FFR-Guided PCI Offers Cost-Effective Benefit Compared with Medical Therapy Alone

Written by ***Lori Alexander***

A cost-effectiveness analysis of the Fractional Flow Reserve (FFR) Guided Percutaneous Coronary Intervention (PCI) Plus Optimal Medical Therapy (OMT) Versus OMT [FAME 2] trial indicates that FFR-guided PCI is economically viable. The initial cost of FFR-guided PCI is higher than that of medical therapy, but the cost gap narrows by >50% at 1 year, said William F. Fearon, MD, Stanford University, Stanford, California, USA, who presented the findings.

The FAME 2 trial showed that FFR-guided PCI plus OMT offered significant benefit compared with OMT alone for patients with stable coronary artery disease (CAD). The trial was prematurely stopped for significantly lower rates of hospitalization for urgent revascularization (p<0.001), but there was no difference in the rate of cardiovascular death or myocardial infarction [De Bruyne B et al. *New Engl J Med* 2012]. The study presented by Dr. Fearon was designed to determine if the benefits of FFR-guided PCI merited the costs.

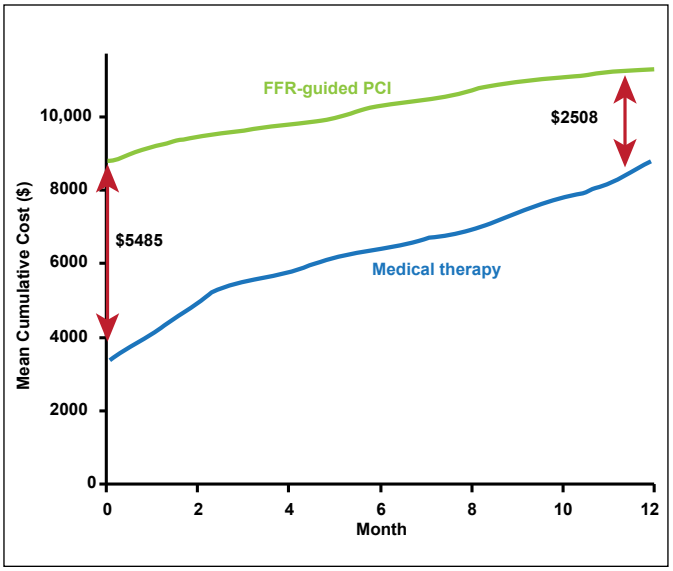
The cumulative costs over 12 months were calculated. Angina was assessed at baseline, and 1, 6, and 12 months. Quality of life (QoL) was measured at baseline and 1 month (since the trial was stopped early) using the European quality of life-5 index scores with US weights. The researchers calculated the cost-effectiveness ratio for the first 12 months and projected the analysis out to 3 years. They assumed that the 1-year cost difference would persist in subsequent follow-up and the 1-month difference would decline linearly over 3 years.

Dr. Fearon reported that the higher baseline cost for FFR-guided PCI ($8790 vs $3305 for medical therapy) was primarily related to the cost of drug-eluting stents (Table 1). The follow-up cost was higher for OMT ($5561 vs $2584 for FFR-guided PCI), with the higher cost primarily related to revascularization. The mean cumulative cost difference at baseline ($5485) decreased more than 50% at 1 year to $2508 (Figure 1). Dr. Fearon noted that the slope of the curves suggests that the cost gap would continue to narrow with further follow-up. He emphasized that (because the trial was stopped early) only a small percentage of the study population (11%) made up the cost estimate at 1 year, so the confidence limits were wide.

Table 1. One Year Cost Estimates Per Patient.

Results		
	FFR-Guided PCI	MT
Baseline	$8790	$3305
Drug-eluting stent(s)	$4304	$48
Follow-up	$2584	$5561
Revascularization	$442	$3928
Total	$11,374	$8866

Figure 1. Cumulative Costs over 12 Months.



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With regard to QoL, significantly more patients in the FFR-guided PCI group were free of or had minimal angina (class 0 or 1) at 1 month (89% vs 71%; p<0.001). The change in the QoL score from baseline to 1 month increased 0.054 in the FFR-guided PCI group but was essentially unchanged (0.003) in the medical therapy group (p<0.001).

The in-trial cost-effectiveness ratio for FFR-guided PCI was $53,000 per quality adjusted life year (QALY). The 3-year projected cost-effectiveness was $32,000/QALY. To provide context for these ratios, Dr. Fearon explained that the traditional standard for hemodialysis cost-effectiveness is <$50,000/QALY. However, the benchmark is considered outdated by some, and the World Health Organization has suggested a new standard of three times the gross domestic product, which would be $150,000/QALY in the United States. Dr. Fearon said that a ratio between $50,000 to $150,000/QALY represents a debatable cost-effectiveness, but the 3-year projection of $32,000 is well below this benchmark.

The study's limitations include the short time horizon and the wide confidence limits of its cost-effectiveness estimates. However, FFR-guided PCI significantly improves angina and QoL compared with medical therapy, and it "appears to be economically attractive."

ISAR-LEFT MAIN 2 Trial: Zotarolimus- Versus Everolimus-Eluting Stents for Treatment of Unprotected Left Main Coronary Artery Lesions

Written by ***Toni Rizzo***

The original Drug-eluting Stents for Unprotected Left Main Stem Disease [ISAR-Left Main] study found no significant difference in outcomes for patients with unprotected left main coronary artery stenosis (uLMCS) who were treated with first generation paclitaxel-eluting versus sirolimus-eluting stents [Mehilli J et al. *J Am Coll Cardiol* 2009]. Since then, the American College of Cardiology Foundation/American Heart Association/Society for Cardiovascular Angiography and Interventions updated the guidelines for percutaneous coronary intervention (PCI) of uLMS to include a class IIa or IIb indication for those patients with uLMCS lesions who have nonextensive coronary disease and are at a low stenting risk or a high surgical risk [Levine GN et al. *Circulation* 2011]. This inclusion into the PCI practice guidelines has led to more widespread use of PCI for the treatment of uLMS.

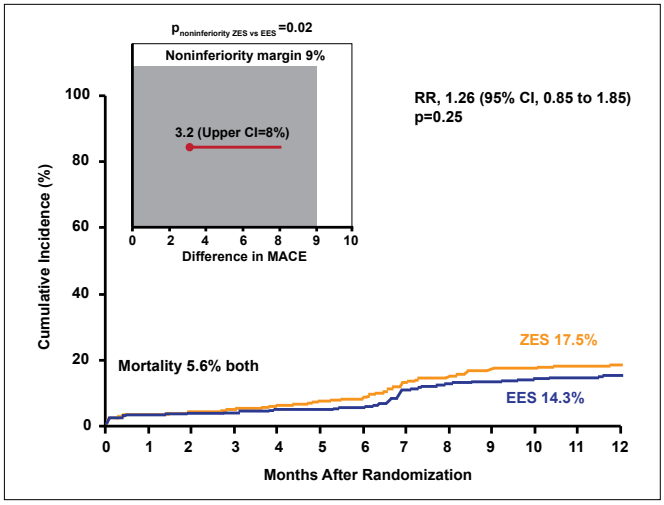
The second generation zotarolimus-eluting stent (ZES) and everolimus-eluting stent (EES) have been shown to perform better than first-generation drug-eluting stents (DES) in nearly all coronary lesion subsets, however there has been no direct comparison of these two platforms in uLMS [Stone GW et al. *New Engl J Med* 2010; von Birgelen C et al. *J Am Coll Cardiol* 2012; Serruys PW et al. *N Engl J Med* 2010; Kim YH et al. *JACC Cardiovasc Interv* 2012].

The objective of the current ISAR-LEFT MAIN 2 trial [NCT00598637] presented by Julinda Mehilli, MD, Klinikum der Universität, Munich, Germany, was to compare the performance of ZES versus EES in patients with uLMCS lesions, using a noninferiority design.

The trial randomized 650 patients with uLMCS to PCI using ZES (n=324) or EES (n=326) after pretreatment with 600 mg of clopidogrel. Follow-up assessments included angiography at 8 months in 237 (73%) patients in the ZES group and 226 (69%) patients in the EES group, and clinical evaluation at 12 months in all patients in both groups. The primary endpoint was the incidence of major adverse cardiac events (MACE), defined as the composite of death, myocardial infarction, and target lesion revascularization at 1-year follow-up. The secondary endpoints were the incidence of definite or probable stent thrombosis at 1 year and angiographic restenosis at 6 to 9 months. The noninferiority margin was calculated at 9%.

At 1-year follow-up, MACE occurred in 17.5% of the ZES group and 14.3% of the EES group (RR, 1.26; 95% CI, 0.85 to 1.85; p=0.25; Figure 1). The mortality rate was 5.6% in both groups. The ZES met the prespecifed noninferiority margin (noninferiority p=0.02).

Figure 1. Major Adverse Cardiac Events.



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Definite and probable stent thrombosis occurred in 0.6% and 0.3% of ZES patients, respectively, and in 0.6% and 0.0% of EES patients, respectively. There was no significant difference between ZES-treated and EES-treated patients with regard to angiographic restenosis (21.5% vs 16.8%; p=0.2) or clinical restenosis (11.7% vs 9.4%; p=0.35) respectively.

The ISAR-LEFT MAIN 2 trial results show that the use of second-generation DES in unprotected left main coronary artery lesions in relatively unselected patients is feasible, safe, and effective. Both stents, the ZES and the EES, provided similar clinical and angiographic outcomes at 1-year follow-up in this high-risk patient population.