What Part of the FFR Link Don’t We Understand?

John McB. Hodgson, MD

Physiologists and physicians have long been interested in blood flow and pressure (i.e., hemodynamics). The importance of the circulatory system in regulating health and disease has been appreciated since the days of blood-letting and leaches. In 1738, Daniel Bernoulli (1) elegantly described the impact of narrowings on pressure and flow in his book *Hydrodynamica*. The principles he described then are still accurate today and underpin our current physiologic measurements. In the mid-19th century, Volkmann (2) was recording arterial pressure waveforms in animals. The importance of translesional gradients was appreciated by Andreas Grünzig (3) from the first percutaneous coronary intervention (PCI). Even using crude measurement techniques, it was possible to show patient benefit when gradients were low post PCI (4). And, in the early 1990s, Nico Pijls et al. (5) validated a lesion specific, simple to use measure to determine the physiologic significance of individual coronary lesions: fractional flow reserve (FFR).

In this issue of the *Journal*, Johnson et al. (6) (with authors from more than 30 institutions) have provided an elegant analysis of FFR data collected over the past 20 years. Using meta-analysis techniques, they have shown a continuous relationship between measured FFR and patient outcome. Although the statistics may be a bit daunting for the average clinician (myself included), the message is quite clear: When FFR values are low, patients benefit from revascularization and when FFR values are high, we can do harm by proceeding with revascularization. Reassuringly, the optimal “cut-point” for determining revascularization strategy using this statistical analysis remains in the 0.75 to 0.80 range. In the age of medical cost containment, a technique that is both less costly and more effective is a rarity. FFR is one such technique (7–10). The current meta-analysis determined that an FFR-guided revascularization strategy (as opposed to an angiographically guided strategy) was associated with a 50% reduction in PCI, while resulting in 10% better angina relief with 20% fewer adverse events. Finally, the results were consistent in 3 important subgroups: left main lesions, diabetic patients, and acute coronary syndrome patients.

At least 3 prior studies have demonstrated that an FFR-guided approach offers patient benefit. The DEFER trial was performed in the early 2000s. Deferring intervention when FFR was not abnormal led to better outcomes than performing PCI (11). In 2005, Legalley et al. (12) showed that compliance with FFR-indicated therapy resulted in improved outcomes. In 2009, The FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) trial results were published and widely acknowledged by the interventional community (13). This randomized trial demonstrated significantly better outcomes when PCI was guided by FFR. Unfortunately, these trials failed to alter the clinical practice of most cardiologists. Figure 1 shows the rate of FFR use during catheterization procedures in U.S. Medicare beneficiaries. Although there was an uptick in FFR use in 2009 following publication of the FAME trial data, as of 2012 the percent of diagnostic catheterizations having FFR performed remained a paltry 4%.
For more than 10 years, as data have been published, the importance of routinely performing FFR has been emphasized in review articles and editorials (14–17). FFR guidance has been shown to be of value in intermediate lesions (5,18), side branches (19,20), left main lesions (21,22), potential bypass graft insertion sites (23,24), and in-stent restenosis lesions (25) to name a few unique applications. An FFR-based interventional strategy has been shown to improve patient outcomes in balloon angioplasty (26), in bare-metal stent PCI (27), in drug-eluting stent PCI (28,29), and in guiding surgical revascularization (23,24,30). The pressure sensor wires are easy to use, the procedure is simple and reproducible, and the FFR strategy is highly cost-effective. Scientific statements specifically devoted to physiologic measures in the catheterization laboratory have been written (31). The multisociety PCI guidelines give FFR a Class IIa indication (32) and the appropriate use criteria for both diagnostic catheterization and revascularization include FFR for any intermediate lesion not already having corresponding non-invasive evidence of stress induced ischemia (33,34). So, one is left wondering what part of the FFR link don’t interventional cardiology understand? The data are clear; the cardiology community should not tolerate continuing to ignore it.

**FIGURE 1** FFR Utilization Trend From 2005 to 2012 in the United States

Percent of diagnostic catheterizations (Diag Cath) (red line) and percutaneous coronary interventional (PCI) (slate line) procedures that also had fractional flow reserve (FFR) performed at the same setting. Data are abstracted from public records detailing procedures performed in U.S. Medicare beneficiaries.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. John McB. Hodgson, Case Western Reserve School of Medicine, MetroHealth Medical Center, 2500 MetroHealth Drive, Cleveland, Ohio 44109. E-mail: jhodgson@metrohealth.org.

REFERENCES


KEY WORDS appropriate use, fractional flow reserve, percutaneous coronary intervention