FRR or Resting Gradients: Rationale and Clinical Data

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

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<th>Affiliation/Financial Relationship</th>
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<td>Consulting Fees/Honoraria</td>
<td>• Abbott Vascular</td>
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<td>• The Medicines Company</td>
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<td>• Volcano Inc.</td>
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Pressure drop *increases* with *stenosis severity*.

Basic Principle of FFR

‘Unmask’ trans-coronary gradients by increase in flow

Pressure drop across stenosis

Coronary flow

Relationship btw. Myocardial Blood Flow and CAD Severity

Minimal Hyperemia in Presence of Stenosis >70%

Myocardial Blood Flow

Coronary Flow Reserve

Relationship of Coronary Flow Reserve and Fractional Flow Reserve

Relationship of Coronary Flow Reserve and Fractional Flow Reserve

N=91

R=0.171; P=0.105

Concordance of Coronary Flow Reserve and Fractional Flow Reserve

Concordance: 51 vessels (56.1%)

Concordance of Coronary Flow Reserve and Fractional Flow Reserve

Discordance of Coronary Flow Reserve and Fractional Flow Reserve

Discordance: 40 vessels (44%)
Discordance of Coronary Flow Reserve and Fractional Flow Reserve

Variability in BP Response to Adenosine

Prevalence of vessels with FFR ≤0.80 and CFR >2 was higher (35.5% vs. 14.5%) in severe hypotensive response group

OR: 3.24
95% CI: 1.17-8.99
P=0.023
Prognostic Value of CFR and SPECT in Intermediate Coronary Lesions

PCI deferred in 182 intermediate lesions based on CFR and SPECT and pt. followed for death/MI/PCI for 1 year

Multivariate analysis revealed CFVR as the only significant predictor for cardiac events

CFVR RR: 3.9 (1.7 to 9.1), p < 0.05
SPECT RR: 0.5 (0.1 to 3.2), p = NS
Association Between Coronary Vascular Dysfunction and Cardiac Mortality

A total of 2783 consecutive patients underwent quantification of CFR by PET and were followed for a median of 1.4 years.
Instant wave-free ratio (iFR)

Detect trans-coronary gradients by using physiologically increased flow during diastole

Mean velocities from ADVISE

Complete cycle flow

Wave-free flow

Increased sensitivity

Graphs showing the relationship between stenosis pressure gradient and coronary flow velocity.
**Definition:**
Instantaneous pressure ratio, across a stenosis during the wave-free period, when resistance is naturally constant and minimised in the cardiac cycle.

\[ \text{iFR} = \text{instantaneous wave-free ratio} \]

iFR closely correlated to FFR in some studies

ADVISE study

Classification Agreement 88%
(+) predictive value 91%
(-) predictive value 85%
Sensitivity 85%
Specificity 91%

RESOLVE Study

- Given conflicting reports, we have formed a collaborative group of independent investigators to perform a large-scale analysis of the diagnostic agreement between iFR and FFR
- Core lab analysis by the Cardiovascular Research Foundation of all published iFR studies as well as consecutive cases from select sites
- Volcano supplied proprietary iFR algorithm to CRF core laboratory

1974 Lesions

1747 Lesions

1691 Lesions

1649 Lesions

1593 Lesions included for analysis

227 Excluded
Insufficient Baseline or Artifact

56 Excluded Not Meeting Inclusion Criteria

42 Excluded Pressure Drift

56 Excluded Other

Correlation iFR vs. FFR

\[ R^2 = 0.66 \]
\[ iFR = 0.21 + 0.85 \text{FFR} \]


- C-Statistic: 0.81
- Sensitivity: 78.9%
- Specificity: 82.4%
- PPV: 85.2%
- NPV: 73.3%
- Accuracy: 80.4%
≥90% Diagnostic Accuracy for iFR vs. FFR

Adenosine Free Zone: 64.9% of Population

Hybrid iFR-FFR Approach

Petraco R et al., EuroIntervention 2013
Adenosine Free Zone


Proportion of lesions not requiring adenosine (%)

Agreement with FFR

iFR Clinical Implementation – SYNTAX II Trial

Patient ‘Signed Off’ by Heart Team for PCI

iFR in all 3 major epicardial vessels*

- iFR < 0.86
- iFR 0.86-0.93
- iFR > 0.93

iFR < 0.86

- Implantation of SYNERGY™ stent(s)
- Optimization by IVUS guidance (modified MUSIC Criteria)

iFR 0.86-0.93

- FFR
- FFR ≤ 0.80
- No stent implantation in lesion
- FFR > 0.80

iFR > 0.93

Optimal medical therapy with a strict control of LDL (≤1.8 mmol)

*FFR with adenosine, iFR/FFR in side branches, all at discretion of the operator
Conclusions

• Despite reasonable statistical correlation with FFR, iFR and Pd/Pa accuracy is only ~80% which is insufficient for clinical decision making

• A hybrid iFR/FFR approach can increase the accuracy to ≥90%, sparing adenosine use in ~60% of the population

• Outcome studies like SYNTAX II will show if this is a clinically feasible approach

• However, given limitations of adenosine in clinical practice, iFR may prove equivalent/superior to FFR – 2 randomized trials ongoing comparing iFR and FFR directly