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EDITORIAL COMMENT

Less Money, Less Problems

Real-World Cost-Effectiveness of Fractional Flow Reserve–Guided Percutaneous Coronary Intervention*

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A wealth of randomized controlled trial (RCT) data over the past 2 decades have proven the clinical value of using fractional flow reserve (FFR) to define coronary artery lesion severity. Collectively, the DEFER (Deferral vs Performance of PCI of Non-Ischemia-Producing Stenoses) and FAME (Fractional Flow Reserve vs Angiography for Multivessel Evaluation) family of trials showed that an FFR-guided percutaneous coronary intervention (PCI) strategy allowed for safe deferral of functionally insignificant lesions and significantly reduced major adverse cardiovascular events compared with an angiography-guided strategy.[1-3] These findings form the basis of the current Class Ia recommendation in the 2021 American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography & Interventions coronary artery revascularization guidelines for FFR guidance in patients with stable angina and angiographically intermediate lesions.[4] Furthermore, real-world registry data have demonstrated a mortality benefit of FFR-guided PCI in this population.[5]

Despite compelling data and strong endorsement from societal guidelines, the use of FFR to direct PCI has remained low worldwide.[6] Many factors have been proposed to explain this gap between evidence and action, including increased procedural time, modest financial renumeration to the operator, operator beliefs and education, patient discomfort from the hyperemic agent, hospital reimbursement, and cost. The perceived hurdle of cost-effectiveness has been investigated previously, with short-term FFR-related cost savings reflecting less stents, shorter hospital admission, and less repeat revascularization.[7,8] However, the analyses to date are limited by generalizability (selected patients from RCTs) and inability to accurately quantify cost or quality of life.

It is with this background we read the timely study by Hong et al[9] in this issue of *JACC: Advances*. Using insurance claims data from the National Health Insurance Service and Health Insurance Review and Assessment databases in Korea, the investigators performed an all-comer multilayered outcome and cost-effectiveness analysis of FFR-guided PCI in 134,613 patients without myocardial infarction (MI) (52% stable angina and 48% unstable angina). Overall, the rate of FFR-guided PCI was 3.8% (4.7% in stable angina vs 2.9% in unstable angina). Compared with the angiography-only group, the FFR group was associated with a significantly lower risk of all-cause death (5.8% vs 7.7%, $P = 0.001$) and spontaneous MI (1.6% vs 2.2%, $P = 0.022$) over a median follow-up of 3 years.

Cost-effectiveness was determined both on an individual patient level by measuring total quality-adjusted life-years (QALYs) and an incremental cost-effectiveness ratio (ICER) and via a simulated model spanning 3 health care systems (Korea, United States, and United Kingdom). Total QALYs represented the sum of QALYs from mortality (years of life lost), MI (years lived with MI), and angina (years lived with angina). ICER was calculated by dividing the

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difference in cost between FFR and angiography-alone cohorts by the difference in total QALYs between the 2 cohorts. Overall, FFR-guided PCI achieved a gain of 0.039 QALYs at a lower cost ($303 cost savings, ICER = −$7,748); this dominant cost-effectiveness was consistent across all major subgroups, including both stable and unstable angina. Finally, utilizing a decision and Markov model over a 10-year horizon, FFR-guided PCI was found to be cost-effective across all 3 health care systems: Korea (0.30 QALYs and ICER = −$7,309), United Kingdom (0.29 QALYs and ICER = −$1,341), and United States (0.37 QALYs and ICER = −$31,267).

Hong et al[9] should be commended for performing this comprehensive and rigorous claims-based, all-comer analysis that meaningfully adds to the limited existing body of cost-effectiveness data in the FFR arena. Key strengths of the study included the ability to capture the entire Korean population, which eliminated selection bias and allowed for a true real-world analysis in comparison to prior RCT-based analyses with selected patient populations. Second, the dual-pronged approach (ie, patient-level and simulated model analyses across health care systems) to assess cost-effectiveness improved the quality and generalizability of the data. In particular, the markedly increased ICER for FFR-guided PCI in the United States is striking and may have policy implications. Lastly, the inclusion of patients with unstable angina—a notoriously subjective diagnosis in which the use of FFR remains uncertain—expands the potential application of FFR beyond the guideline-recommended domain of stable angina.

Nonetheless, there are a few limitations that should be noted when contextualizing this study. First, the claims-based data lacked the granularity to discriminate lesion and procedural characteristics. The cost-effectiveness of FFR-guided PCI almost certainly would be magnified in the subset of patients with angiographically intermediate lesions. More importantly, it is possible that some patients who underwent FFR-guided PCI had an angiographically severe disease, rendering FFR interrogation unnecessary and possibly falsely diluting its cost-effectiveness. Second, the markedly low rate of FFR-guided PCI in this analysis, which reflects practice patterns and reimbursement criteria in Korea during the study period, may somewhat limit the application of these data more ubiquitously. For instance, a recent U.S. registry-based study reported that 75% of patients with a stable angina and angiographically intermediate disease undergoing PCI had FFR guidance.[5] Third, the cost-effectiveness of FFR-guided PCI in this study appears to be primarily driven by the observed survival benefit, which may be subject to both measured (eg, younger age and aspirin adherence) and unmeasured confounding, thus limiting the weight of the findings. Lastly, these data do not capture the potential cost-effectiveness of post-PCI FFR assessment, a growing area of physiology-guided PCI in the current era.

In conclusion, the work by Hong et al[9] is an important contribution to the existing FFR cost-effectiveness landscape and supports FFR-guided PCI as a strategy to improve not only outcomes but also the quality of life at a lower cost irrespective of health care system dynamics. It remains to be seen if cost-effectiveness impacts health care policies or FFR adoption globally, but the data herein certainly reinforce that “less money, less problems” is attainable with FFR guidance.

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REFERENCES

1. Pijls NHJ, Fearon WF, Tonino PAL, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention in patients with multivessel coronary artery disease. *J Am Coll Cardiol*. 2010;56(3):177-184. https://doi.org/10.1016/j.jacc.2010.04.012

2. Xaplanteris P, Fournier S, Pijls NHJ, et al. Five-year outcomes with PCI guided by fractional flow reserve. *N Engl J Med*. 2018;379(3):250-259. https://doi.org/10.1056/nejmoa1803538

3. Bech GJ, De Bruyne B, Pijls NHJ, et al. Fractional flow reserve to determine the appropriateness of angioplasty in moderate coronary stenosis. *Circulation*. 2001;103(24):2928-2934. https://doi.org/10.1161/01.cir.103.24.2928

4. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: a report of the American

College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. *Circulation*. 2022;145(3). https://doi.org/10.1161/cir.0000000000001038

5. Parikh RV, Liu G, Plomondon ME, et al. Utilization and outcomes of measuring fractional flow reserve in patients with stable ischemic heart disease. *J Am Coll Cardiol*. 2020;75(4):409-419. https://doi.org/10.1016/j.jacc.2019.10.060

6. Götberg M, Cook CM, Sen S, Nijjer S, Escaned J, Davies JE. The evolving future of instantaneous wave-free ratio and fractional flow reserve. *J Am Coll Cardiol*. 2017;70(11):1379-1402. https://doi.org/10.1016/j.jacc.2017.07.770

7. Tanaka N, Kohsaka S, Murata T, et al. Treatment strategy modification and its implication on the medical cost of fractional flow reserve-guided percutaneous coronary intervention in Japan. *J Cardiol*. 2019;73(1):38-44. https://doi.org/10.1016/j.jjcc.2018.05.018

8. Fearon WF, Bornschein B, Tonino PAL, et al. Economic evaluation of fractional flow reserve-guided percutaneous coronary intervention in patients with Multivessel disease. *Circulation*. 2010;122(24):2545-2550. https://doi.org/10.1161/circulationaha.109.925396

9. Hong D, Kim H, Lee H, et al. Long-term cost-effectiveness of fractional flow reserve-based percutaneous coronary intervention in stable and unstable angina. *JACC Adv*. 2022;1:100145.

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