JAMA Insights | CLINICAL UPDATE

Fractional Flow Reserve Measurement for the Physiological Assessment of Coronary Artery Stenosis Severity

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Invasive coronary angiography is an imperfect criterion standard for assessment of coronary artery disease severity. Decisions about treatment strategy, including medical therapy or percutaneous or surgical revascularization, are made based on angiographic results. However, coronary angiograms can overestimate or underestimate lesion severity, especially when only moderate stenosis (40%-80%) is present. Several factors other than the percentage of luminal narrowing may determine if a stenosis actually causes ischemia. The length of the stenosis, serial lesions, the amount and viability of the myocardium the vessel serves, and presence of collateral flow are some of the key determinants of why a 70% stenosis, for example, may cause marked ischemia in one patient but not in another. Adding to the complexity of angiographic interpretation, experienced angiographers may disagree about the severity of intermediate lesions.

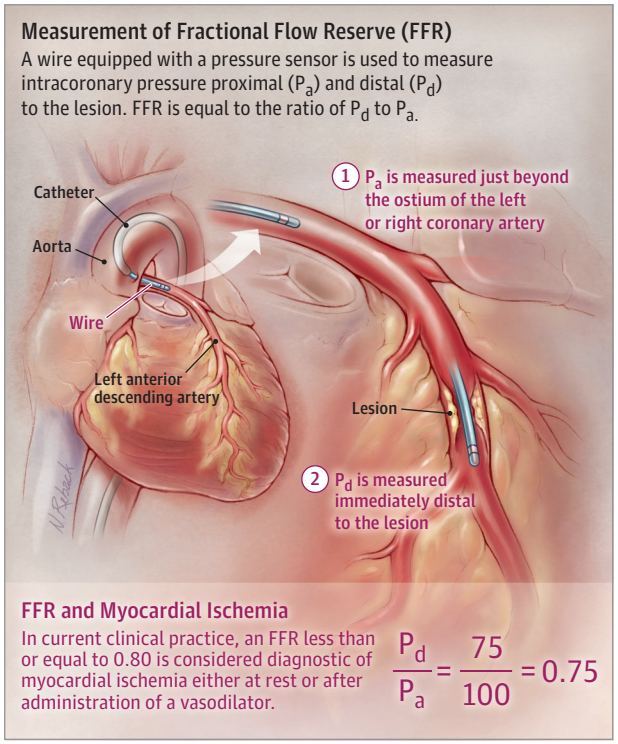
Addition of fractional flow reserve (FFR) measurements to angiography helps physicians to understand better the clinical significance of angiographically ambiguous lesions. FFR is measured by passing a wire with a pressure sensor into the coronary artery via a catheter and determining the ratio of the intracoronary pressure distal to a lesion to the aortic pressure proximal to the lesion (**Figure**).[1]

When there is no lesion, the FFR is 1.0. An FFR of less than or equal to 0.75 to 0.80 correlates with ischemia. Revascularization of lesions below this range results in better outcomes than does medical therapy. FFR is measured at a steady state and can be followed with administration of a vasodilator such as adenosine. The resultant hyperemic flow serves as an invasive pharmacological stress test. In current clinical practice, a steady-state FFR of less than or equal to 0.80 is considered diagnostic for myocardial ischemia. Myocardial ischemia is also diagnosed if the initial FFR is greater than 0.80 but falls below that value following vasodilation.

The Fractional Flow Reserve vs Angiography for Multivessel Evaluation (FAME) 2 trial randomized 888 patients with stable coronary artery disease in whom the FFR was less than or equal to 0.80 to receive either medical therapy or percutaneous coronary intervention (PCI).[2] Patients randomized to the PCI group had fewer ischemic events, largely driven by a reduction in the need for urgent revascularization procedures. The validity of this end point has been criticized because of some subjectivity in determining who needs urgent revascularization. The counterargument is that most of the urgent revascularization procedures were performed after obtaining objective measures of ischemia, such as electrocardiographic changes or the patient having a documented myocardial infarction.

Recently, 5-year outcomes from FAME 2 revealed that the primary composite end point of death, myocardial infarction, or urgent revascularization was significantly reduced with PCI compared with medical therapy (13.9% vs 27.0%; hazard ratio, 0.46; $P < .001$) for patients who had an FFR less than or equal to 0.80.[3] There was also better angina relief with PCI. There was no significant difference in mortality rates between the 2 strategies, although there were fewer myocardial infarctions in the PCI group than the medical therapy group (hazard ratio, 0.66; 95% CI, 0.43-1.00). Approximately half of the patients randomized to receive medical therapy eventually required PCI. Consequently, FAME 2 underestimated the benefits of PCI in patients with an FFR of less than or equal to 0.80.

Figure. Physiological Assessment of Coronary Artery Lesion Severity Using Fractional Flow Reserve



A value of 1.0 indicates normal flow. The corresponding instantaneous wave-free ratio (iFR) cutoff value for ischemia is less than or equal to 0.89.

Limitations of FFR include the potential need for vasodilator administration that may have adverse effects such as transient dyspnea or bradycardia.[1] FFR requires more time than angiography to perform, and it is costlier, especially if several arteries must be assessed when multivessel disease is present. The coronary artery may be injured requiring immediate stenting in approximately 0.5% of the patients. Extreme vessel tortuousity and other anatomical factors may increase this risk. Serial lesions within an artery create complex interdependent flow dynamics, making it difficult to assess one lesion's physiological severity.[1] For these reasons, improvements in the technical aspects of the procedure and the evolution of related procedures, such as the instantaneous wave-free ratio (iFR), simplify invasive physiological measurements of flow.[4] Use of iFR does not require a vasodilator, allowing quicker measurements. With iFR, the

cutoff value is less than or equal to 0.89. Potentially, developments such as iFR may lower the barrier to performing physiological measurements, which still occur only in the minority of PCI cases.

Trial data show lower use of stents when FFR is measured since it may avoid placing stents across lesions that are worrisome in appearance but have adequate blood flow. Thus, physiological assessment of moderate stenoses could help reduce the costs of management of coronary artery disease while enhancing the efficacy of PCI in the patients who end up receiving it.[5] In certain situations, use of FFR or iFR would direct patients toward PCI when medical therapy would have otherwise been used, in others to medical therapy when PCI would have been used, and yet in other cases influence the choice of PCI vs coronary artery bypass grafting. In actual practice, widespread use of FFR and iFR would likely lead to a net decrease in the number of PCI cases performed for stable angina.

Ongoing trials are evaluating other related indices of physiology and flow. The role in determining which vessels to bypass during coronary artery bypass grafting is being examined.[6] The ability to guide interventional cardiologists in treating multivessel disease in the context of ST-elevation myocardial infarction is also being evaluated.[7] Noninvasive FFR coupled with computed tomography may provide information about both anatomy and physiology. Thus, the future is bright for physiological assessment of the hemodynamic significance of angiographic coronary artery stenoses.

However, even once it is determined with FFR or iFR that a lesion is causing ischemia, a further challenge is that not all ischemia actually results in angina. Additionally, even with a normal FFR, there may still be angina due to coronary artery disease because of microvascular disease (although there are modalities to sort that out, such as noninvasive positron emission tomography or invasive coronary flow reserve). Thus, use of invasive physiological assessment does not diminish the importance of proper clinical history or noninvasive imaging, though FFR or iFR is very useful as an adjunct to determine objectively if intermediate severity coronary stenoses are indeed causing ischemia.

ARTICLE INFORMATION

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Published Online: September 13, 2018. doi:10.1001/jama.2018.10683

Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Bhatt reports advisory board participation with Cardax, Elsevier Practice Update Cardiology, Medscape Cardiology, and Regado Biosciences; board of directors: Boston VA Research Institute, Society of Cardiovascular Patient Care, TobeSoft, and the American Heart Association quality oversight committee (chair); data monitoring committee: Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute [for the PORTICO trial]; funded by St Jude Medical [now Abbott]), Cleveland Clinic, Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine, and the Population Health Research Institute; honoraria: American College of Cardiology (senior associate editor, Clinical Trials and News, ACC.org; vice-chair, ACC accreditation committee), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute [RE-DUAL PCI clinical trial steering committee]; funded by Boehringer Ingelheim), Belvoir Publications (editor in chief, Harvard Heart Letter), Duke Clinical Research Institute (clinical trial steering committees), HMP Global (editor in chief, *Journal of Invasive Cardiology*), *Journal of the American College of Cardiology* (guest editor; associate editor), Population Health Research Institute (COMPASS clinical trial steering committee [funded by Bayer]), Slack Publications (chief medical editor, *Cardiology Today's Intervention*), Society of Cardiovascular Patient Care (secretary/treasurer), and WebMD (CME steering committees); other: *Clinical Cardiology* (deputy editor), NCDR-ACTION registry steering committee (chair), and VA CART research and publications committee (chair); research funding: Abbott, Amarin, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Chiesi, Eisai, Ethicon, Forest Laboratories, Idorsia, Ironwood, Ischemix, Lilly, Medtronic, PhaseBio, Pfizer, Regeneron, Roche, Sanofi Aventis, Synaptic, and The Medicines Company; royalties: Elsevier (editor, *Cardiovascular Intervention: A Companion to Braunwald's Heart Disease*); site coinvestigator: Biotronik, Boston Scientific, St Jude Medical (now Abbott), and Svelte; trustee: American College of Cardiology; and unfunded research: FlowCo, Merck, Novo Nordisk, PLx Pharma, and Takeda.

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