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Noninvasive FFR Measures Match Wire-Based Assessment: ALL RISE and FAST III

While the noninvasive methods used different technologies to calculate flow, both were noninferior to the gold standard.

by L.A. McKeown MARCH 29, 2026

NEW ORLEANS, LA—Treatment decisions for intermediate coronary lesions based on noninvasive fractional flow reserve (FFR) measurements yield similar clinical outcomes as conventional wire-based physiology assessments 1 year after revascularization, according to two studies presented here at the American College of Cardiology 2026 Scientific Session.

In ALL-RISE, the composite of death, MI, or unplanned, clinically indicated coronary revascularization was 6.9% in the group with procedures guided by angiography-derived FFR (FFRangio; CathWorks) and 7.1% with conventional pressure-wire-based assessment (noninferiority $P < 0.001$).

Similarly, in FAST-III, the composite of death from any cause, any MI, or any revascularization was 7.5% at 1 year with a different automated

system (vFFR; Pie Medical Imaging) and 7.5% in the pressure-wire group (noninferiority $P = 0.004$).

"With the data we have thus far, I think we [have] made a huge step in the direction in which angio-based physiology can replace wires in a large number of patients," FAST-III lead investigator Joost Daemen, MD, PhD (Erasmus University Medical Center in Rotterdam, the Netherlands), told TCTMD in a media briefing.

Despite recommendations in both the European and US guidelines to use FFR for guiding revascularization decisions related to angiographically intermediate stenoses, such testing is used in less than 20% of cases, the ALL-RISE investigators note.

The technologies used in ALL-RISE and FAST III to help operators make a physiological assessment without invasively placing a pressure wire are among several under investigation. The CathWorks FFRangio technology involves calculating FFR based on the coronary angiogram using computer software and artificial intelligence (AI). With vFFR from Pie Medical, FFR is calculated using angiographic images and three-dimensional quantitative coronary angiography.

Both Kirtane and Daemen said while angiography-derived guidance is headed toward becoming an integrated part of workflow in cath labs, caution should be used in suggesting any type of class effect among these varied systems.

"Clearly with both these studies you're seeing the ability to potentially supplant the wire and that should increase physiologic adoption as a whole, and then where these individual technologies lie would be determined by ease of use, feasibility, [etc]," Kirtane told TCTMD.

"We've seen the results of predicate trials being either very positive or perhaps somewhat less positive, if not negative," Daemon said. He noted that given how the fast iterations are occurring in these technologies, "I think they would need proper prospective randomized trials to assess their safety and efficacy."

Both ALL-RISE and FAST III were simultaneously published in the *New England Journal of Medicine*.

William Fearon, MD (Stanford University, CA), the lead author of ALL-RISE, noted the similarities despite the use of different technologies to derive the FFR.

"When I look at FAST-III in comparison to ALL-RISE, I'm struck by how concordant a lot of the results are—the age of the patients, their risk factors, their presentation, the percent of lesions requiring PCI, the slightly higher PCI rate in the angio-derived physiology arm in both studies, the event rates and of course noninferiority. And it's all very reassuring to the field of angiography derived physiology."

ALL-RISE

Kirtane, Fearon, and colleagues randomized 1,930 patients (mean age 68.4 years; 25% women) to physiological assessment with FFRangio or a pressure-wire-based approach. Half of lesions in both groups were in the left anterior descending (LAD) artery.

PCI was performed in 44% of patients in the FFRangio arm, and in 35% of patients in the pressure wire arm.

Time to calculate FFR was 2 minutes shorter with FFRangio, and total contrast volume, total fluoroscopy time, and total procedure time also were all lower, with an average of 5 minutes saved per procedure, compared with the pressure wire.

Ther were no differences seen between groups in rates of early or late revascularization, incidence of bleeding, acute kidney injury, or procedure-related adverse events.

FAST III

Daemon and colleagues randomized 2,211 patients (mean age 67 years; 24% women) from seven countries to vFFR or pressure wire-based FFR assessment. ACS was present in 18.7%, more than one-third had a

prior history of PCI, and more than 50% had lesions in the LAD.

Any revascularization (PCI or CABG) was performed in 59% of the vFFR group and 52% of the pressure-wire group. In those receiving PCI, procedure times were a mean of 5 minutes shorter with vFFR.

Study-vessel failure, a secondary endpoint consisting of the composite of death from cardiac causes, study-vessel MI, or clinically indicated study vessel revascularization occurred at rates of 4.6% and 4% in the pressure wire and vFFR groups, respectively. Analyses of the individual components of the primary and secondary endpoints showed a pattern consistent with the main findings. Additionally, there were no differences between groups in rates of serious adverse events.

More functionally significant lesions were identified with vFFR than with the pressure wire, which yielded a between-group difference of 9 percentage points in patients who underwent revascularization. A similar observation was also made in FAVOR III Europe. Daemen and colleagues say while it is unclear which factors may have contributed to these differences, more analysis is needed "to determine whether the higher percentage of patients in the vFFR group than in the FFR group who underwent revascularization indicates that vFFR better detected physiologically relevant lesions or whether there was a systemic shift in decision thresholds on the basis of patient characteristics and lesion location."

Not Throwing the Wire Out Just Yet

To TCTMD, Kirtane said as far as FFRangio being useful in the lab, he views it as a judicious alternative to standard pressure wire, although not as a replacement for it. In practice, he said, it can be set up seamlessly so that images automatically flow to the console, allowing the operator to use it at any time in the case.

"I've actually used it after the fact," he noted. "There were questions in the case [about significance of a lesion] and they wished they had done the pressure wire, and [I did it] post hoc."

Commenting on the results of ALL-RISE, David Moliterno, MD (University of Kentucky, Lexington), said, “I think this is what we’ve been looking for and I think this is a call, no pun intended, that we should ‘all rise’ in the cath lab and use physiology more.”

However, Moliterno said in some core lab analyses of non-pressure-wire assessments, the area under the curve (AUC) has been less than ideal and there has been a suggestion of discordance in measurements

systems available to noninvasively calculate FFR, Kirtane noted they differ in requirements from the software as to how many angiograms are needed.

Speaking in a media briefing about FAST-III, Benny Levenson, MD (Kardiologische Gemeinschaftspraxis, Berlin, Germany), said he views the results as superior as opposed to noninferior and said he looks forward to using the technology.

“It's superior because I think we all agree that any device which does not need to go into the patient is a good device,” he said. “I think it's important to create an infrastructure in the cath lab, which should be very feasible. On the other hand, the question remains what do we do if we have poor quality angiograms? Does it still work in this case?”

Daemen said it’s true that the technology simply won’t work if the angiography quality is poor. That being said, “I do think that in, let's say 80 to 90 percent of the patients, this could be a very attractive alternative to wire-based physiology. But I would not throw the invasive wire out yet.”

by **L.A. McKeown** **Editor, CV Team Forum**

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