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Reproducibility Assessment of Different Functional Intracoronary Diagnostic Techniques

Fernando Rivero-Crespo[1], Javier Cuesta[2], Amparo Benedicto[3],
Teresa Bastante-Valiente[3], Jorge-Andrés Restrepo[4], Guillermo Diego-Nieto[3],
Fernando Alfonso
[1]Hospital Universitario de la Princesa, Madrid, Spain, [2]Hospital Universitario de la
Princesa, Madrid, MS, [3]Hospital Universitario de la Princesa, Madrid, España,
[4]Hospital Universitario de la Princesa, Madrid, Spain, [5]Hospital Universitario
Clinico San Carlos. Madrid, Madrid, Spain

Background: Current guidelines recommend the use of fractional flow reserve (FFR) for guiding the decision for coronary revascularization. Recently, new parameters are being validated for intracoronary ischemia detection.There are few data on the intrinsic biological variability of these measurements. The objective of this study was to evaluate the reproducibility of the different methods of intracoronary diagnosis.
Methods: We prospectively enrolled consecutive intermediate coronary lesions during a 6-month period. In all cases we systematically obtained measurements of the following parameters (in the same lesion using the same sequence): Pd/Pa, iFR, FFRic (after 80 mg intracoronary adenosine) and FFRiv (after intravenous adenosine at 140 mg/kg/min). At least two measurements of each parameter were obtained separated by a minimum interval of 3 minutes. The agreement between the measurements of each parameter was assessed using the intra-class correlation coefficient (ICC) and the Bland-Altman method. The variability of the four parameters was estimated using the variation coefficient (VC).
Results: Fifty three lesions were included. The mean values of each parameter were: 94.2 ± 4.8 for Pd/Pa; 88.0 ± 8.1 for iFR; 81.3 ± 8.3 for FFRic and 81.6 ± 11.3 for FFRiv. The concordance of each parameter was very good, with coefficients close to 1 in all determinations and with very precise ICC confidence intervals. The ICC values were 0.95 (95%CI: 0.91-0.97) for Pd/Pa ; 0.99 (95%CI: 0.98-0.99) for iFR ; 0.97 (95%CI: 0.96-0.98) for FFRic; and 0.97 (95%CI: 0.95-0.98) for FFRiv. The mean difference was not different from 0 for any parameter (Student-t test for related samples with p values < 0.05 in all cases). The Bland-Altman analyses showed a good agreement in all cases. The CV, however, showed greater variability for FFRiv, with a CV of 13.8% compared with 5.1%, 9.2% and 10.2% of Pd/Pa , iFR and FFRic, respectively.
Conclusions: Our findings suggest that the reproducibility of the different methods of functional diagnosis is excellent. Nonetheless, the variability of these parameters should be taken into account when making treatment decisions.

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FFR-guided complete revascularization during primary PCI: Preliminary data from the COMPARE ACUTE trial
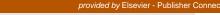
Pieter C. Smits[1], Georgios J. Vlachojannis[2], Ketil Lunde[3], Elmir Omerovic[4],
Carl E. Schotborgh[5], Gert Richardt[6], Mohamed Abdel-Wahab[7],
Franz-Josef Neumann[8], Rainer Hambrecht[9], Adrian Wlodarczak[10], Petr Kala[11],
Z. Piroth[12], Christoph A. Nienaber[13]
[1]Maasstad Hospital Rotterdam, Rotterdam, Netherlands, [2]Maasstad Hospital,
Rotterdam, Netherlands, [3]Oslo University Hospital, Oslo, Norway, [4]Sahlgrenska
University Hospital, Gothenburg, Sweden, [5]Haga Hospital, The Hague, Zuid-
Holland, [6]Segeberger Kliniken, Bad Segeberg, Germany, [7]Heart Center, Segeberger
Kliniken, Bad Segeberg, Germany, [8]Universitaets-Herzzentrum Freiburg Bad
Krozingen, Bad Krozingen, Germany, [9]Klinikum, Bremen, Bremen, Germany,
[10]Miedziowe Centrum Zdrowia Lubin, Lubin, Poland, [11]Internal and Cardiology
Department, Masaryk University and University Hospital Brno, Czech Republic,
Brno, Czech Republic, [12]Hungarian Instititute of Cardiology, Budapest, Hungary,
[13]University of ROSTOCK, Rostock, Germany

Background: Current guidelines deem percutaneous coronary intervention (PCI) of a non-infarct related artery (n-IRA) at the time of primary PCI (pPCI). This approach is being challenged by recent studies, which show benefits of complete rather than culprit vessel-only revascularization at the time of pPCI. However, these studies assessed grade of stenosis in the n-IRA by visual estimate. The impact of fractional-flow reserve (FFR) measurements during n-IRA PCI has not been assessed.
Methods: COMPARE ACUTE is an ongoing prospective, randomized trial carried out at 14 sites across Europe and Asia. Patients were randomly allocated (2:1) to receive either FFR guided multi-vessel (MV) PCI vs. culprit vessel-only PCI in the setting of STEMI. The primary study endpoint is MACCE defined as death, myocardial infarction, any revascularization, or cerebral accident at 12 months. FFR measurements were done at the discretion of the operator directly after completion of pPCI in all n-IRA with visual estimate of ≥50% stenosis. Positive FFR measurement was defined as ≤0.80 under maximal hyperemia. Here we report analysis of the preliminary FFR data.
Results: Since July 2011, 408 patients (613 FFR measurements) undergoing primary PCI with multi-vessel disease were enrolled. Mean age was 60.8 ± 13.2 (78.6% male) with Killip class I at presentation in 96%. In 35.6% the pPCI was performed in the LAD, 45.7% in the RCA and 18.6% in the RCX. Successful pPCI defined as TIMI 3 flow was achieved in 95.3%. FFR-measurements of n-IRA were performed in the LAD in 40.2%, RCA 26.8% and RCX 33.0%. In 56.5% the FFR measurement of a n-IRA was negative and in 43.5% positive.

Conclusions: This preliminary data from the COMPARE ACUTE trial indicates the high portion of negative FFR-measurements in lesions found in non-infarct related arteries and visual estimated stenosis of >50%. This aspect should be paid regard to in the debate on multi-vessel primary PCI in STEMI.

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Combined use of iFR and FFR With High-Dose Intracoronary Adenosine for the Classification of Intermediate Coronary Lesions

Fernando Rivero-Crespo[1], Javier Cuesta[2], Amparo Benedicto[3],
Teresa Bastante-Valiente[3], Jorge-Andrés Restrepo[4], Guillermo Diego-Nieto[3],
Fernando Alfonso[4]
[1]Hospital Universitario de la Princesa, Madrid, Spain, [2]Hospital Universitario de la
Princesa, Madrid, MS, [3]Hospital Universitario de la Princesa, Madrid, España,
[4]Hospital Universitario de la Princesa, Madrid, Spain

Background: iFR is a new, non-hyperemic, physiologic pressure index proposed for the assessment of intermediate coronary lesions. Recently, it has been suggested the value of a combined approach using iFR and FFR with intravenous adenosine (FFRiv) for the classification of coronary lesions located within the "grey zone" of physiologic severity. The intracoronary use of adenosine at high dose (FFRic) in combination with iFR might facilitate the widespread clinical use of these physiologic studies, as FFRic remains a simpler and less invasive technique that is associated with less side effects. The objective of this study was to determine the diagnostic accuracy of a systematic combined use of iFR and FFRic versus the classical FFRiv -used as the gold standard- for the assessment of intermediate coronary lesions.
Methods: 38 consecutive patients with 44 intermediate coronary lesions (30-80% by QCA) were included in the study during a 6 month-period. iFR, FFRic (600 μg ic adenosine) and FFRiv (200 μg/kg/min) were systematically determined in all patients. The diagnostic accuracy of the 2 tests were calculated against the reference standard of FFRiv using a cut-off diagnostic threshold set at 0.80. The area under the curve of each test was also analyzed.
Results: 44 lesions were included. The mean age of patients was 66 ± 11, 81% were male and 29% were diabetics. The most frequent indication was stable angina (56%) and the more frequent vessel was left anterior descending coronary artery (47%) and most lesions were located at mid coronary segments (51%). The average angiographic severity was $51\%\pm 9$ and the mean FFRiv was 0.81 ± 0.09. iFR (optimal cut-off value found:0,89)sensitivity (100%) was higher than FFRic (89%). However, the specificity of iFR (70%) was less than that of FFRic (96%). Using a sequential approach (initial determination of iFR and then FFRic for cases positive according to iFR) an AUC of 0.98 (0.92-1) was obtained.
Conclusions: Our findings suggest that iFR as a high sensitivity whereas FFRic has a high specificity, as compared with FFRiv. The sequential combined use of both tests appears to be very simple, provides a very high diagnostic yield.

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Does Coronary Physiology or Anatomy Better Predict the Capacity of Stenting to Increase Flow?

Sukhjinder S. Nijjer[1], Sayan Sen[2], Ricardo Petraco[3], Tim P. van de Hoef[4],
Martijn A. van Lavieren[5], Rasha Al-Lamee[2], Mauro Echavarria-Pinto[6],
Darrel P. Francis[2], Carlo Di Mario[2], Javier Escaned[7], Jan Piek[8], Justin E. Davies[2]
[1]Imperial College London, London, London, [2]Imperial College London, London,
United Kingdom, [3]Imperial College, London, United Kingdom, [4]Academic Medical
Center - University of Amsterdam, Amsterdam, Noord Holland, [5]Academic Medical
Center, Amsterdam, Noord Holland, [6]Hospital Universitario Clinico San Carlos,
Madrid, Spain, [7]Hospital Clinico San Carlos, Madrid, Spain, [8]Academic Medical
Center, Amsterdam, Netherlands

Background: Coronary stenoses are stented to improve coronary flow with the majority selected using angiographic anatomical parameters. We sought to quantify the change in coronary flow velocity after angiographically successful stenting and quantify the predictive capabilities of anatomical parameters to predict flow increase after stenting and compared them to physiological indices of lesion severity.
Methods: 75 stenoses (67 patients, 62 ± 9 years) selected for PCI on the basis of anatomical findings, had hyperemic transtenotic mean coronary flow velocity measurements using a combined Doppler flow and pressure wire, before and after stenting. The relationship between the change in hyperemic flow after stenting and both anatomical parameters (measured by quantitative coronary angiography) and physiological indices (FFR, measured during hyperemia and the instantaneous wave-free ratio (iFR) measured at rest) was assessed.
Results: Before PCI, stenosis diameter was $61\pm14\%$; FFR was 0.68 ± 0.17 and iFR was 0.73 ± 0.23. Hyperemic flow velocity rose significantly after PCI (30 ± 20cm/s to 51 ± 25cm/s, p< 0.001). Anatomical parameters had a weak but significant relationship with the change in hyperemic flow: diameter stenosis (R^2 0.18, p=0.0002) and stenosis area (R^2 0.11, p=0.008). Physiological indices, in contrast, were strongly predictive: iFR R^2 0.51, p< 0.001, FFR R^2 0.42, p< 0.001. For intermediate stenoses (50-70% lesions), physiological parameters retained their stronger predictive value, iFR R^2 0.38, p< 0.001, FFR R^2 0.35, p< 0.001, while the anatomical parameters had little value (diameter stenosis R^2 0.0015 p=0.80; stenosis area R^2 0.07 p=0.16).
Conclusions: Both resting and hyperemric pressure-only physiological indices are better than anatomical parameters in predicting the capacity of stenting to increase