INTERVENTIONAL CARDIOLOGY

Cost-effectiveness of PCI guided by fractional flow reserve

Doralisa Morrone and William S. Weintraub

In 2009, the FAME investigators reported that percutaneous coronary intervention guided by fractional flow reserve (FFR) could reduce the incidence of cardiovascular events when compared with angiographically guided PCI. The economic study conducted on the basis of FAME has now shown that an FFR-guided approach can also result in reduced costs.

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Coronary revascularization strategies have been evaluated in numerous clinical trials. As coronary revascularization has become more common, concerns over financial costs have increased.[1] Studies of the costs involved in revascularization therapy, including cost-effectiveness analysis, have been conducted alongside clinical trials for 30 years. William F. Fearon and his co-investigators in the Fractional Flow Reserve versus Angiography for Multivessel Evaluation (FAME) trial[2] have now reported that a strategy of fractional flow reserve (FFR) guidance is a cost-effective alternative to angiographic guidance of percutaneous coronary intervention (PCI), with overall costs at 1 year of US$14,315 in the FFR group versus $16,700 in the angiography group.[3]

> “FAME is … unusual in finding that FFR guidance resulted in improved outcomes at lower cost”

FAME is an important randomized, multicenter trial comparing outcomes of PCI using either angiographic guidance alone or angiographic guidance plus fractional flow reserve (FFR) guidance to select lesions for intervention.[2] FFR is used to assess the pressure differences across a coronary stenosis by measuring the pressure in the coronary artery proximal and distal to the stenosis. In the FFR-guided arm of FAME, lesions with a substantial pressure drop were targeted, whereas those without a pressure drop were not. In the angiographic arm, the coronary arteriogram was used to guide revascularization. The primary end point in FAME was a composite of major cardiac events, which included death, myocardial infarction, and repeat revascularization at 1 year. The primary end point occurred in significantly fewer of the patients in the FFR-guidance group than in the angiographic-guidance group (13.2% versus 18.3%, $P=0.02$).[2]

On the basis of FAME, Fearon *et al.* have now conducted a prospective economic evaluation of FFR-guided PCI compared with angiographically guided PCI.[3] The FAME economic study was a stochastic analysis in which patient-level data on costs and effects were used, as opposed to an analysis based on averages of composite data from the literature. Microcosting was used to assess the costs of the initial hospitalization, using US site-cost weights for specific resources, such as stents. Subsequent cardiovascular hospitalization costs were calculated on the basis of Medicare reimbursement rates by diagnosis-related group. Outpatient costs and indirect costs were not assessed.

Quality-adjusted life years (QALYs) were calculated by multiplying survival by utility, which was assessed using responses to the EQ-5D® (Stichting EuroQol Group, Dordrecht, The Netherlands) questionnaire collected at baseline, after 1 month, and at 1 year. QALYs at 1 year after randomization tended to be greater in the FFR arm (0.853 versus 0.838, $P=0.20$) than in the angiography arm. Costs of the index procedure, hospitalization, repeat PCI, and CABG surgery, as well as costs associated with myocardial infarction (MI) and MI with PCI were lower in the FFR arm ($14,315 versus $16,700, $P<0.0001$). The confidence intervals for differences in QALYs and costs between the two arms were estimated using bootstrap analysis, which showed that FFR was cost-saving in 90.74% bootstrap replications. Moreover, in 99.96% of simulations, the incremental cost-effectiveness ratio was below the commonly used societal willingness-to-pay threshold of $50,000. In addition to bootstrap analysis, sensitivity analysis indicated that the results were robust within reasonable limits of parameter values. Thus, Fearon *et al.* found FFR-guided therapy to be the appropriate approach compared with angiographic guidance, offering both improved patient outcomes and saving money.[3]

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The FAME cost-effectiveness analysis follows a long history of economic studies conducted alongside trials of revascularization strategies. In the Emory Angioplasty

versus Surgical Trial (EAST),[4] percutaneous transluminal coronary angioplasty (PTCA) was compared with CABG surgery. Fewer patients in the surgery group than in the angioplasty group reported angina (12% versus 20%, $P = 0.039$) at 3 years follow-up. Although initial hospital costs and professional fees were lower in the angioplasty group, this difference disappeared by 8 years of follow-up.[5]

In the Randomized Intervention Treatment of Angina (RITA) economic evaluation,[6] in which PTCA was compared with CABG surgery, the prevalence of angina during follow-up was greater in the PTCA group and antianginal drugs were prescribed more frequently to patients undergoing PTCA. Although initial hospital costs were lower in the PTCA arm, again, this difference disappeared at 5 years of follow-up.[6]

In 2007, the results of the Clinical outcomes Utilizing Revascularization and aggressive DruG Evaluation (COURAGE) trial[7] showed that PCI in addition to medical therapy did not reduce risk of death or MI when compared with medical therapy alone, although an improvement in symptoms was reported with PCI for a period of between 1 and 3 years. Results from the COURAGE cost-effectiveness analysis were published in 2008 and showed that PCI plus medical therapy was more expensive than medical therapy alone.[8]

Studies of coronary revascularization strategies have generally shown that the therapy offering the better outcome does so at increased cost. FAME is, therefore, relatively unusual in finding that FFR guidance resulted in improved outcomes at lower cost when compared with angiographic guidance.

Some limitations of this study should be noted. The first is that the time horizon was limited to 1 year. A lifetime analysis would be likely to reveal increased costs associated with FFR guidance compared with angiographic guidance owing to prolongation of life. Thus, a lifetime study might show in the future that FFR should not be a dominant strategy. The cost analysis was also limited in that outpatient services, outpatient medications, and noncardiac hospitalizations were not included. In addition, the methods of costing the initial hospitalization were dependent on microcosting in just one center in the USA. Furthermore, the difference in QALYs between the two arms of the study was small and did not reach statistical significance. Finally, FAME was a fairly small study with just 1,005 patients, and has not yet been replicated.

> **"Application of an FFR-guided approach to PCI has increased ... in part because of the ... results from FAME"**

FAME and its associated economic study are of great interest. Application of an FFR-guided approach to PCI has increased in the past couple of years, in part because of the publication of the results from FAME. FFR guidance for PCI in patients with lesions of uncertain severity now has a class IIa recommendation in the ACC/AHA guidelines[9] and a class Ia recommendation in the European Society of Cardiology guidelines.[10] However, to what extent the results of FAME can be generalized, and just how widely an FFR-guided approach to PCI should be applied awaits further study.

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Competing interests
The authors declare no competing interests.

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ATRIAL FIBRILLATION

Therapy with omega-3 fatty acids—is the case closed?

Stanley Nattel and David R. Van Wagoner

Omega-3 fatty acids have anti-inflammatory, antioxidant and membrane-stabilizing properties that indicate they could be useful in suppressing cardiac rhythm disorders. These natural dietary constituents are of particular interest for the treatment of atrial fibrillation, a common and problematic cardiac arrhythmia. However, a new, well-designed clinical study has raised major questions about their value for this indication.

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Atrial fibrillation (AF) is a very common arrhythmia, and its therapy remains a challenge. Presently available drug therapy is inadequate and great interest exists in developing improved therapeutic approaches for this indication.[1] Extensive evidence points to potentially beneficial effects of fish oils, in particular omega-3 polyunsaturated fatty acids (PUFAs), on AF.[2] Since PUFAs are a natural dietary constituent and have very few adverse effects, any efficacy of PUFAs against AF would be likely to translate into important clinical applications. Although many observational and unblinded studies point to the value of PUFAs in treating AF, few rigorous randomized double-blind