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Clinical evidence for CAAS vFFR

FAST Study series

Pre-stent scenario

- The **initial FAST I**[1] study evaluated 100 patients and assessed the diagnostic accuracy of vFFR to predict invasive FFR $\leq$ 0.8. The diagnostic accuracy (AUC) was 0.93 and a high reproducibility was shown with a correlation coefficient of 0.95.

- In the **FAST Extend**[2] study 294 patients were evaluated confirming the high diagnostic accuracy (AUC) was 0.94 of vFFR to predict FFR $\leq$ 0.8.

- The **FAST II**[3] study was an international multi-center prospective trial in 6 countries (Netherlands, Germany, Italy, France, Unites States and Japan) evaluating the diagnostic accuracy and reproducibility of vFFR in an in-hospital and off-line core laboratory setting. The diagnostic accuracy (AUC) to predict FFR ≤ 0.8 for both corelab and (al, 2022) in-hospital were very high 0.93 and 0.91, respectively. Reproducibility between in-hospital and corelab also demonstrated to be very high at 0.87.

- The **FAST III**[4] trial was an international, multi-center, prospective study in which 2,235 patients were enrolled across 37 sites in 7 European countries, making it the largest European study to date evaluating an angiography-based FFR approach against the invasive gold standard.
  The primary endpoint was assessed in 1,116 patients in the vFFR group and 1,095 patients in the FFR group. At 1 year, vFFR-guided revascularization was demonstrated to be non-inferior to FFR-guided revascularization, with a composite rate of death, myocardial infarction, or repeat revascularization of 7.5%.

- The **AIR-STEMI**[5] trial evaluated whether functional coronary angiography could improve the guidance of complete revascularization in STEMI patients with multivessel coronary artery disease. In this international randomized trial of 1,823 patients, physiology-guided revascularization was compared with conventional angiography-guided revascularization. At a median follow-up of 17.9 months, the physiology-guided strategy resulted in lower risk of primary-outcome events (8.9% vs. 13.7%) and fewer safety events (4.6% vs. 7.1%). **Caas vFFR** was one of the angio-based FFR methodologies used for functional assessment in the study, demonstrating its role to help guide revascularization.

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[1] Masdjedi et al. Validation of 3-Dimensional Quantitative Coronary Angiography based software to calculate Fractional Flow Reserve: Fast Assessment of STenosis severity (FAST)-study. 2020:591-599doi: 10.4244/EIJ-D-19-00466.

[2] Neleman et al. Extended Validation of Novel 3D Quantitative Coronary Angiography-Based Software to Calculate vFFR: The FAST EXTEND Study. JACC Cardiovasc Imaging. 2021

[3] Masdjedi et al. Vessel fractional flow reserve (vFFR) for the assessment of stenosis severity: the FAST II study. EuroIntervention 2022

[4] Joost Daemen et al. Angiography-Based Physiology to Guide Coronary Revascularization, New England Journal of Medicine. 2026 doi:10.1056/NEJMoa2601841

[5] Simone Biscaglia et al. Complete Revascularization Guided by Functional Coronary Angiography in STEMI, New England Journal of Medicine.2026 doi:10.1056/NEJMoa2605373

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Post-stent scenario

- The **FAST Post**[6] study evaluated 100 patients and assessed the diagnostic accuracy of vFFR to predict invasive FFR $\leq$ 0.9 after stent implantation. The diagnostic accuracy (AUC) was 0.98 and high reproducibility was shown with a correlation coefficient of 0.95.

- In the **FAST Outcome**[7] study vFFR was carried out post-stenting in 800 patients and related to 1-year clinical outcome in these patients. The study demonstrated that patients with a post-stent vFFR < 0.9 showed a significantly higher rate of target vessel revascularization at 1 year.

- The **FAST Residual vFFR**[8] study evaluated the correlation of residual vFFR as calculated on the pre-stent angiogram with the post-stent invasive FFR. Residual vFFR was effective in identifying which lesions had a post-PCI FFR (fractional flow reserve) below 0.90. The overall accuracy was very high, with an area under the curve (AUC) of 0.93, indicating a strong performance. Additionally, using vFFR for virtual stenting accurately predicted the FFR results after PCI.

Various scenarios

Caas vFFR has been evaluated across multiple applications and diverse scenarios, with a few examples highlighted below:

- In the **VERMONT**[9] study vFFR showed excellent diagnostic performance, with an AUC of 0.92 (95% CI: 0.89–0.96) for identifying lesions with FFR ≤ 0.80. Sensitivity was 90%, specificity 79%, with a negative predictive value of 93% and a positive predictive value of 74%. Interobserver agreement was excellent ($r = 0.97$, $p < 0.001$). Notably, real-time vFFR computation was on average 13.9 minutes faster than wire-based FFR ($p < 0.001$). Real-time vFFR has low exclusion rate, rapid analysis time, and minimal interobserver variability, highlighting its practicality as a reliable screening tool in routine clinical practice.

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[6] Masdjedi et al. Validation of novel 3-dimensional quantitative coronary angiography-based software to calculate fractional flow reserve post stenting. Catheter Cardiovasc Interv. 2020

[7] Masdjedi et al. The Prognostic Value of Angiography-Based Vessel-FFR After Successful Percutaneous Coronary Intervention: The FAST Outcome Study.

[8] Tomaniak, M.; Neleman, T.; et al. Diagnostic Accuracy of Coronary Angiography-Based Vessel Fractional Flow Reserve (vFFR) Virtual Stenting. J. Clin. Med. 2022, 11, 1397. https://doi.org/10.3390/jcm11051397

[9] D.Akrawi, K.Kadappu, J.Xu, et al., "VERMONT: Vessel Fractional Flow Reserve (vFFR) Assessment of Stenosis Severity: A Prospective Study," Catheterization and Cardiovascular Interventions106 (2025): 3757-3765, https://doi.org/10.1002/ccd.70250.

- The **FAST dPR**[10] study investigated the diagnostic performance of vFFR and dPR, using FFR as a reference. The study found that while both vFFR and dPR strongly correlated with FFR, vFFR had a significantly higher correlation and diagnostic agreement with FFR than dPR, despite some discordance in specific patient subgroups. Overall, vFFR is supported as a less invasive method with good diagnostic performance, potentially enhancing the adoption of angio-based FFR.

- The **vFFR vs RFR**[11] study conducted at University Hospital Cologne aimed to compare the diagnostic performance of vessel fractional flow reserve (vFFR) to the non-hyperemic pressure ratio resting full-cycle ratio (RFR). Analysing 986 lesions from 705 patients, vFFR showed a strong correlation with RFR and demonstrated high diagnostic accuracy with 77% sensitivity, 93% specificity, and an AUC of 0.92. The findings confirmed vFFR's high diagnostic performance for evaluating coronary stenoses, including in specific subgroups like those with diabetes, severe aortic stenosis, and lesions in the left anterior descending artery.

- The **FAST OCT**[12] trial an *international multi-center prospective trial* focused on the association of vFFR with OCT. While vFFR demonstrated a significant association with MLA during univariable analysis, its independent predictive value for MLA was confirmed with respect tp multivariable analyses and these findings were discussed during TCT 2023.

- The **FAST Left Main**[13] study investigated the correlation between vFFR and IVUS for left main coronary stenosis. Amongst all the patients investigated in the study for 3D QCA and vFFR analyses, a strong correlation was observed. The diagnostic accuracy of vFFR ≤0.8 in identifying lesions with MLA < 6.0 mm^2 was high with the AUC of 0.95. In patients with good quality angiographic visualization and complete IVUS footage, 3D-QCA-based vFFR assessment reliably correlates with IVUS-assessed LMCA MLA.

[10] Scoccia et al. Comparison of diagnostic accuracy measures of novel 3D quantitative coronary angiography based software and diastolic pressure ratio for fractional flow Reserve. A single center pooled analysis of FAST EXTEND and FAST II studies

[11] Lake et. al. Comparison of vessel fractional flow reserve with invasive resting full-cycle ratio in patients with intermediate coronary lesions. International Journal of Cardiology 2023

[12] Annemieke C Ziedses des Plantes, Alessandra Scoccia et. al. Association of vessel fractional flow reserve (vFFR) with luminal obstruction and plaque characteristics as detected by optical coherence tomography (OCT) in patients with NSTE-ACS: the FAST OCT study, European Heart Journal - Cardiovascular Imaging, Volume 26, Issue 1, January 2025, Pages 49–59, https://doi.org/10.1093/ehjci/jeae212

[13] Tomaniak M et al. Correlation between 3D-QCA based FFR and quantitative lumen assessment by IVUS for left main coronary artery stenoses. Catheter Cardiovasc Interv. 2020