BMC2 Best Practice Protocol

Best Practice Protocol for the Blue Cross Blue Shield of Michigan Cardiovascular Consortium

## Fractional Flow Reserve (FFR)/ Instantaneous wave-Free Ratio (iwFR) Measurements

Physiologic assessment of coronary artery disease has become one of the cornerstones of decision-making for myocardial revascularization. Multiple indices exist to determine the hemodynamic significance of intermediate coronary artery stenoses (50-90%) in the absence of non-invasive proof of ischemia in the corresponding territory of interest.

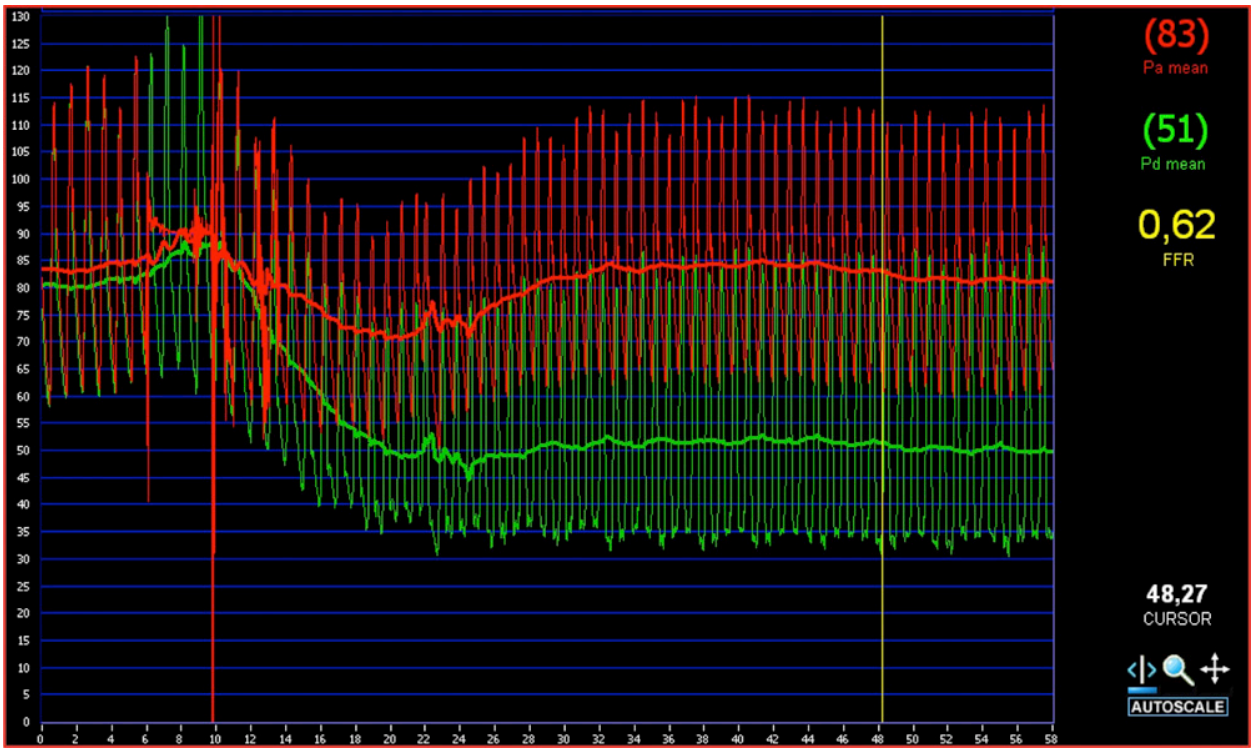
The prognostic impact of FFR/iwFR measurement has been validated in multiple randomized trials and shown that revascularization can be safely deferred if FFR is > 0.80 or iwFR > 0.89. FFR measurements have also been shown to guide treatment in patients with multivessel disease and in patients presenting with STEMI and non-culprit vessels stenosis.

**Recommendations on functional testing and intravascular imaging for lesion assessment**

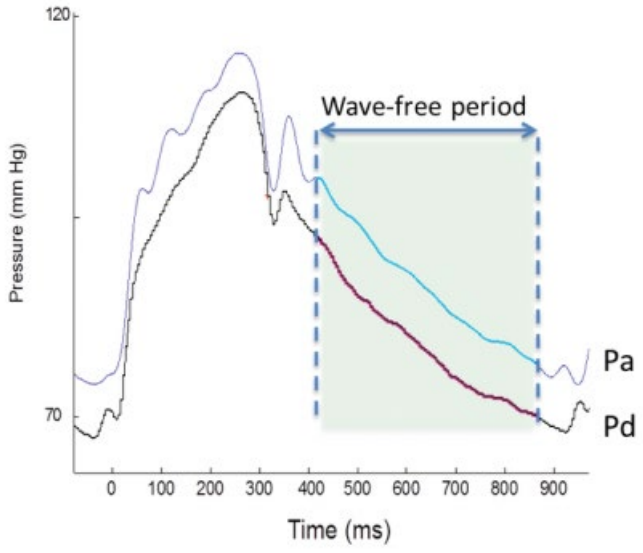
| Recommendations | Class[a] | Level[b] |
|---|---|---|
| When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.[15,17,18,39] | I | A |
| FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI.[29,31] | IIa | B |

**Definition:**

1) FFR is calculated as the ratio of distal coronary pressure (Pd) over proximal aortic pressure (Pa) during maximal hyperemia (see figure below). It is a highly reproducible diagnostic measure as long as attention is given to careful procedural steps prior to any measurements.




2) iwFR is measured as the mean ratio of instantaneous phasic distal coronary pressure to aortic pressure during a diastolic window free of newly generated wave activity called the “wave-free period” (see figure below).



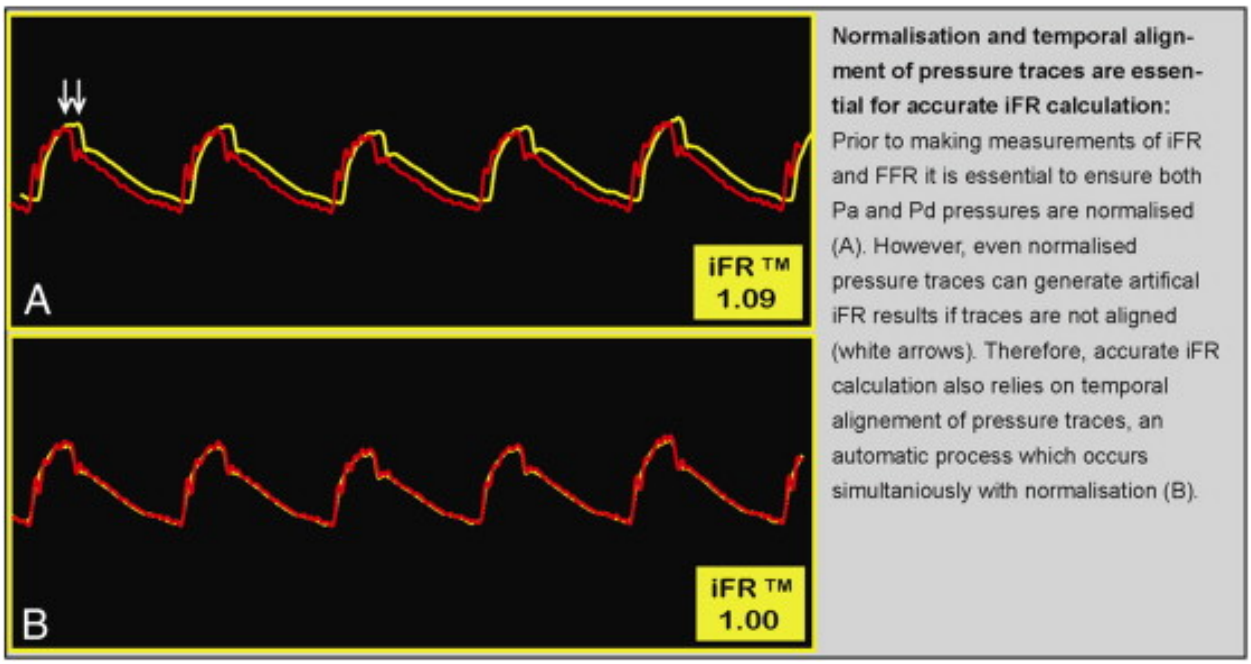
Wave Free Period[1]

**Other resting indices (whole cycle/diastolic):**
While many non-hyperemic pressure ratios indices (NHPR) are commercially available, the BPP Task Force elected to focus on the methodology with the most robust supporting data for its use.

**Patient Preparation:**
Patients should abstain from caffeine for 24 hours prior to FFR evaluation. Administration of adenosine can cause flushing or chest pain, so patients need to be warned of possible side effects. Proper anticoagulation with UFH (60 u/kg) should be given and ensure that ACT is > 200.

**Zeroing of FFR/iwFR wire:**
As soon as the wire is electronically connected to the console, the “zero reference” is taken automatically or manually.

**Normalization/Equalization:**
Catheters should be flushed with normal saline to get rid of contrast. You should be able to see a dicrotic notch in the aortic tracing. A wire introducer may be utilized to facilitate advancing the wire in the coronary past the stenosis but should be removed and the Tuohy or Copilot tightened for normalization (see figure below). While catheter selection (<6Fr size, diagnostic catheters as opposed to guiding catheters) are left to the discretion of the operator, we believe that best practice for physiologic assessment warrant use of a 6Fr guiding catheter (without sideholes) to optimize reproducibility of findings.




**Calibration:**
The wire should be advanced until the end of the radiopaque tip of the wire is just outside the guiding catheter (either in the ascending aorta or in the proximal unobstructed vessel) and then calibrate the distal pressure (Pd) to the proximal pressure (Pa), ensuring that the catheter waveform is not ventricularized or dampened as this will lead to inaccurate measurements.

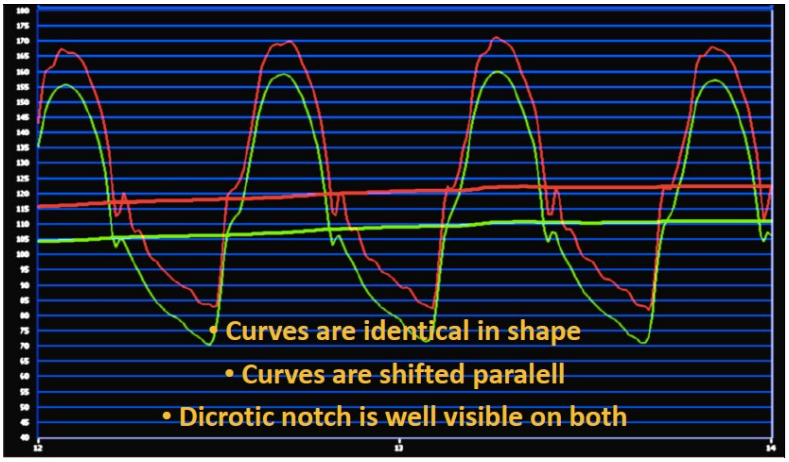
**Measurement of Resting Indices:**
Full vasodilation of the epicardial artery should be routinely done by intracoronary administration of nitrate (300 mcg) as soon as selective guide engagement is established and ideally before introducing the wire. One should wait at least 30 seconds after administering NTG to check resting indices. Pd/Pa and iFR Measurements should be repeated at least twice. The wire should be advanced at least 3 cm past the stenosis for accurate measurements. Contrast injections can cause transient hyperemia and it is important to wait at least 30 seconds after a contrast injection to check the resting indices.

**Measurement of Hyperemic Indices:**
Intracoronary adenosine is given (200mcg for the left coronary arteries and 100mcg for the right coronary artery). Intravenous adenosine can also be used and infused at 0.140 mg/kg/min over 4 minutes through a peripheral venous line. FFR values < 0.80 or iwFR

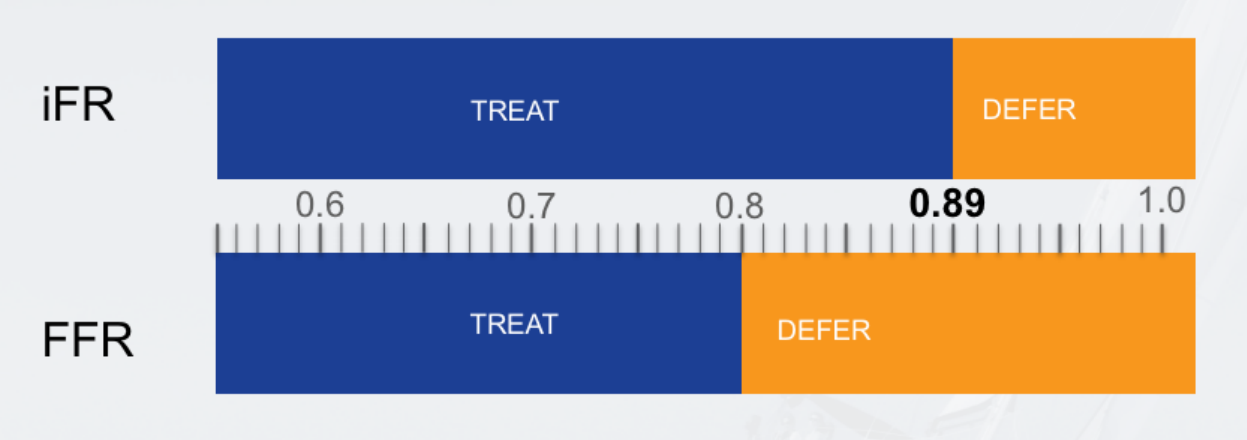
values < 0.89 are consistent with ischemia in the artery being evaluated. Values are to be measured at the *nadir* of the Pd/Pa tracings.

**Pullback Measurement:**
This is best done with continuous intravenous administration of adenosine while performing a slow pullback of the wire which is the best means to assess the distribution of the abnormal epicardial resistance which is extremely important in the case of multiple sequential lesions.

**Checking for Signal Drift:**
Pressor sensors have a tendency to drift that will offset readings from the original calibrated state and underestimate the physiologic measurement. During measurements, always compare Pd to Pa waveform (see figure below). The wire should be pulled back at the end of measurements and positioned 1-2 mm distal to the tip of the guiding catheter and Pd/Pa measured again. The 2 should be identical, if not suspect a drift.



**Treatment Algorithms:**




**Pearls and Pitfalls:**

1. For hyperemic measurements, theophylline should be interrupted for 12 hours prior to study. Overall influence of caffeine appears to be minimal especially when consumed in small amount and > 1 hour prior to measurement.
2. Guiding catheters should not obstruct ostium or display a “ventricularized” signal. Guide should be completely disengaged in case of ostial stenosis.
3. When performing equalization of pressure, introducer must be completely removed and hemostatic valve completely closed. A second wire can create artifact and should be avoided.
4. FFR wire can interact with vessel wall specially in small vessel caliber, so placement of the sensor in segments with substantial tortuosity should be avoided.
5. Viscous contrast agent can affect resting gradient Pd/Pa
6. In case of left main (LM) disease, FFR/iFR can be used as long as there is no significant lesion in the proximal vessel where the sensor is advanced (LAD or LCx).
7. In case of serial stenosis, the distal measured value represents the combined effect of all the lesions. Pullback should be helpful to guide intervening first on the most significant lesion with the higher pressure step up.
8. When measuring FFR/iFR in a vessel supplying collateral blood flow, careful attention and consideration should be given to evaluate whether the collateral blood flow is supplying a territory that is viable or not, and the amount of myocardium supplied when interpreting FFR/iFR value.
9. There are limited data on FFR measurements in stenotic bypass vessels.

10. FFR is helpful in guiding revascularization decision in non-culprit vessels in STEMI and NSTEMI patients.
11. Side branch lesions can be assessed for hemodynamic significance using FFR. If FFR<0.8, it is associated with higher event rate

**Disclaimer:**
BMC2 Best Practice Protocols are based on consortium-wide consensus at the time of publication. Protocols will be updated regularly, and should not be considered formal guidance, and do not replace the professional opinion of the treating physician.

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