic and physiologic determinants of the

Abbreviations: CFR, coronary flow reserve; CX, circumflex artery; FFR, fractional flow reserve; HMR, hyperemic microvascular resistance; IMR, index of microvascular resistance; LAD, left anterior descending artery; MR, microvascular resistance; PCI, percutaneous coronary intervention.; RCA, right coronary artery; TVR, target vessel failure; HSR, hyperemic stenotic resistance.

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Microvascular resistance
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relative changes of MR and its association to target vessel failure (TVF) has not been investigated previously. This study aims to evaluate the association between changes in MR and TVF.
Methods: This is a sub-study of the Inclusive Invasive Physiological Assessment in Angina Syndromes (ILIAS) registry which is a global multi-centre initiative pooling lesion-level coronary pressure and flow data.
Results: Paired pre-post PCI haemodynamic data were available in $n = 295$ vessels out of $n = 828$ PCI treated patients and of these paired data on MR was present in $n = 155$ vessels. Vessels were divided according to increase vs. decrease % in microvascular resistance following PCI ($\Delta MR\ \% \leq 0$ vs. $\Delta MR > 0\%$). Decreased microvascular resistance $\Delta MR\ \% \leq 0$ occurred in vessels with lower pre-PCI fractional flow reserve (0.67 ± 0.15 vs. 0.72 ± 0.09 $p = 0.051$), coronary flow reserve (1.9 ± 0.8 vs. 2.6 ± 1.8 $p < 0.0001$) and higher hyperemic microvascular resistance (2.76 ± 1.3 vs. 1.62 ± 0.74 $p = 0.001$) and index of microvascular resistance (24.4 IQ (13.8) vs. 15. 8 IQ (13.2) $p = 0.004$). There was no difference in angiographic parameters between $\Delta MR\ \% \leq 0$ vs. $\Delta MR > 0\%$. In a cox regression model $\Delta MR\ \% > 0$ was associated with increased rate of TVF (hazard ratio 95% CI 3.6 [1.2; 10.3] $p = 0.018$).
Conclusion: Increased MR post-PCI was associated with lesions of less severe hemodynamic influence at baseline and higher rates of TVF at follow-up.

1. Introduction

The coronary arterial circulation comprises of epicardial arteries (> 400 μm) ensuring conductance of blood, and pre-arterioles (100-400 μm) and arterioles (10-100 μm) serving as resistance vessels regulating perfusion of the capillary bed, typically referred to as the coronary microvasculature [1]. Coronary microvascular dysfunction (CMD) is clinically diagnosed as reduced vasodilator capacity of the coronary circulation expressed by the coronary flow reserve (CFR) and increased minimal resistance in the microcirculation expressed by the hyperemic microvascular resistance index (HMR) or index of microcirculatory resistance (IMR). CMD is increasingly recognized as an important determinant of angina pectoris both in the presence and absence of obstructive epicardial coronary artery disease, and is linked to co-morbidities such as hypertension and diabetes [2–4].

In concomitant epicardial and microvascular disease, the individual role of epicardial and microvascular pathology remains elusive, and data on the impact of percutaneous coronary intervention (PCI) on microvascular function and its relation to clinical outcome is scarce. PCI improves flow and perfusion pressure distal to a stenosis, and increases the distal artery diameter through endothelium dependent vasodilation [5]. It offsets the low-flow-mediated vasoconstriction [6] that occurs due to epicardial stenosis, and increases distal coronary perfusion pressure. In a healthy microcirculation the compensatory vasodilatation increases the flow up the point of microcirculation's capacity. As vascular resistance is inversely dependent of fourth power of vessel radius even relatively small changes in vessel diameter have large impact on microvascular resistance. High microvascular resistance following PCI predicts poor outcome in chronic coronary syndrome [7], and is associated with larger infarct size in ST-segment elevation myocardial infarction [8]. However, the clinical relevance of the microvascular function response to PCI has not been studied. We aimed to evaluate the anatomic and hemodynamic predictors of microvascular resistance improvement after PCI, and the prognostic value of microvascular resistance improvement after PCI for target vessel failure (TVF).

2. Methods

2.1. The ILIAS registry

This is a sub-study of the Inclusive Invasive Physiological Assessment in Angina Syndromes (ILIAS) (ClinicalTrials.gov Identifier NCT04485234) which is a global multi-centre initiative of pooled lesion level physiological and clinical outcome data. It comprises of 20 expert institutions in Netherlands, Korea, Japan, Spain, Denmark, Italy and the United States of America. The data was prospectively collected from patients who underwent clinically indicated invasive coronary angiography and had comprehensive invasive physiological assessment of at least one native coronary artery. Patients with hemodynamic instability, significant valvular disease and prior coronary artery bypass graft surgery, as well as culprit vessels of acute coronary syndromes were excluded. Individual patient data for pooled analysis were collected using standardized spreadsheets and a fully compliant cloud-based clinical data platform (Castor EDC, Amsterdam, The Netherlands). Standardized definitions were used for all variables.

2.2. Coronary angiography and physiological evaluation

Coronary angiography and physiological evaluation were conducted according to local practice. After diagnostic coronary angiography, invasive physiological indices were measured using either separate pressure- (PressureWire, RADI medical – now Abbott Vascular, St Paul, MN) and Doppler velocity sensor-equipped coronary guidewires (FloWire, Endosonics – now Philips-Volcano, San Diego, CA), dual pressure- and Doppler flow velocity-equipped guide wire (ComboWire, Volcano Corp. – now Philips-Volcano, San Diego, CA), or a temperature-sensitive pressure sensor-equipped guide wire (PressureWire, St Jude Medical- now Abbott Vascular, St. Paul, MN) using routine techniques. Intracoronary nitrate (100 or 200 μg) was administered before physiologic measurements. Using the Doppler velocity technique, baseline (bAPV) and hyperemic average peak flow velocities (hAPV) were labelled baseline and hyperemic flow, respectively. Using the coronary thermodilution technique, resting and hyperemic thermodilution curves were obtained in triplicate using three injections (4 mL each) of room-temperature saline, and the inverse of the average basal (bTmn) and hyperemic mean transit times (hTmn) was labelled baseline and hyperemic flow, respectively. Hyperemia was induced by intravenous infusion of adenosine (140 μg/kg per min) or adenosine triphosphate (ATP) (150 μg/kg per min) through a peripheral or central vein, intracoronary bolus injection of adenosine (20-200μg), or intracoronary bolus injection of nicorandil (3 mg), according to local standards [9,10].

2.3. Clinical follow up

Clinical follow-up was obtained at outpatient clinic visits or by telephone contact to ascertain the occurrence of target vessel failure (TVF). TVF was defined as the composite of cardiac death, target vessel-related acute myocardial infarction, and clinically driven (urgent) revascularization of the target vessel by means of coronary artery bypass graft surgery or PCI. All patient-reported events were verified by evaluating hospital records or contacting the treating cardiologist or general-practitioner.

2.4. Statistics

Demographic variables were analyzed on per-patient level and hemodynamic and anatomic variables on per-vessel level. Continuous variables were presented as mean ± SD or median (interquartile range)

as appropriate and tested with analysis of variance, and categorical variables were presented as numbers (%) and tested with Mann-Whitney *U* test. Non-parametric test of medians were used when unequal variance were observed. TVF was tested with a Cox proportional hazard model using gender, hypertension and diabetes as covariates. Delta microvascular resistance (ΔMR %) was defined as: $IMR_{post\text{-}PCI} - IMR_{pre\text{-}PCI} / IMR_{pre\text{-}PCI}$ x 100% or $HMR_{post\text{-}PCI} - HMR_{pre\text{-}PCI} / HMR_{pre\text{-}PCI}$ x 100% for thermodilution-based and Doppler velocity- based assessments, respectively. The cohort was divided according to ΔMR % ≤ 0 vs. ΔMR % > 0, representing a physiological improvement in minimal microvascular resistance versus status quo or deterioration of minimal microvascular resistance following PCI. A *p* value <0.05 was considered significant. Data was analyzed with SPSS (version 27, IBM, USA).

3. Results

3.1. Study population

The ILIAS-registry has *n* = 3046 vessel specific data out of which *n* = 828 (27%) underwent PCI. Post-PCI physiological evaluation with FFR and CFR was conducted in *n* = 295 and in *n* = 155 vessels post-PCI MR was measured (Fig. 1). Combined pre-post measurements on microvascular resistance were available in 155 vessels and including outcome data in 146 vessels. The mean age of the population was 63 ± 10 years and consisted of primarily males (72%). The proportion of hypertension and diabetes was 58% and 28% respectively (Table 1).

Table 1
Baseline characteristics (patient level).

	Mean SD /N (%)
Age	66 ± 10
BMI kg/m^2	26 ± 4
LVEF %	61 ± 10
Male gender	86 (75)
Hypertension	72 (63)
Diabetes	24 (34)
Current smoking	27 (23)
Primary indication	
Stable angina pectoris	84 (73)
UAP/NSTEMI	31 (27)
Previous MI	30 (26)
Previous PCI	35 (30)
Left main	5 (4)
LAD	77 (67)
LCx	16 (14)
RCA	22 (19)
Aspirin	102 (89)
Beta-blocker	72 (63)
Calcium channel blocker	53 (46)
ACE-I/ARB	57 (50)
Nitrate	40 (35)

ACE-I: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker, BMI: body mass index, LVEF: left ventricular ejection fraction, MI: myocardial infarction, NSTEMI: non-ST-elevation myocardial infarction, PCI: percutaneous coronary intervention, UAP: unstable angina pectoris.

3.2. Anatomic data according to the change in microvascular resistance

When divided according to the change in hyperemic microvascular resistance in response to PCI i.e. decreased (ΔMR ≤ 0%) vs. increased (ΔMR > 0%) microvascular resistance, there was no between-group difference in angiographic reference vessel diameter (3.1 ± 0.7 vs. 3.3 ± 1.0 mm, *p* = 0.34), minimum lumen diameter (1.1 ± 0.5 vs. 1.1 ± 0.4 mm, *p* = 0.45), diameter stenosis (64 ± 16 vs. 65 ± 18%, *p* = 0.69), or lesion length (18.3 ± 15 vs. 20.5 ± 13, *p* = 0.56) (Table 2).

Table 2
Lesion characteristics and changes in microvascular resistance (vessel level).

	ΔMR ≤ 0% *N* = 113	ΔMR > 0% *N* = 42	P
Reference diameter mm	3.1 ± 0.7	3.3 ± 1.0	0.34
Minimum lumen diameter mm	1.1 ± 0.5	1.1 ± 0.4	0.45
Diameter stenosis %	64 ± 16	65 ± 18	0.69
Lesion length mm	18.3 ± 15	20.5 ± 13	0.56

One-way analysis of variance test of anatomic features between vessels with reduced and increase microvascular resistance (ΔMR ≤ 0% vs. ΔMR > 0%) pre vs. post percutaneous coronary intervention.

3.3. Hemodynamic data according to the change in microvascular resistance

Table 3 show the hemodynamic differences between the two ΔMR sub-groups. Lesions with a decrease in hyperemic microvascular resistance following PCI (ΔMR ≤ 0%) tended to have lower pre-PCI FFR (0.67 ± 0.15 vs. 0.72 ± 0.09, *p* = 0.051), lower pre-PCI CFR (1.9 ± 0.8 vs. 2.6 ± 1.8, *p* < 0.0001), lower pre-PCI Pd/Pa (0.82 ± 0.15 vs. 0.86 ± 0.09, p 0.02), and higher pre-PCI HMR (2.76 ± 1.3 vs. 1.62 ± 0.74 mmHg/cm/s, *p* = 0.001) or IMR 24.4 (20.9) vs. 15.8 (13.2), *p* = 0.004). Vessels with ΔMR ≤ 0% had highest proportion of FFR ≤ 0.80 and CFR

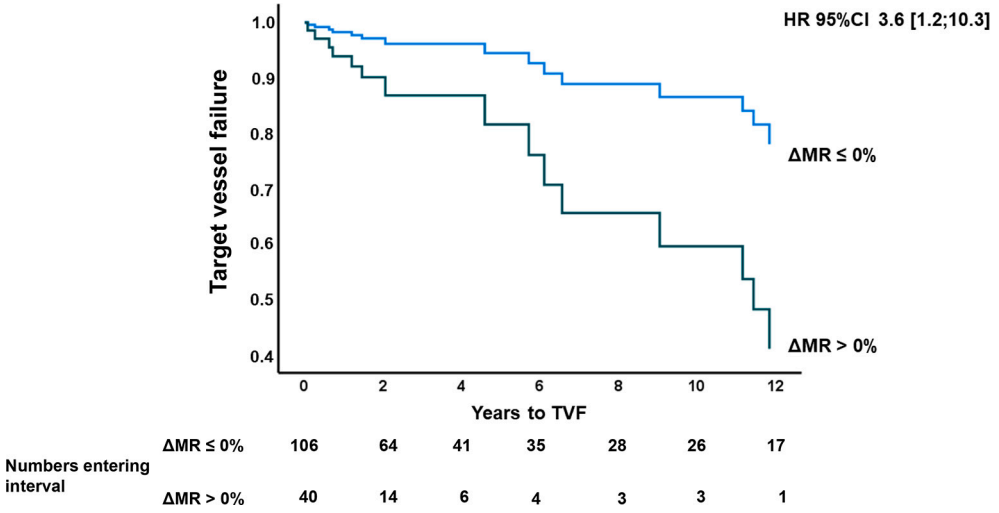

Fig. 1. Cox regression model of target vessel failure (TVF) between lesions with delta microvascular resistance ≤0% and > 0% (ΔMR ≤ 0% vs. ΔMR > 0%) following percutaneous coronary intervention.

Table 3
Pressure/flow and changes in microvascular resistance (vessel level).

	ΔMR ≤ 0% N = 113	ΔMR > 0% N = 42	P
Pre-FFR	0.67 ± 0.15	0.72 ± 0.09	0.051
Post-FFR	0.88 ± 0.06	0.87 ± 0.07	0.24
Pre-CFR	1.9 ± 0.8	2.6 ± 1.8	<0.0001
Post-CFR	3.1 ± 1.5	2.3 ± 1.3	0.003
Pre-Pd/Pa	0.82 ± 0.15	0.86 ± 0.09	0.02
Post-Pd/Pa	0.95 ± 0.04	0.94 ± 0.04	0.12
Pre-b-APV cm/s	14.6 ± 6.4	26.4 ± 15.6	<0.0001
Post-b-APV cm/s	19.6 ± 8.0	23.2 ± 9.1	0.123
Pre-h-APV cm/s	25.3 ± 13.6	49.0 ± 32.3	<0.0001
Post-h-APV cm/s	51.5 ± 19.4	44.5 ± 12.5	0.183
Pre-b-tmn	1.0 ± 0.46	0.84 ± 0.49	0.18
Post-b-tmn	0.75 ± 0.33	5.5 ± 24	0.22
Pre-h-tmn	0.58 ± 0.4	0.36 ± 0.26	0.02
Post-h-tmn	0.26 ± 0.19	0.49 ± 0.36	0.001
Pre-HMR mmHg/cm/s	2.76 ± 1.3	1.62 ± 0.74	0.001
Post-HMR mmHg/cm/s	1.72 ± 0.69	1.96 ± 0.68	0.240
Pre-IMR	24.4(20.9)	15.8(13.2)	0.004
Post-IMR	13.6(11.6)	24.3(24.9)	0.002
Pre-HSR mmHg/cm/s	1.79 ± 1.7	0.76 ± 0.41	0.023
Post-HSR mmHg/cm/s	0.19 ± 0.12	0.28 ± 0.20	0.027

b-APV: baseline average peak velocity, b-tmn: baseline transit mean time, CFR: coronary flow reserve, FFR: fractional flow reserve, h-APV: hyperemic average peak velocity, HMR: hyperemic microvascular resistance, HSR: hyperemic stenotic resistance, h-tmn: hyperemic transit mean time, IMR: index of microvascular resistance.

< 2.0 (Figs. 2-3). Supplemental Table 1 show the hemodynamic values (ΔMR > 0% vs. ΔMR ≤ 0%) when pre-FFR > 0.80 subtracted. Supplemental Table 2 show equal distribution of vessels with pre-FFR > 0.80 between the ΔMR > 0% vs. ΔMR ≤ 0% (Fisher's exact test $p = 0.73$). Doppler derived pre-CFR was significantly lower than thermodilution derived pre-CFR (supplemental Table 3). The different hyperemic agents had an effect on post-FFR and pre-CFR with intracoronary nicorandil having the most potent effect on post-FFR and post-CFR was lowest when intravenous adenosine or intracoronary nicorandil were used (supplemental Table 4).

3.4. Target vessel failure and ΔMR %

In Cox regression analysis for target vessel failure (TVF), using gender, diabetes and hypertension as covariates, an increase in microvascular resistance after PCI (ΔMR > 0%) was associated with increased rate of TVF during median follow up time of 3.3 years (Hazard Ratio (95% CI) 3.6 (1.3; 10.3) and $p = 0.018$), and subtracting lesions with pre-PCR FFR > 0.80 the Hazard Ratio for TVF was borderline significant

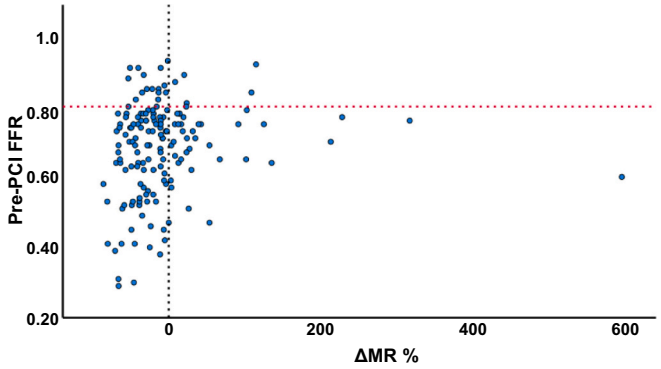

Fig. 2. Pre percutaneous coronary intervention (Pre-PCI) fractional flow reserve (FFR) according to delta microvascular resistance (ΔMR %) following PCI. The black and red dot line indicate ΔMR = 0% and FFR cut off level 0.80. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

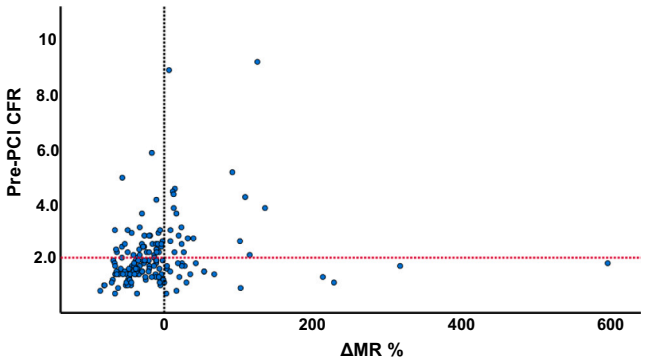

Fig. 3. Pre percutaneous coronary intervention (Pre-PCI) coronary flow reserve (CFR) according to delta microvascular resistance (ΔMR %) following PCI. The black and red dot line indicate ΔMR = 0% and CFR cut off level 2.0. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

2.3 (0.9; 6.0) (Table 4).

3.5. Pre- and post-PCI hemodynamic data

Pre-PCI, mean FFR was 0.68 ± 0.1, CFR 2.3 ± 1.3, HMR 2.6 ± 1.3 mmHg/cm/s, IMR 22.7 (20.7) and HSR 1.4 ± 1.4 mmHg/cm/s. Except for IMR, all values improved significantly following PCI: FFR 0.88 ± 0.1 ($p < 0.0001$ versus pre-PCI FFR), CFR 3.2 ± 2.1 ($p < 0.0001$ versus pre-PCI CFR), HMR 1.8 ± 0.7 mmHg/cm/s ($p < 0.0001$ versus pre-PCI HMR), HSR 0.21 ± 0.14 mmHg/cm/s ($p < 0.0001$ versus pre-PCI HSR). IMR corrected for collateral flow contribution using Yong's formula was not different compared to the apparent IMR values (Table 5).

4. Discussion

This is a multicentre observational cohort study with pooled post-PCI data comprised of pressure, flow, and microvascular resistance. The main aim was to evaluate the prognostic value of changes of microvascular resistance following PCI and relate it to hemodynamic and anatomic parameters. The main results are that an increase in hyperemic microvascular resistance following PCI was 1) associated with a higher rate of TVF and 2) occurred in vessels with higher pre-PCI FFR and CFR values.

Previously, it has been demonstrated that an improvement in flow velocity following PCI occurs only in vessels with FFR ≤ 0.80, and dominantly occurs in vessels with FFR values below 0.60 [5]. According to Ohm's law of resistance, flow is reciprocal of microvascular resistance assuming laminar flow conditions. In the current study, improvement in microvascular resistance occurred in lesions with the worst pre-PCI values: lowest FFR, CFR and hyperemic average peak velocity, and highest resistance. Therefore, the effect of PCI of on the microcirculation is dependent on the degree of epicardial disease (i.e. impairment of FFR and CFR). A minority of the lesions had pre-PCI FFR > 0.80 distributed

Table 4
Target vessel failure rate during follow up (vessel level).

	ΔMR ≤ 0% N (%)	ΔMR > 0% N (%)	Hazard ratio 95% CI	P
TVF	9 (7.9)	6 (14.3)	3.6 [1.2;10.3]	0.018
TVF (without pre-PCI FFR > 0.80)	8 (7.1)	4 (9.5)	2.3 [0.9; 6.0]	0.086

Multivariate model adjusted to hypertension, diabetes and gender evaluating target vessel failure (TVF) rate between vessel with reduced vs. increased post-PCI microvascular resistance (ΔMR ≤ 0% vs. ΔMR > 0%).

Table 5
Pre/Post-PCI changes in pressure, flow and microvascular resistance.

	Pre-PCI	Post-PCI	P
FFR $n = 284$	0.68 ± 0.1	0.88 ± 0.1	<0.0001
CFR n = 295	2.3 ± 1.3	3.2 ± 2.1	<0.0001
HMR $n = 88$	2.6 ± 1.3	1.8 ± 0.7	<0.0001
IMR $n = 67$	22.7 (20.7)	16.9 (13.3)	0.11
IMRcor n = 67	19.8 (19.9)	16.5 (15.4)	0.38
HSR n = 88	1.4 ± 1.4	0.21 ± 0.14	<0.0001

CFR: coronary flow reserve, FFR: fractional flow reserve, HMR: hyperemic microvascular resistance, HSR: hyperemic stenotic resistance, IMR: index of microvascular resistance. IMRcor: IMR corrected with Yong's formular.

equally between the two groups of ΔMR. Subtracting these lesions showed a borderline significant TVF rate for ΔMR > 0% which is probably a power issue due to the relative small number of events. The overall mean FFR in lesions undergoing PCI and divided according to changes in microvascular resistance were comparable to previous randomized trials [11–13]. FFR is dependent on microvascular resistance i.e. a low FFR value implies a low microvascular resistance for moderate disease whereas in severe epicardial disease the main determinant of FFR is HSR [14]. Baseline microvascular resistance in both revascularized and medically treated lesions is not associated to TVF [14]. Lower TVF was seen in the ΔMR ≤ 0% group which had the lowest FFR and CFR prior to PCI, whereas the ΔMR > 0% group with higher baseline FFR and CFR, had worse outcome. Subtracting vessels with pre-FFR > 0.80 showed a still increased Hazard Ratio and TVF-rate when ΔMR > 0%, although it was not statistically significant due to the overall low number of events in this population. This apparent paradox is explained by the observational nature of this study and therefore confers no causation. The median follow-up time in this study was 3.3 years and therefore TVF occurred relatively lately, and not immediately after the index procedure. The late occurrence of TVF suggests that it is related to the subsequent microvascular impairment. Until recently microvascular dysfunction was considered a benign condition, but there is mounting evidence that microvascular and endothelial dysfunction are associated with MACE and poor outcome [15].

The results were based upon apparent values of HMR and IMR and not corrected for collateral flow contribution by wedge pressure or Yong's formula [16]. Coronary wedge pressure has been considered as a surrogate for coronary collateral flow contribution [17]. Based upon the assumption that collateral flow increases with lesion severity, using the apparent distal flow and pressure values overestimates microvascular resistance values prior to PCI and confounds serial assessments of microvascular resistance pre- and post-PCI. However, two points question this notion. First, coronary collateral flow contribution is reportedly negligible distal to coronary stenosis with FFR > 0.6 [18]. The mean FFR was above 0.6 in both study groups in this analysis (i.e. increased vs. decreased microvascular resistance following PCI) and the inter-group difference was not statistically significant. Second, coronary wedge pressure is determined by many other factors than the collateral circulation such as heart rate, contractility, and venous backpressure [19], and the contribution of collateral flow to the measured wedge pressure in moderate epicardial disease is at best minimal. The main finding is this study was that increases in apparent resistance values are associated to TVF, and therefore correcting microvascular resistance to account for collaterals is not necessary when evaluating moderate epicardial coronary artery disease.

The current study did not show any significant difference in the anatomic parameters between the two groups determined by microvascular resistance responses following PCI. The anatomic parameters were derived by quantitative angiographic analysis of the angiographic data, and therefore crude by nature without any specific details of plaque composition and burden. Intravascular imaging data was not available to establish a link between plaque composition and post-PCI physiological parameters. Distal embolization following PCI (mainly in acute coronary syndromes) is linked to plaque burden and can offset PCI-related improvement in coronary flow and resistance [20]. The current study is based upon evaluation of stable lesions with a steady-state condition between plaque composition and downstream physiology. This is different in the culprit lesion in the setting of acute coronary syndromes where thrombus formation and inflammation contribute to impairment of the microcirculation [21]. Understanding the relationship between physiological changes and lesion severity and composition can be addressed by combining physiology and intra vascular imaging in future studies.

4.1. Limitations

There are several limitations in study. First, the observational nature of this study should be taken in account when viewing the conclusions. Second, a minority of patients underwent PCI with paired pre and post-PCI measurements, which could bias the results due to missing data. Third, intravascular imaging data was not available and therefore the anatomic data are based upon quantitative angiographic analysis of angiographic data. Fourth, there is no data of periprocedural myocardial infarction, as this could increase MR and drive the association to TVF. Fifth, this a population of mainly stable coronary artery disease with a relatively low number of events.

5. Conclusion

In conclusion, the improvement of minimal microvascular resistance following PCI, defined as a relative reduction in hyperemic microvascular resistance in response to revascularization, is associated with a significantly lower rate of TVF during follow-up. This finding was observed in patients with chronic coronary syndrome and, by definition, in lesions with stable plaque composition. The improvement in microvascular resistance following PCI occurred in vessels with lower FFR, lower CFR, and higher HMR/IMR values prior to PCI, compared to vessels where no improvement in microvascular resistance was observed after PCI.

CRediT authorship contribution statement

Ashkan Eftekhari: Conceptualization, Writing – review & editing, Investigation. **Tim P. van de Hoef:** Supervision, Project administration, Software, Investigation. **Masahiro Hoshino:** Investigation, Resources. **Joo Myung Lee:** Investigation, Resources. **Coen K.M. Boerhout:** Investigation, Resources. **Guus A. de Waard:** Investigation, Resources. **Ji-Hyun Jung:** Investigation, Resources. **Seung Hun Lee:** Investigation, Resources. **Hernan Mejia-Renteria:** Investigation, Resources. **Mauro Echavarria-Pinto:** Investigation, Resources. **Martijn Meuwissen:** Investigation, Resources. **Hitoshi Matsuo:** Investigation, Resources. **Maribel Madera-Cambero:** Investigation, Resources. **Mohamed A. Effat:** Investigation, Resources. **Koen Marques:** Investigation, Resources. **Joon-Hyung Doh:** Investigation, Resources. **Rupak Banerjee:** Investigation, Resources. **Chang-Wook Nam:** Investigation, Resources. **Giampaolo Niccoli:** Investigation, Resources. **Tadashi Murai:** Investigation, Resources. **Masafumi Nakayama:** Investigation, Resources. **Nobuhiro Tanaka:** Investigation, Resources. **Eun-Seok Shin:** Investigation, Resources. **Paul Knaapen:** Investigation, Resources. **Niels van Royen:** Investigation, Resources. **Javier Escaned:** Investigation, Resources. **Bon Kwon Koo:** Investigation, Resources. **Steven A.J. Chamuleau:** Investigation, Resources. **Tsunekazu Kakuta:** Investigation, Resources. **Jan J. Piek:** Investigation, Resources. **Evald Høj Christiansen:** Supervision, Conceptualization, Investigation.

Declaration of Competing Interest

There are no conflicts of interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2023.131296.

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