FiGARO trial

FFR versus iFR in assessment of lesion hemodynamic significance using gene polymorphism and lesions morphology assessed by OCT

NCT03033810

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- Charles University Hospital in Prague
- Czech Republic

FiGARO - background

- Both FFR and iFR have IA class recommendation for coronary lesions assessment in the current ESC guidelines
- However, FFR / iFR discrepancy can be found in 12-20% of measurements

Hypotheses

- **I/ Morphology of the atherosclerotic plaques plays a role in coronary flow and therefore it can be related to the FFR/iFR discrepancy**

  - plaque rupture and plaque erosion lead to the turbulent flow in coronary arteries (even more during hyperemia), which may causes a **false positive FFR**
  - plaques were examined by optical coherecne tomography

- **II/ Polymorphism in gene for endothelial synthase (Glu298Asp) and in a promotor of gene for hemoxygenase-1 may cause lower than expected reaction to adenosin**

  - carrieres of risk type of these gene polymorphisms have lower chance for maximal vasodilatation after adenosin administration, which may cause a **false negative FFR**

FiGARO – data sources

- 1953 lesions from 1626 patients
  - ACS - 254 patients (18.03%)
- Czech hospitals:
  - Charles University Hospital in Prague
  - Podlesi Hospital, Trinec
  - University Hospital Ostrava
  - Homolka Hospital Prague
  - Masaryk University Hospital, Brno
  - Municipal Hospital, Ostrava
- International hospitals:
  - Gifu Heart Center, Gifu, Japan
  - Favaloro Hospital Universitario Buenos Aires, Argentina

Journal of the American Heart Association

ORIGINAL RESEARCH

Fractional Flow Reserve Versus Instantaneous Wave-Free Ratio in Assessment of Lesion Hemodynamic Significance and Explanation of their Discrepancies. International, Multicenter and Prospective Trial: The FiGARO Study

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BACKGROUND: The FiGARO (FFR versus iFR in Assessment of Hemodynamic Lesion Significance, and an Explanation of Their

Correlation between FFR and iFR

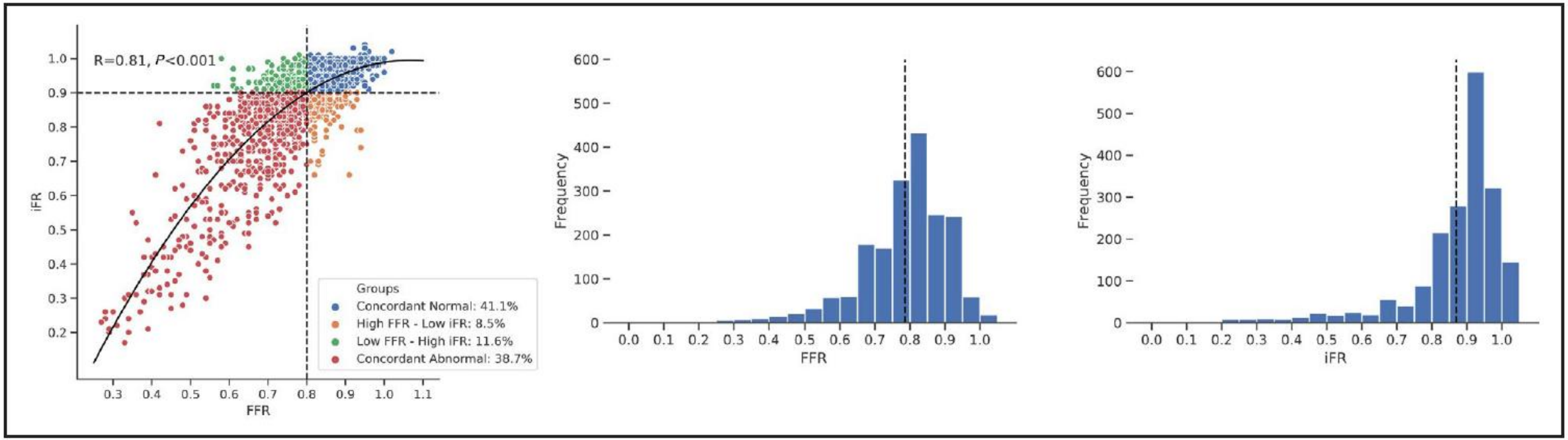

Figure 2. Correlation between FFR and iFR values and histograms for FFR and iFR values.
FFR indicates fractional flow reserve; and iFR, instantaneous wave-free ratio.

FFR and iFR correlation in borderline lesions:
for iFR (0.85-0.95) **R=0.45**, p<0.0001
for FFR (0.75- 0.85) **R=0.33**, p<0.0001

Diskrepant measurements were found in 393 (20.9%) of cases:
FFR positive / iFR negative in 264 lesions (14.1%)
FFR negative / iFR positive in 129 lesions (6.8%)

Plaque morphology and FFR / iFR discrepancies

- During interim analysis of OCT from 40 patients we did not find any morphology differences between lesions with and without FFR / iFR discrepancies, therefore we decided not to continue with this type of analysis

Table 3. Predictors for FFRp/iFRn According to Angiographic Parameters

Parameters included in model	Unstandardized coefficient B	SE	Wald	*P* value for significance
Proximal location	–0.09	0.183	0.23	0.63
Diameter stenosis	0.005	0.008	0.36	0.55
Lesion location in Right coronary artery	0.75	0.195	14.7	0.0001
Tandem lesion	0.153	0.21	0.51	0.48

Model for prediction of FFRp/iFRn type of discrepancy. Nagelkerke R Square 0.029. Hosmer-Lemeshow test: chi-square 9673, *P* value 0.289.
CFR indicates coronary flow reserve; FFR indicates fractional flow reserve; iFR, instantaneous wave-free ratio; n, negative; and p, positive.

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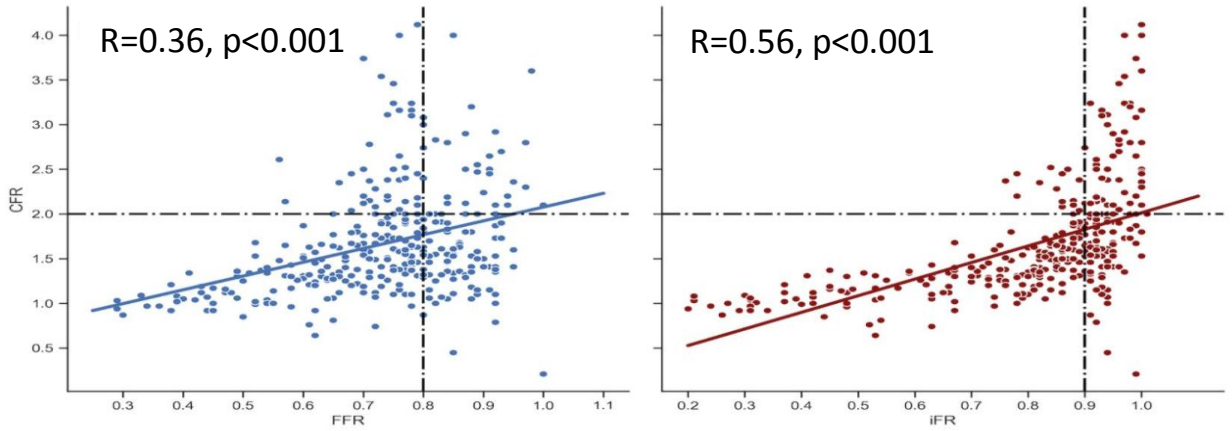
Endothelial dysfunction assessed by digital tonometry and discrepancy between fraction flow reserve and instantaneous wave free ratio

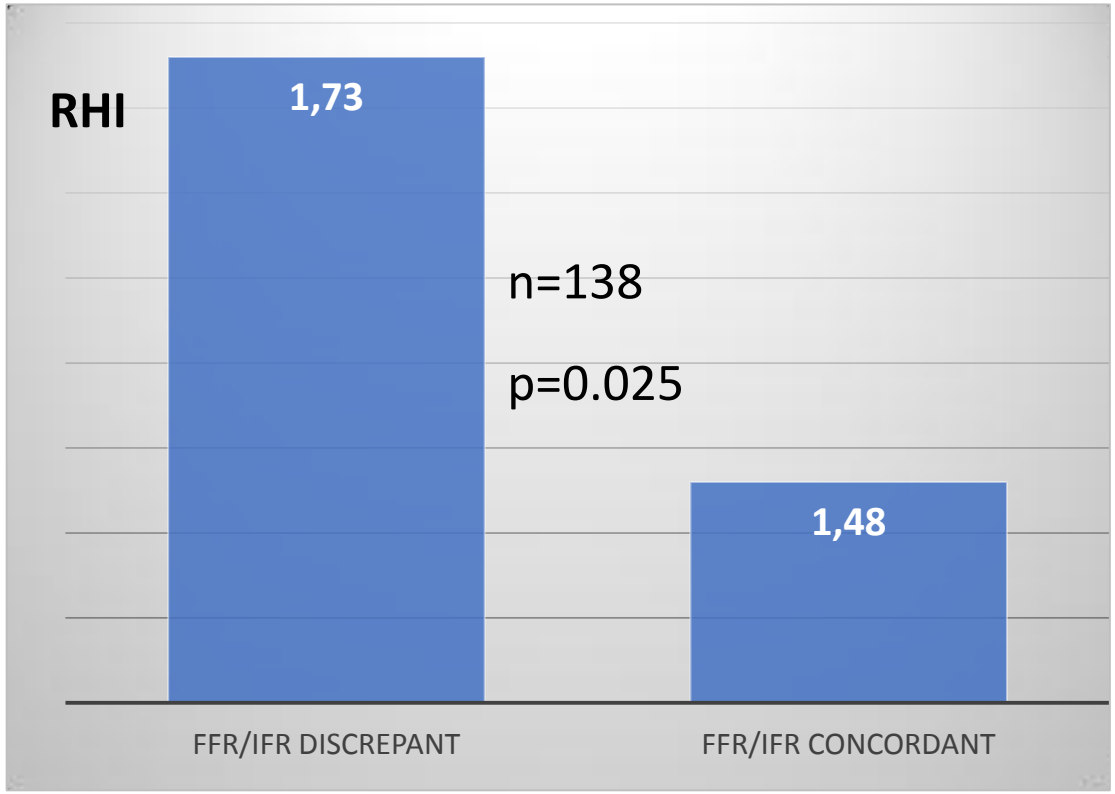
Stepan Jerabek, David Zemanek, Jan Pudil, Kristyna Bayerova, Ales Kral, Karel Kopriva, Yoshiaki Kawase, Hiroyuki Omori, Toru Tanigaki, Zhi Chen, Alexandra Vodzinska, Marian Branny, Hitoshi Matsuo, Martin Mates, Milan Sonka & Tomas Kovarnik

Coronary flow reserve and FFR / iFR discrepancies



Type lézí podle FFR a iFR	CFR1	CFR2	p
1/ FFRp/iFRn vs. 2/ FFRp/iFRp	2.24 ± 0.70	1.39 ± 0.36	<0,0001
1/ FFRp/iFRn vs. 2/ FFRn/iFRn	2.24 ± 0.70	1.8 ± 0.64	<0,0001
1/ FFRn/iFRp vs. 2/ FFRp/iFRp	1.41 ± 0.37	1.39 ± 0.36	0,85
1/ FFRn/iFRp vs. 2/ FFRn/iFRn	1.41 ± 0.37	1.8 ± 0.64	0,011

Endothelial dysfunction and FFR / iFR discrepancies



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Genetic analysis

- 224 patients
- risk types of polymorphism were found in :
  - 112 pacients (51.1%) in gene for ENOS
  - 60 pacients (27.4%) in gene for HO-1
  - 28 pacients (12.8%) in both genes

Table 7. FFR/iFR Discrepancy and Type of Polymorphism in Genes for ENOS and HO-1

	FFR/iFR discrepancy	FFR/iFR agreement	*P* value
$ENOS_r$	37 (55.2%)	75 (49.3%)	0.42
$HO\text{-}1_r$	21 (31.3%)	39 (25.6%)	0.39
$ENOS_r$ and $HO\text{-}1_r$	10 (14.9%)	18 (11.8%)	0.53
$ENOS_p$ and $HO\text{-}1_p$	19 (28.4%)	56 (36.8%)	0.22

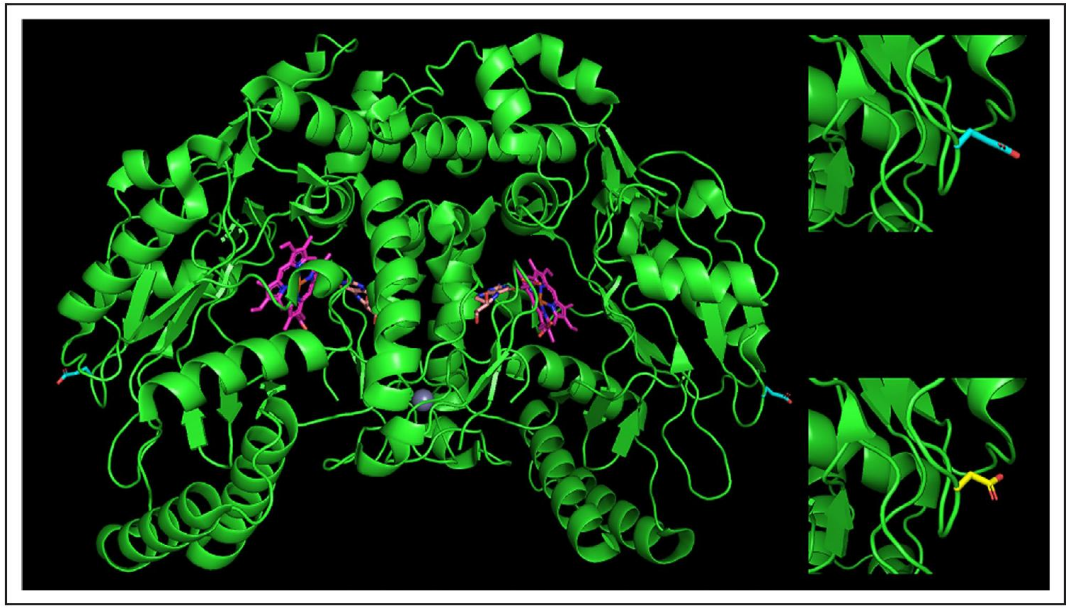

Figure 1. A 3-dimensional image of the ENOS heme domains.

Genetic analysis II

- **FFR negative / iFR positive** type of discrepancy was found more frequently in patients with risk type polymorphism in both genese:
  - *8 patients (24.2%) vs. 2 patients (5.9%), p= 0.03*

Further predictors of FFR / iFR discrepancies

Table 4. Predictors for the FFRp/iFRn Type of Discrepancy

Parameters included in model	Unstandardized coefficient B	SE	Wald	Significance
Sex	0.66	0.22	9.4	0.002
Age	-0.02	0.009	7.1	0.008
Using beta blockers	-0.21	0.17	1.43	0.23
Ejection fraction of left ventricle	0.01	0.008	2.27	0.13

Table 5. Predictors for FFRn/iFRp Type of Discrepancy

Parameters included in model	Unstandardized coefficient B	SE	Wald	Significance
Weight	–0.01	0.008	3.16	0.08
Using diuretics	0.5	0.29	2.9	0.09
Hemoglobin, g/L	–0.01	0.007	3.9	0.05
Smoking	0.67	0.29	5.4	0.02
Chronic kidney disease	0.89	0.37	5.8	0.02

Conclusions

- FFR / iFR discrepancy was found in 21% measurements
- **FFRp/iFRn** type of discrepancy is probably caused by well preserved endothelial functions and it was more frequently found in:
  - in the right coronary artery
  - younger patients
  - males
- **FFRn/iFRp** type of discrepancy can be caused by non-adequate reaction to adenosin administration and it was found more frequently in:
  - carriers of risk type polymorphisms in genes for ENOS and HO-1
  - smokers
  - patients with chronic kidney disease

The marriage of Figaro has been still performed in the same theater in Prague since 1786

… conducted by W.A. Mozart in 1787

FiGARO investigators

- H. Matsuo, S. Jerabek, Y. Kawase, H. Omori, T. Tanigaki, D. Zemanek, A. Kral, J. Pudil, A. Vodzinska, M. Branny, R. Stipal, P. Kala, J. Mrozek, T. Grezl, K. Novobilsky, O. Mendis, K. Kopriva, M. Mates