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Acute-setting vs. staged-setting vessel fractional flow reserve of intermediate non-culprit lesions in patients with ST-segment elevation myocardial infarction (FAST STAGED study)

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Complete revascularization in patients with ST-segment elevation myocardial infarction (STEMI) and multivessel disease improves clinical outcome [1,2].

Several trials investigated the additional value of fractional flow reserve (FFR) to guide complete revascularization. FFR of intermediate non-culprit lesions (NCL) with ≥50% angiographic diameter stenosis (DS) appeared negative in 30–50%, questioning the need for percutaneous coronary intervention (PCI) [3–5].

Vessel fractional flow reserve (vFFR) is a novel 3D-quantitative coronary angiography (3D-QCA)-based technology that does not require the use of dedicated pressure wires or hyperemic agents. vFFR proved to have a good diagnostic agreement with pressure wire-based FFR [6–8]. More recently, we demonstrated the potential impact of acute-setting vFFR of intermediate NCL on revascularization strategy and clinical outcome in STEMI patients [9]. In this setting, vFFR had a diagnostic accuracy of 83.3% with pressure wire-based FFR as a reference [9]. The latter makes vFFR a promising alternative to conventional FFR, which was the decision tool in previous trials [3–5].

Temporary microvascular changes in the acute setting have been linked to higher FFR values (underestimation) or lower non-hyperemic pressure ratio (NHPR) values (overestimation) [10,11]. Where previous work demonstrated a decrease in classification agreement when the time between repeated measurements increased, the optimal timing of pressure wire-based physiological NCL assessment in patients presenting with STEMI remains topic of debate [10,12]. In contrast to FFR and NHPR, vFFR should not be hampered by temporary changes in the microcirculation. Hence, the aim of this study was to compare acute- vs. staged-setting vFFR of intermediate NCL in STEMI patients.

This was a single-center, retrospective cohort study. All STEMI patients from January 1st, 2018, to December 31st, 2021, undergoing primary PCI followed by a staged procedure (within 3 months) for an intermediate lesion (30–80% angiographic DS with a reference diameter ≥2.00 mm by visual estimation or QCA) in a non-culprit vessel were screened for eligibility. Patients with prior coronary bypass surgery, heart transplantation, cardiac arrest or cardiogenic shock, or coronary angiograms that appeared not feasible for vFFR computation, were excluded. The Ethical Committee of the Erasmus University Medical Center approved the study protocol and waived the need for informed consent.

vFFR analysis method has been described before [6,7,9]. In brief, analyses were performed offline in random sequence by an academic corelab specialist using CAAS workstation 8.5.1 (Pie Medical imaging, Maastricht, the Netherlands). Acute- or staged-setting pressure wire-based physiological NCL assessment was infrequent (n = 15/92) and disregarded for the present analysis.

The Shapiro-Wilk test and visual inspection of distribution plots were used to evaluate whether continuous variables followed normal distribution. Continuous variables were presented as mean ± standard deviation (SD) or as median with 25th–75th percentiles, as appropriate. Categorical variables were reported as counts with percentages. Normally distributed paired continuous variables were compared with the paired *t*-test. The correlation for acute- and staged-setting vFFR was displayed in a scatter plot and numerically expressed with the Pearson's correlation coefficient (r). The diagnostic performance of acute- vs. staged-setting vFFR was determined for the cutoff value of ≤0.80. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the discriminative value of acute-setting vFFR to detect staged-setting vFFR ≤0.80. If patients had multiple eligible non-culprit vessels with an intermediate lesion, the vessel with the lowest acute-setting vFFR value was used for the analysis.

Out of 181 screened patients, 92 patients were included. vFFR computation appeared not feasible in 47 patients (26.0%), which was

Abbreviations: 3D-QCA, 3D-quantitative coronary angiography; DS, diameter stenosis; FFR, fractional flow reserve; iFR, instantaneous wave-free ratio; NCL, non-culprit lesion; NHPR, non-hyperemic pressure ratio; PCI, percutaneous coronary intervention; ROC, receiver operating characteristic; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction; vFFR, vessel fractional flow reserve.

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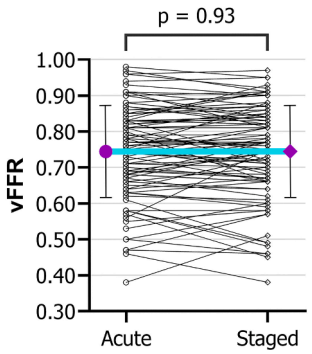

Fig. 1. Change in vFFR from the acute to the staged setting: The black lines illustrate the change in vFFR from the acute to the staged setting for all 92 patients individually. The purple characters and black whiskers indicate mean vFFR ± standard deviation for the acute and staged setting. Mean vFFR (0.74 in both settings) did not change over time as highlighted by the light blue line. The median (25th–75th percentiles) time between the primary PCI and staged procedure was 14.5 (3.0–30.0) days. vFFR = vessel fractional flow reserve. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

mainly due to missing coronary angiograms with a rotation/angulation of at least 30 degrees in either the acute or staged setting. Mean age was 64.9 (±10.4) years and 65 (70.7%) patients were male. The median time between the primary PCI and staged procedure was 14.5 (3.0–30.0) days. Mean systolic blood pressure (in mmHg) was 123.3 (±23.2) in the acute setting vs. 119.7 (±21.9) in the staged setting (p = 0.19), while mean diastolic blood pressure was 72.3 (±13.5) in the acute setting vs. 67.5 (±12.5) in the staged setting (p = 0.002).

Acute- vs. staged-setting mean vFFR did not differ (0.74 (±0.13) vs. 0.74 (±0.13), p = 0.93) (Fig. 1). The correlation (r) was 0.89 (p < 0.001) (Fig. 2). From the acute to the staged setting, vFFR changed from ≤0.80 to >0.80 and vice versa in 6 patients (6.5%). The diagnostic performance of acute-setting vFFR with staged-setting vFFR as the reference standard had a sensitivity of 96.4%, specificity of 88.9%, diagnostic accuracy (classification agreement) of 93.5%, positive predictive value of 93.1%, and negative predictive value of 94.1% (Fig. 2). ROC curve analysis revealed an excellent discriminative ability of acute-setting vFFR to predict staged-setting vFFR ≤0.80, with an area under the curve of 0.97 (p < 0.001). The classification agreement between acute- and staged-setting vFFR did not differ for patients with a staged procedure within or after 14 days (93.5% for both, p = 1.00).

In summary, mean vFFR of intermediate NCL in STEMI patients did not change over time and the overall classification agreement between the acute and staged setting was 93.5%. These findings confirm our hypothesis that vFFR is not affected by temporary microvascular changes in the acute setting.

vFFR seems a more consistent classifier of intermediate NCL in STEMI patients as compared to both FFR (classification agreement of 80.8%) and instantaneous wave-free ratio (iFR) (classification agreement of 78.2–82.2%) [11,12]. Two other studies assessed the repeatability of FFR and iFR without providing the precise classification agreement for the cutoff values of ≤0.80 and ≤0.89, respectively, but no significant differences in mean values were observed from the acute to the staged setting [13,14].

Both online and offline computation of acute-setting vFFR may be attractive in the context of STEMI with multivessel disease, as it can preclude (hyperemic) pressure wire-based measurements during either the primary PCI or staged procedure, enhance Heart Team decision making, and avoid potential staged procedures focusing on invasive physiological NCL assessment (appearing negative).

Our results are in line with two other studies comparing acute- vs. staged-setting quantitative flow ratio and add to the evidence that angiography-based technologies could play a future role in this subset of patients [15,16].

This study was limited by its single-center and retrospective design. Furthermore, angiographic projections used for acute- and staged-setting vFFR computation differed inevitably. Nevertheless, the classification agreement was 93.5%. Finally, vFFR has largely been validated in patients with stable coronary artery disease and non-ST-segment elevation acute coronary syndrome. Despite promising results in the retrospective FAST STEMI I study, the ongoing FAST STEMI II study (NCT05698719) will shed more light on the validation of acute-setting vFFR as compared to acute-setting FFR, NHPR and microvascular resistance indices.

In conclusion, acute-setting vFFR has the potential to further enhance the uptake of physiology-guided intermediate NCL revascularization in STEMI patients, thereby reducing pressure wire-based physiological lesion assessment during either primary PCI or staged procedures.

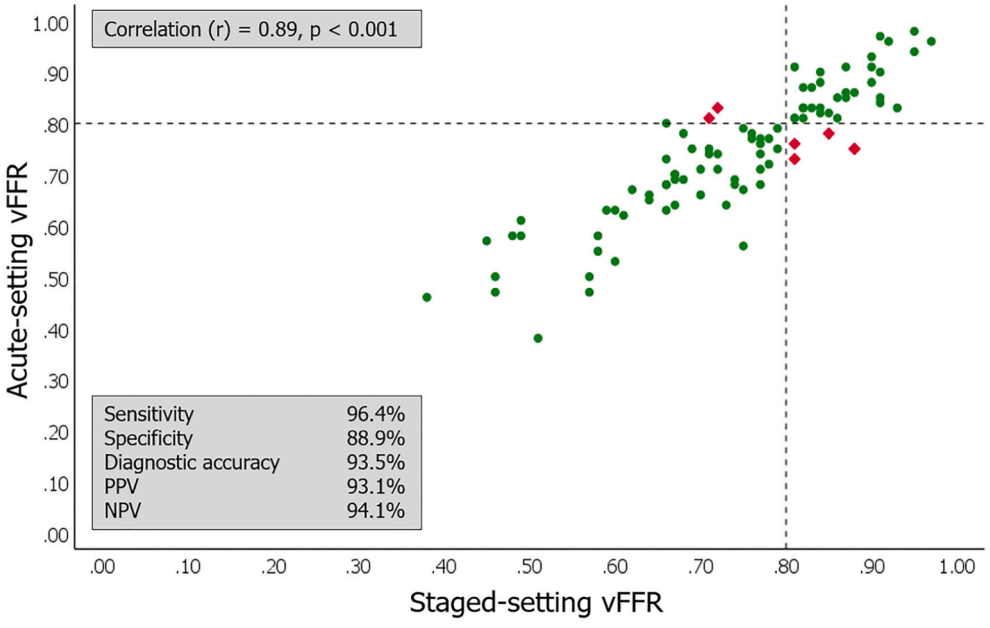

Fig. 2. Diagnostic performance of acute-setting vFFR with staged-setting vFFR as the reference standard: The green dots indicate agreement between acute- and staged-setting vFFR, while the red squares indicate disagreement between acute- and staged-setting vFFR (based on the cutoff value of ≤0.80). The grey box below displays the diagnostic performance of acute-setting vFFR with staged-setting vFFR as the reference standard. NPV = negative predictive value, PPV = positive predictive value, vFFR = vessel fractional flow reserve. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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Declaration of Competing Interest

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Jager Huang[1], Frederik T.W. Groenland[1], Alessandra Scoccia, Annemieke C. Ziedses des Plantes, Tara Neleman, Nicolas M. Van Mieghem, Joost Daemen[*]
Department of (Interventional) Cardiology, Thoraxcenter, Erasmus University Medical Center, Rotterdam, 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).

[1] Shared first authorship, both authors contributed equally.