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Correspondence

Post percutaneous coronary intervention physiology in patients presenting with ST-segment elevation myocardial infarction

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Post percutaneous coronary intervention (PCI) fractional flow reserve (FFR) can be used to evaluate procedural success and to guide stent optimization [1,2]. Several studies have demonstrated that reduced FFR following PCI in patients presenting with chronic coronary syndrome (CCS) or non-ST-segment elevation acute coronary syndrome (NSTE-ACS) is associated with adverse outcome [3]. Conversely, the use of post-PCI physiology in patients presenting with ST-segment elevation myocardial infarction (STEMI) has been criticized due to the temporarily elevated microvascular resistance [4]. The aim of this study was to compare post-PCI FFR and diastolic pressure ratio (dPR) between (1) patients presenting with vs. without STEMI and (2) in culprit and non-culprit vessels of STEMI patients.

The FFR SEARCH registry was a single-center, prospective, observational cohort study (n = 1000) [5]. Consecutive patients undergoing PCI with stent implantation were screened for eligibility, irrespective of clinical presentation. Following angiographically successful PCI, post-PCI physiology was obtained using a dedicated microcatheter (Navvus RXi, ACIST Medical Systems). No further optimization was performed following post-PCI FFR measurement. dPR computation was performed offline using dedicated software [6]. The study protocol was approved by the local Ethical Committee. All patients provided informed consent.

Patients were categorized into 2 groups based on clinical presentation. The primary outcome was the difference in post-PCI FFR and dPR in patients presenting with vs. without STEMI. Secondary outcomes included differences in post-PCI FFR and dPR in culprit vs. non-culprit vessels of STEMI patients.

Standard statistical tests were applied to compare patient-level variables, and (generalized) linear mixed models with random intercepts were used to compare vessel-level variables. All post-PCI physiology outcomes (presented as means ± SD) were assessed at vessel level. Multivariable models were built with post-PCI physiology as the dependent variable to adjust for potential confounders. Multicollinearity was tested. Statistical analysis was performed with SPSS version 28 and R version 4.2.0 (packages: lme4, lmerTest). A 2-sided p < 0.05 was considered statistically significant.

Post-PCI FFR was successfully measured in 959 patients (1165 vessels) of which 322 (33.6 %) patients (371 vessels) presented with STEMI and 637 (66.4 %) patients (794 vessels) presented without STEMI. In STEMI patients, post-PCI FFR was available for 315 culprit vessels and 56 non-culprit vessels. In patients presenting without STEMI, 285 patients (353 vessels) had CCS and 352 patients (441 vessels) had NSTE-ACS.

STEMI patients were younger (61.5 ± 12.7 vs. 65.2 ± 11.3, p < 0.001) and more often male (77.3 % vs. 70.0 %, p = 0.017). STEMI patients presented less often with a history of hypertension (35.8 % vs. 59.8 %), diabetes (9.3 % vs. 23.7 %), prior myocardial infarction (9.9 % vs. 25.3 %), and prior revascularization (13.4 % vs. 32.7 %) (p < 0.001 for all).

The left anterior descending (LAD) was the study vessel in 43.1 % in the STEMI group vs. 47.4 % in the without STEMI group (p = 0.18). Median stent diameter and length (both in mm) were 3.2 (3.0–3.5) and 22.0 (15.0–35.0) in STEMI vs. 3.0 (2.9–3.5) and 24.0 (15.0–38.0) in without STEMI (p < 0.001 and p = 0.13, respectively). Both predilatation and postdilatation were less frequently performed in the STEMI group (58.2 % vs. 69.6 %, p < 0.001, and 51.8 vs. 62.9, p < 0.001).

Mean post-PCI FFR was 0.93 ± 0.06 in STEMI vs. 0.90 ± 0.07 in without STEMI (p adjusted = 0.006) (Fig. 1A), while mean post-PCI dPR was 0.96 ± 0.06 in STEMI vs. 0.95 ± 0.07 in without STEMI (p adjusted = 0.33) (Fig. 1B). Post-PCI FFR was <0.90 in 89 vessels (24.0 %) of STEMI patients and in 351 vessels (44.2 %) of patients without STEMI (p < 0.001).

Focusing on STEMI patients, mean post-PCI FFR and dPR were numerically higher in culprit vs. non-culprit vessels, but these differences were not statistically significant (Fig. 1). In STEMI culprit vessels with TIMI 0 flow at baseline (46.0 %), mean post-PCI FFR was 0.94 ± 0.05 vs. 0.93 ± 0.06 in STEMI culprit vessels with TIMI 1–3 flow (p unadjusted = 0.016, p adjusted = 0.29), while mean post-PCI dPR was 0.96 ± 0.06 vs. 0.96 ± 0.05, respectively (p unadjusted = 0.66, p adjusted = 0.08).

Abbreviations: CCS, chronic coronary syndrome; dPR, diastolic pressure ratio; FFR, fractional flow reserve; LAD, left anterior descending; NSTE-ACS, non-ST-segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

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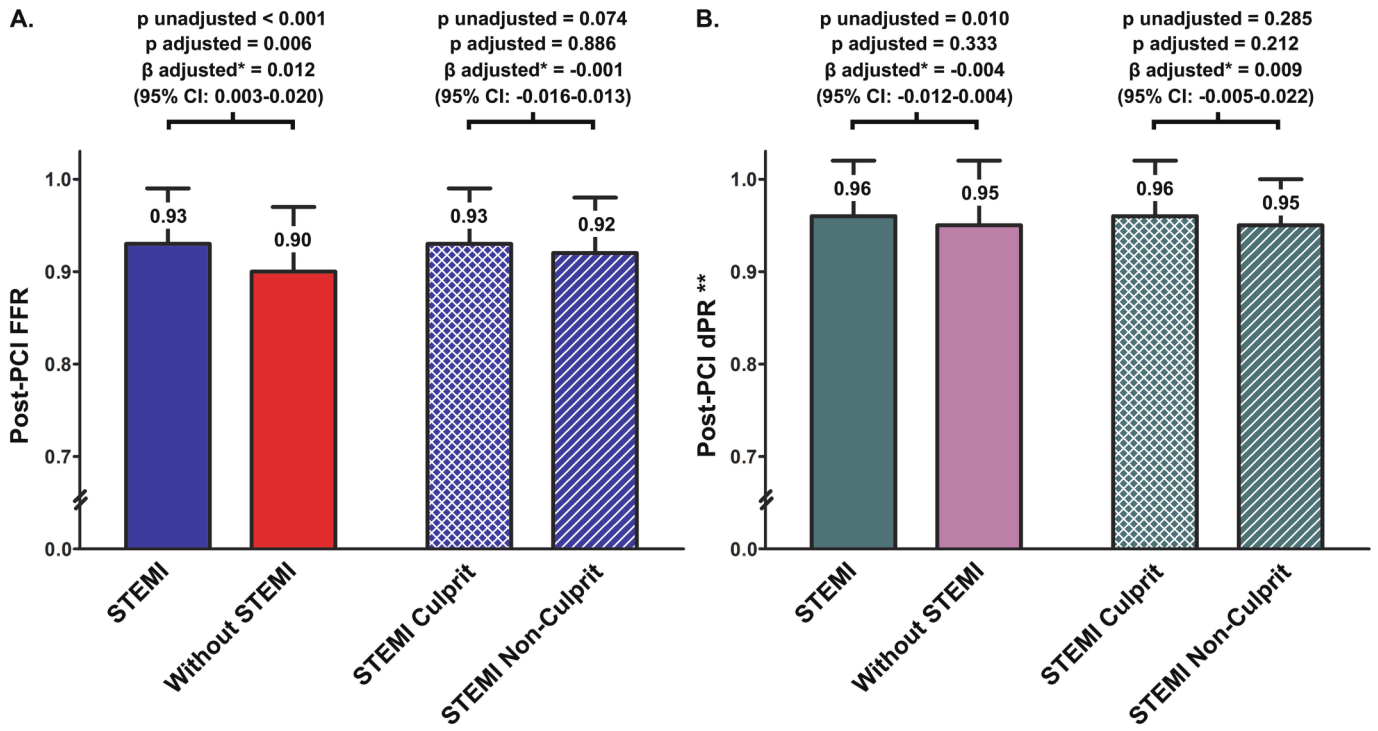

Fig. 1. Differences in post-PCI FFR and dPR according to clinical presentation with vs. without STEMI and for culprit vs. non-culprit vessels within STEMI. Vessel-level data, presented as means with standard deviations (whiskers). CI = confidence interval, dPR = diastolic pressure ratio, FFR = fractional flow reserve, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction. * The adjusted β (including the 95 % confidence interval) represents the mean difference in the physiological index that is related to presentation with vs. without STEMI following multivariable adjustment (independent association). A positive value indicates a higher adjusted post-PCI FFR or dPR in the STEMI group, while a negative value indicates a higher adjusted post-PCI FFR or dPR in the without STEMI group. Variables included in the multivariable model: Age, gender, hypertension, hypercholesterolemia, diabetes, smoking, prior myocardial infarction, prior PCI, prior coronary bypass surgery, peripheral arterial disease, left anterior descending, lesion type, calcification, in-stent restenosis, thrombus, quantitative coronary angiography (QCA) diameter stenosis pre, QCA minimal lumen diameter pre, predilatation, stent length, stent diameter, number of stents, postdilatation, QCA diameter stenosis post, QCA minimal lumen diameter post. ** dPR was available for 1126/1165 (96.7 %) vessels.

Finally, the impact of STEMI on post-PCI FFR did not depend on LAD vs. non-LAD as the interrogated study vessel (p for interaction = 0.47).

In summary, (1) post-PCI FFR measured directly after angiographically successful PCI was significantly higher in patients presenting with vs. without STEMI, (2) no significant difference in post-PCI dPR was observed in patients presenting with vs. without STEMI, and (3) no significant difference in post-PCI FFR and dPR was observed between culprit vs. non-culprit vessels of STEMI patients.

To the best of our knowledge, this is the first study to provide real-world physiological confirmation on higher post-PCI FFR in STEMI patients as compared to patients presenting without STEMI. Our findings support the concept of a blunted hyperemic response in patients who are subject to microvascular impairment as in the context of STEMI [4,7,8].

More specifically to STEMI patients, post-PCI FFR appeared higher in culprit vessels with TIMI 0 flow, suggesting the presence of increased amount of thrombus. This finding is in line with previous work demonstrating the association between higher thrombus burden and microvascular dysfunction [9]. Furthermore, there was no significant difference in post-PCI FFR between culprit and non-culprit vessels of STEMI patients, which fits with the concept that microvascular dysfunction in a primary PCI setting is not limited to the culprit territory [10,11]. However, we did find a numerically higher post-PCI FFR in STEMI culprit as compared to STEMI non-culprit vessels, which reflects on studies showing the unfavorable impact of higher thrombus burden on microvascular function, as well as that non-culprit vessels appear not overly affected by microvascular impairment in patients with acute myocardial infarction [9,10,12].

The difference in post-PCI dPR in patients with vs. without STEMI was less pronounced than for post-PCI FFR and did not hold after multivariable adjustment. In the acute phase of STEMI, the impact of microvascular impairment and increased zero flow pressure with FFR seems higher as compared to the effect of augmented resting flow with non-hyperemic pressure ratios [13,14]. The latter is reinforced by a recent study demonstrating that FFR but not instantaneous wave-free ratio in non-culprit vessels of STEMI patients significantly decreased a month after primary PCI [15].

Finally, no significant interaction in the effect of STEMI on post-PCI FFR in LAD vs. non LAD vessels was observed.

Altogether, our findings dispute the use of a universal physiological cut-off for FFR following angiographically successful PCI in patients presenting with vs. without STEMI, whereas the latter does not hold for dPR. Future research is needed to establish specific post-PCI cut-offs for both FFR and dPR to predict future adverse events and to guide optimization respective to clinical presentation with STEMI [16].

This study has limitations. First, this was an observational study reflecting local practice in a single center. Second, physiological assessment was performed using a microcatheter that proved to result in a slight overestimation of FFR as compared to pressure wires [17]. Third, despite large sample size, post-PCI physiology was available in only 56 non-culprit vessels of STEMI patients. The comparison with 315 culprit vessels should be interpreted carefully. Finally, specific data on thrombus burden and microvascular function (e.g. coronary flow reserve and index of microvascular resistance) were not available, but would have provided relevant insight in the rationale behind higher post-PCI FFR in STEMI patients.

In conclusion, this large prospective study is the first to demonstrate that post-PCI FFR, but not dPR, is significantly higher in patients presenting with vs. without STEMI.

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CRediT authorship contribution statement

Frederik T.W. Groenland: Conceptualization, Investigation, Methodology, Visualization, Writing – original draft. **Annemieke C. Ziedses des Plantes:** Conceptualization, Formal analysis, Investigation, Methodology, Writing – review & editing. **Alessandra Scoccia:** Formal analysis, Methodology, Software, Visualization, Writing – review & editing. **Tara Neleman:** Formal analysis, Methodology, Software, Writing – review & editing. **Kaneshka Masdjedi:** Conceptualization, Formal analysis, Methodology, Writing – review & editing. **Isabella Kardys:** Formal analysis, Methodology, Writing – review & editing. **Roberto Diletti:** Conceptualization, Methodology, Writing – review & editing. **Nicolas M. Van Mieghem:** Conceptualization, Methodology, Writing – review & editing. **J. Daemen:** Conceptualization, Methodology, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Joost Daemen received institutional grant/research support from Abbott Vascular, ACIST Medical, Boston Scientific, Medtronic, Microport, Pie Medical, and ReCor Medical, and consultancy and speaker fees from Abbott, Abiomed, ACIST medical, Boston Scientific, CardiacBooster, Cardialysis BV, Kaminari Medical, Medtronic, ReCor Medical, Pie Medical, PulseCath, and Siemens Health Care. Nicolas van Mieghem received institutional research grant support from Abbott Vascular, Biotronik, Boston Scientific, Daiichi Sankyo, Edwards Lifesciences, and Medtronic, and consultancy fees from Abbott, Abiomed, Amgen, Anteris, Boston Scientific, Daiichi Sankyo, JenaValve, Medtronic, PulseCath BV, and Teleflex. Tara Neleman has received institutional grant support from ACIST Medical Systems. The remaining authors report no relationships that could be construed as a conflict of interest.

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Frederik T.W. Groenland[a], Annemieke C. Ziedses des Plantes[a], Alessandra Scoccia[a], Tara Neleman[a], Kaneshka Masdjedi[b], Isabella Kardys[a], Roberto Diletti[a], Nicolas M. Van Mieghem[a], Joost Daemen[a,*]

[a] *Department of (Interventional) Cardiology, Thoraxcenter, Erasmus University Medical Center, Rotterdam, the Netherlands*

[b] *Department of Cardiology, Admiraal de Ruyter Hospital, Goes, the Netherlands*

[*] Corresponding author at: Department of Cardiology, Thoraxcenter, Erasmus University Medical Center, Dr. Molewaterplein 40, Room Rg-628, 3015 GD, Rotterdam, the Netherlands.
E-mail address: j.daemen@erasmusmc.nl (J. Daemen).