Do the Angiographically-Derived FFR Systems Have a Class Effect?

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After a decade of validation and clinical studies, adoption is increasing, particularly after the recent completion of several large randomized clinical trials.[4,5]

Cath labs across the country are now using angiographically-based physiology systems to derive fractional flow reserve (FFR) without need for a wire or adenosine. Given the low use and perceived challenges to wire-based FFR, these systems are a welcome reality. Angiographically-derived physiology (ADP) is proposed to reduce procedure time, radiation, and cost, while improving procedure safety (recall there is no need for an intracoronary guidewire or adenosine) and maintaining strong diagnostic performance. After attending discussions of the various systems at the recent Society for Cardiovascular Angiography and Interventions meeting in Montreal, I thought this would be a good time to address a question that's frequently asked: Are these systems all the same?

Before addressing the question, let's look at what angiographically-derived physiology (ADP) provides.

A 72-year-old man with chest discomfort and an equivocal exercise tolerance test comes to the cath lab. The left anterior descending (LAD) coronary artery has an intermediate 50-70% narrowing (Figure 1). A pressure wire FFR was 0.88, a non-ischemic value. For our own comparison, we also performed an online FFRangio (CathWorks, now Medtronic), which demonstrated an angiographically-derived FFR of 0.89. After using the FFRangio system for several years, we have good confidence that it can provide an accurate FFR in most circumstances. Questions about accuracy of ADP for complex anatomy (left main, bifurcations, grafts) are still under investigation.

The Medtronic system is one of several commercially available ADP systems.[1-3] After a decade of validation and clinical studies, adoption is increasing, particularly after the recent completion of several large randomized clinical trials.[4,5] Each system generates an angiography-derived FFR value designed to approximate invasive wire-based FFR. The systems are distinguished by proprietary algorithms, different coronary and microvascular resistance assumptions, workflow (i.e., number of angiographic views needed), and operator interactions (number of screen clicks) to get to the FFR answer. Faria et al[3] examined the differences among the systems such as the need for arterial pressure input, impact of coronary microvascular disease, contribution of side branches, and quality and quantity of current clinical data (Figure 2). At this point, any differences among results from different ADP systems have not been fully quantified.

How is Angiographically-Derived Physiology (ADP) Generated?

Since all angio FFR systems produce a similar result, given the potential limitations and differences, are they comparable enough to consider them as having a class effect? Before we can answer the question fully, it is important to understand how ADP is produced.

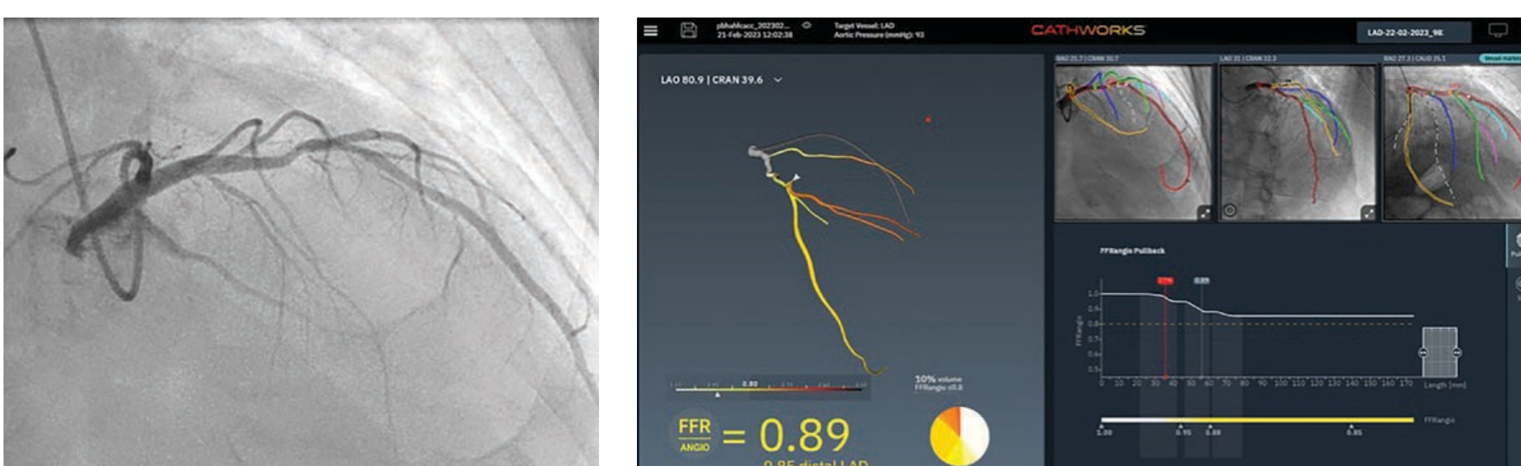

Figure 1. A 72-year-old man who has coronary artery disease risk factors, chest discomfort and equivocal exercise tolerance test shows the angiogram on the far left with an intermediately severe left anterior descending (LAD) lesion. Pressure wire-based fractional flow reserve (FFR) was 0.88. The angiograms were submitted to the online FFRangio system (Medtronic) which demonstrated the color-coded FFR map in the middle, a resulting FFR of 0.89 in the LAD. The far-right panel shows the longitudinal vessel map of the FFR.

Figure 2. Comparison of major angiography-derived fractional flow reserve (FFR) systems. The table summarizes selected workflow requirements and functional features of QFR, CAAS vFFR, caFFR, FFRangio, and µQFR, including the number of angiographic projections required, need for aortic pressure input, incorporation of microcirculatory assessment, accounting for side branches, and relative amount of published supporting data. Color coding indicates the relative strength of each feature: green = favorable, yellow = intermediate, and red = unfavorable. Abbreviations: CAAS vFFR, vessel fractional flow reserve; caFFR, computational pressure-flow dynamics-derived FFR; FFRangio, angiography-derived FFR; QFR, quantitative flow ratio; µQFR, Murray law-based quantitative flow ratio.

Adapted with permission from Faria D, Hennessey B, Shabbir A, et al. Functional coronary angiography for the assessment of the epicardial vessels and the microcirculation. EuroIntervention. 2023 Jun 19; 19(3): 203-221. doi:10.4244/EIJ-D-22-00969.

The systems are distinguished by proprietary algorithms, different coronary and microvascular resistance assumptions, workflow (i.e., number of angiographic views needed), and operator interactions (number of screen clicks) to get to the fractional flow reserve (FFR) answer.

Let's review the steps needed to generate a functional angiographic image (Figure 3).

Step 1. A standard coronary angiography is performed and analyzed, creating a three-dimensional anatomic model.

Step 2. Using the system's physiologic model, the mathematical formulas (Navier-Stokes equations, resistance equations, and some other simplified flow calculations) are applied using predetermined boundary conditions (either assumed or measured) of pressure and flow.

Step 3. The computer then solves the equations for flow (at rest and during an assumed hyperemia state) and computes the FFR along the vessel.

Step 4. Functional indices (FFRangio, quantitative flow ratio [QFR], vessel FFR [vFFR], etc.), are then displayed on the monitor.

It should be noted that significant and operationally meaningful differences in cath lab workflow predominantly involve image-acquisition requirements (time, training and angiographic quality).

Validation and Clinical Data

The validation studies show strong correlation and diagnostic accuracy for angio FFR vs wire FFR, typically with the area under the curve (AUC) in the 0.90–0.97 range in early single-system trials. The studies show similar diagnostic performances compared to wire-based FFR, with only modest differences in accuracy and sensitivity (Table 1). An anonymous comparison of various angiography-derived FFR software was reported by Ninomiya et al.[6] The study was a prospective, head-to-head comparison of 5 ADP methods vs pressure-wire FFR/instantaneous wave-free ratio (iFR) and retrospectively reviewed 390 angiograms with each system analyzed by 4 blinded reviewers (Table 2; note FFR-angio was not included in this head-to-head comparison). A core lab provided identical angiographic views and frame selection to each vendor, with blinded, anonymized analysis. Comparing the 5 angiography-derived FFR systems with invasive FFR and 2D QCA (% diameter stenosis), Ninomiya et al found

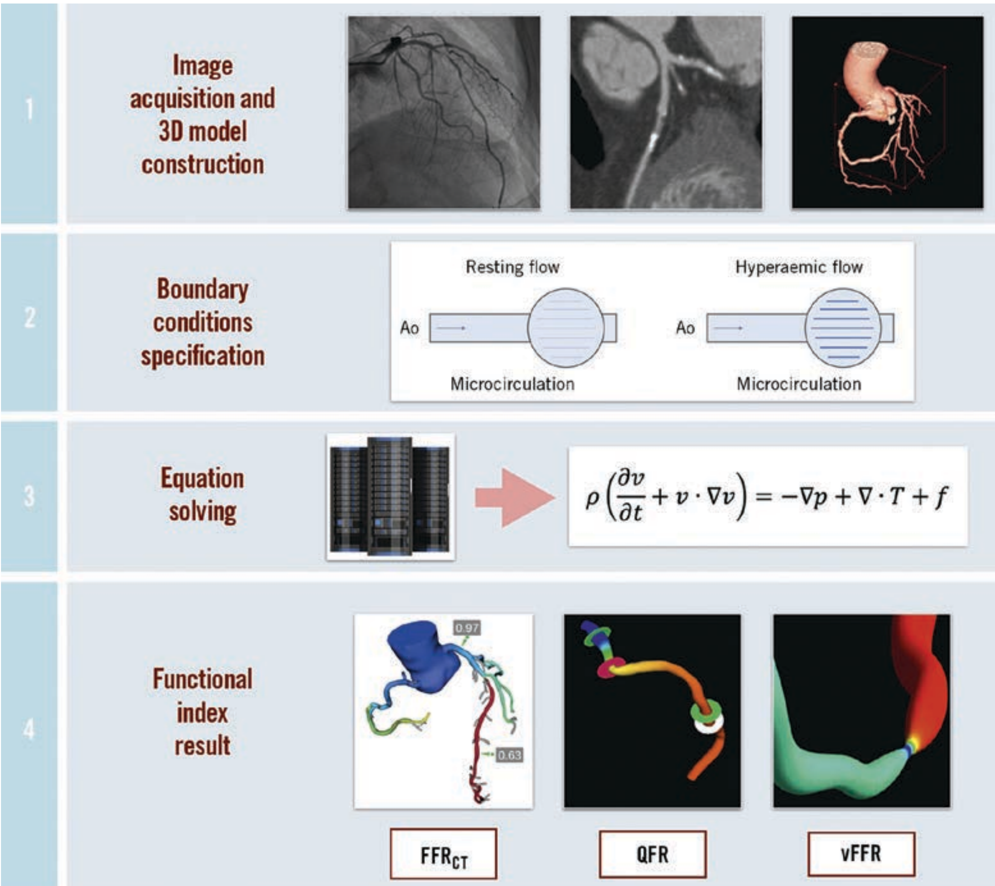

Figure 3. Steps needed to generate a functional angiographic image. *Step 1:* A standard coronary angiography is performed and subsequently analyzed, creating a three-dimensional anatomic model. *Step 2:* A physiologic model is selected. The mathematical formulas are applied whereby boundary conditions of pressure and flow are specified. *Step 3:* Once boundary conditions are specified, the patient-specific data (e.g., assumed resting coronary flow is proportional to subtended myocardial mass, and microvascular resistance is generally inversely correlated to vessel size and reduced during maximal hyperemia), the physical laws of fluid dynamics are applied, solving the Navier-Stokes equations, resistance equations, and/or some other simplified flow calculation. *Step 4:* Finally, the functional index of FFR, QFR, and/or vFFR is computed from the proprietary algorithms and displayed on the monitor.

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the following:

1) High analyzability across systems (92–100% of vessels);
2) For prediction of invasive FFR ≤0.80, area under the curve (AUC) values were 0.75, 0.74, 0.74, 0.73, and 0.73 for the five angiography-derived FFR systems, compared with 0.65 for QCA (Figure 4).
3) Differences between systems were small and not clinically meaningful. All outperformed pure angiographic stenosis assessment and all fell short of prior validation data with their initially published results. Overall, these data suggest there is a class effect when tested under identical conditions, without identifying a single standout technology.

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Across the broader angiographically-derived physiology literature, QFR and FFRangio currently have the most randomized and multicenter data, while some newer platforms such as caFFR and AccuFFR have smaller or more regional datasets.

TABLE 1. Validation studies of ADP vs pressure wire.

Platform	Study	N (lesions)	Accuracy (%)	Sensitivity (%)	Specificity (%)
QFR	FAVOR 11 China	308	93	95	92
QFR	FAVOR 11 Europe-Japan	329	87	87	87
vFFR	FAST-EXTEND	294	88	75	94
vFFR	FAST 11	334	90	81	95
FFRangio	FAST-FFR	301	92	94	91

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TABLE 2. Angiographically-derived fractional flow reserve (FFR) systems as compared by by Ninomiya et al.[4] (Note FFRangio was not included in this head-to-head comparison.)	
1.	Quantitative flow ratio (QFR) is calculated using the QAngio XA 3D 2.1 software package (Medis Medical Imaging System BV)
2.	Vessel FFR (vFFR) computation on the CAAS workstation (Pie Medical Imaging)
3.	Coronary angiography-derived fractional flow reserve (caFFR) analysis, FlashAngio software (Rainmed Ltd)
4.	Murray Law-based quantitative flow ratio (2DμQFR) (Pulse Medical Imaging Technology, Shanghai Co., Ltd.)
5.	Murray Law-based quantitative flow ratio (3D μQFR) (Pulse Medical Imaging Technology, Shanghai Co., Ltd.)

TABLE 3. Randomized controlled trials of angiographically-derived physiology (ADP).

Platform	Trial	Comparator	N	Primary Outcomes	Key Results
QFR	FAVOR III China	Angiography-guided PCI	3825	1-year MACE	QFR reduced MACE (HR=0.55), fewer PCIs
QFR	FAVOR III Europe	Wire-based FFR	2000	1-year MACE	QFR not noninferior, more stents, increased MI
FFRangio	PROVISION	Wire-based FFR	401	Revascularization rate	Met noninferiority, decreased cost and radiation
FFRangio	ALL-RISE	Wire-based FFR	1930	1-year MACE	Demonstrated noninferiority of FFRangio to FFR/NHPR
vFFR	FAST III	Wire-based FFR	2235	1-year MACE	Demonstrated noninferiority of FFRangio to FFR
vFFR	LIPISIASTRATEGY	Wire-based FFR	~2000	1-year MACE	Pending

Adapted from Amponsah DK, Fearon WF. From evidence to practice: the growing role of angiography-derived physiology. J Clin Med. 2025 Nov 20; 14(22): 8219. doi:10.3390/jcm14228219. Licensed under CC BY 4.0. QFR = quantitative flow ratio; vFFR = vessel fractional flow reserve; PCI = percutaneous coronary intervention; MACE= major adverse cardiac events; HR = hazard ratio; FFR = fractional flow reserve; NHPR = non-hyperemic pressure ratio; MI = myocardial infarction.

platforms such as caFFR and AccuFFR have smaller or more regional datasets. QFR has the largest number of studies and several randomized trials, with QFR-guided percutaneous coronary intervention (PCI) showing better outcomes vs angiography-only guidance,[7] but QFR-guided PCI failed a non-inferiority trial vs wire FFR[8].

ADP Workflow

ADP systems differ in the number and angle of required projections, tolerance for angiographic artifacts, such as vessel overlap and foreshortening, need for manual contouring vs automation, time of signal acquisition, and ease of use (fewer clicks). It is likely these differences could translate into a superior platform and better real-world success. Those systems with the lowest additional lab workflow impingement may be preferred, having similar underlying physiologic results and clinical outcomes.

Angiographically-derived physiology (ADP) systems differ in the number and angle of required projections, tolerance for angiographic artifacts, such as vessel overlap and foreshortening, need for manual contouring vs automation, time of signal acquisition, and ease of use (fewer clicks). It is likely these differences could translate into a superior platform and better real-world success.

The Bottom Line

Commercially available ADP platforms are FDA approved with features and limitations that distinguish one vendor system over another.[9] Despite what appears to be a marked step forward toward ease of use with very good diagnostic accuracy, there is reticence among operators to adopt the technology. Barriers to adoption include perceived limited large clinical outcome evidence, lack of reimbursement, training requirements and change in operator angiographic techniques, cath lab workflow integration, and operator–machine interaction requirements (Figure 5). Updated guidelines on the use of ADP will likely follow as more clinical studies become available.

To the main question, are these systems similar enough to have a class effect? In our view, the answer is 'yes' for determination of an accurate FFR value and 'no' regarding the

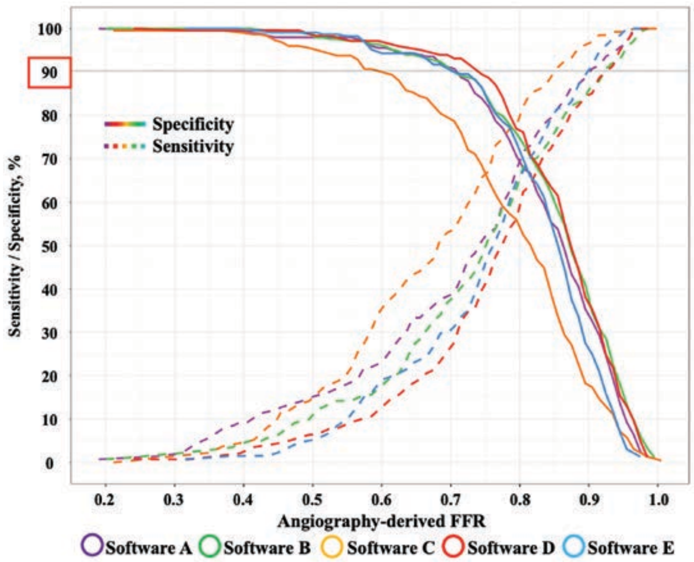

Figure 4. Sensitivity and specificity curves for five angiography-derived FFR systems in predicting invasive FFR ≤0.80, with corresponding area under the curve (AUC) values. (Note: FFRangio was not included in this study). *Reprinted with permission from Ninomiya K, Serruys PW, Kotoku N, et al. Anonymous comparison of various angiography-derived fractional flow reserve software with pressure-derived physiological assessment. JACC Cardiovasc Interv. 2023 Jul 24; 16(14): 1778-1790. doi:10.1016/j.jcin.2023.04.026.*

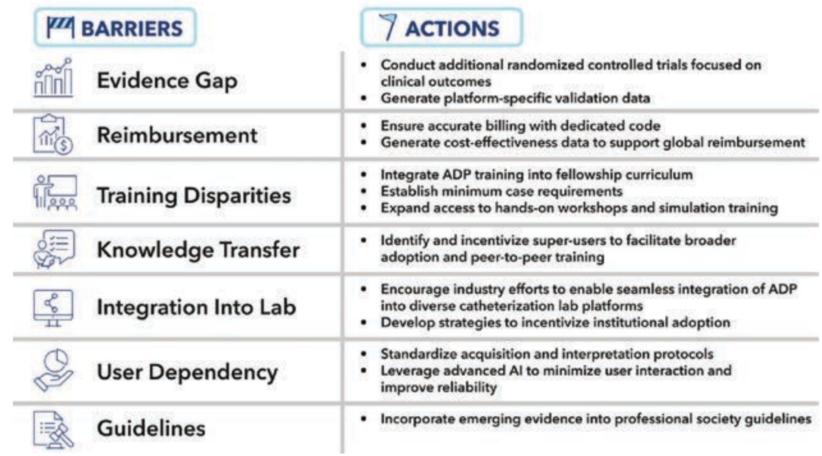

Figure 5. Barriers to adoption of angiographically-derived physiology (ADP) and potential solutions.

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available clinical outcome studies and cath lab workflow. The answer will become clearer as the industry and interventionists use these tools to discover new applications for better results for our patients. ■

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