Comparison of Fractional Flow Reserve–Guided PCI and Coronary Bypass Surgery in 3-Vessel Disease


Study Overview
Objective: To determine whether fractional flow reserve (FFR)–guided percutaneous coronary intervention (PCI) is noninferior to coronary-artery bypass grafting (CABG) in patients with 3-vessel coronary artery disease (CAD).
Design: Investigator-initiated, multicenter, international, randomized, controlled trial conducted at 48 sites.
Setting and participants: A total of 1500 patients with angiographically identified 3-vessel CAD not involving the left main coronary artery were randomly assigned to receive FFR-guided PCI with zotarolimus-eluting stents or CABG in a 1:1 ratio. Randomization was stratified according to trial site and diabetes status.
Main outcome measures: The primary endpoint was major adverse cardiac or cerebrovascular event, defined as death from any cause, myocardial infarction (MI), stroke, or repeat revascularization. The secondary endpoint was defined as composite of death, MI, or stroke.
Results: At 1 year, the incidence of the composite primary endpoint was 10.6% for patients with FFR-guided PCI, and 6.9% for patients with CABG (hazard ratio [HR], 1.5; 95% CI, 1.1-2.2; P=.35 for noninferiority,) which was not consistent with noninferiority of FFR-guided PCI compared to CABG. The secondary endpoint occurred in 7.3% of patients in the FFR-guided PCI group compared with 5.2% in the CABG group (HR, 1.4; 95% CI, 0.9-2.1). Individual findings for the outcomes comprising the primary endpoint for the FFR-guided PCI group vs the CABG group were as follows: death, 1.6% vs 0.9%; MI, 5.2% vs 3.5%; stroke, 0.9% vs 1.1%; and repeat revascularization, 5.9% vs 3.9%. The CABG group had more extended hospital stays and higher incidences of major bleeding, arrhythmia, acute kidney injury, and rehospitalization within 30 days than the FFR-guided PCI group.
Conclusion: FFR-guided PCI was not found to be noninferior to CABG with respect to the incidence of a composite of death, MI, stroke, or repeat revascularization at 1 year.

Commentary
Revascularization for multivessel coronary artery disease can be performed by CABG or PCI. Previous studies have shown superior outcomes in patients with multivessel CAD who were treated with CABG compared to PCI.1-3 The Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial, which compared CABG to PCI in patients with a multivessel disease or unprotected
left main CAD, stratified the anatomic complexity based on SYNTAX score and found that patients with higher anatomic complexity with a high SYNTAX score derive larger benefit from CABG compared to PCI.\textsuperscript{4} Therefore, the current guidelines favor CABG over PCI in patients with severe 3-vessel disease, except for patients with a lower SYNTAX score (<22) without diabetes.\textsuperscript{5,6} However, except for a smaller size study,\textsuperscript{3} the previous trials that led to this recommendation used mostly first-generation drug-eluting stents and have not evaluated second-generation stents that have lower rates of in-stent restenosis and stent thrombosis. In addition, there have been significant improvements in the PCI techniques since the study period, including the adoption of a radial approach and superior adjunct pharmacologic therapy. Furthermore, previous studies have not systematically investigated the use of PCI guided by FFR, which has been shown to be superior to angiography-guided PCI or medical treatment alone.\textsuperscript{7-9}

In this context, Fearon and the investigators of the FAME 3 trial investigated the use of FFR-guided PCI with second-generation zotarolimus drug-eluting stent compared to CABG in patients with 3-vessel CAD. They randomized patients with angiographically identified 3-vessel CAD in a 1:1 ratio to receive FFR-guided PCI or CABG at 48 sites internationally. Patients with left main CAD, recent ST-elevation MI, cardiogenic shock, and left ventricular ejection fraction <30% were excluded. The study results (composite primary endpoint incidence of 10.6% for patients with FFR-guided PCI vs 6.9% in the CABG group (HR, 1.5; 95% CI, 1.1-2.2; \(P=0.35\) for non-inferiority) showed that FFR-guided PCI did not meet the noninferiority criterion.

Although the FAME-3 study failed to show noninferiority in the overall population, when stratified by the SYNTAX score, the major adverse cardiac event rate for the PCI group was numerically lower than that of the CABG group. The results from the FAME-3 study are overall in line with the previous studies and the current guidelines. Future studies are necessary to assess the outcomes of multivessel PCI compared to CABG using the most contemporary interventional practice and achieving complete revascularization in the PCI arm.

Applications for Clinical Practice
In patients with 3-vessel disease, FFR-guided PCI was not found to be noninferior to CABG; this finding is consistent with previous studies.

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Disclosures: None.
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References
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