Fractional Flow Reserve for Coronary Bifurcation Lesions

Can Fractional Flow Reserve–Guided Side Branch Intervention Strategy Improve Clinical Outcomes Compared With Angiography-Guided Strategy?*

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Fractional flow reserve (FFR) is an invasive physiological index to define ischemia-causing stenosis in patients with coronary artery disease. FFR represents the ratio of blood flow distal to a stenotic lesion to normal maximal flow and can be easily measured using a pressure sensor-tipped guidewire in a cardiac catheterization laboratory. FFR is helpful for clinical decision making in patients with angiographically intermediate or ambiguous coronary stenosis. Previous studies have demonstrated the clinical benefit of FFR-guided revascularization strategy over angiography-guided strategy or medical treatment (1,2).

The bifurcation lesion is one of the most challenging lesion subset in the field of percutaneous coronary intervention (PCI). Several clinical trials were designed and performed to prove the benefit of side-branch stenting over balloon angioplasty or medical treatment, but failed, even with the advent of drug-eluting stents. Therefore, a provisional side-branch intervention strategy is regarded as the standard approach for general bifurcation lesions. During the provisional strategy, the operator decides whether to intervene on the side-branch ostial stenosis after main-branch stent implantation. However, there has been no universal criterion for jailed side-branch intervention. Because anatomic assessment generally overestimates the lesion severity of jailed side branches (3–6), an FFR-guided revascularization strategy can reduce unnecessary complex intervention and associated complications. Although a previous case-control study demonstrated that FFR use resulted in less frequent side-branch intervention without a difference in clinical outcomes compared with conventional strategy (6), no randomized study has been performed to prove the clinical benefit of an FFR-guided side-branch intervention strategy over an angiography-guided strategy.

In this issue of JACC: Cardiovascular Interventions, Chen et al. (7) present the first randomized study comparing FFR-guided and angiography-guided side-branch intervention strategies in patients with bifurcation lesions. The authors randomized 320 patients with true bifurcation lesions (Medina 1,1,1 or 0,1,1) with a planned provisional side-branch intervention strategy to angiography-guided (Angio group) and FFR-guided (FFR group) groups. In the Angio group, the side branch was dilated when the Thrombolysis In Myocardial Infarction flow was <3, dissection was greater than type A, or ostial stenosis was >70%. Side-branch stenting was performed if any of these criteria persisted after kissing balloon inflation. In the FFR group, kissing balloon inflation was performed when jailed side-branch FFR was <0.8 and side-branch stenting when post-kissing balloon inflation FFR was <0.8. The major finding of the study was that the 1-year composite rate of major adverse cardiac events (cardiac death, myocardial infarction, and clinically driven target...
vessel revascularization) was similar in both groups (18.1% in both groups, hazard ratio: 0.91, 95% confidence interval: 0.48 to 1.88). The 1-year target vessel revascularization and stent thrombosis rates were 6.9% and 5.6% (p = 0.82) and 1.3% and 0.6% (p = 0.56) in the Angio group and FFR group, respectively. Therefore, the investigators’ conclusion was that angiography- and FFR-guided provisional side-branch stenting of true bifurcation lesions provided similar 1-year clinical outcomes.

Because this study was designed to prove the clinical benefit of an FFR-guided side-branch intervention strategy, the results can be disappointing, especially considering the results of the FAME (Fractional Flow Reserve versus Angiography for Multivessel Evaluation) study (1). In the FAME study, 1,005 patients with multivessel disease were randomized to angiography-guided or FFR-guided drug-eluting stent implantation. The 1-year event rate (death, nonfatal myocardial infarction, and repeat revascularization) was 18.3% in the angiography-guided group and 13.2% in the FFR-guided group (p = 0.02) (1). Why were these findings not reproduced in this DKCRUSH-VI (Double Kissing Double CRUSH VI) study? To answer this question, the difference between the main branch and side branch needs to be understood. It is well-known that a certain amount of ischemic burden is required to prove the benefit of revascularization over medical treatment. Because the side-branch myocardial territory is smaller than that of the main branch, the clinical impact of different strategies for side branches will be less than that for main branches. This may be the main reason why there has been no clinical difference in the most conservative strategy (leave-it-alone) and the most aggressive strategy (side-branch stenting) in previous randomized trials. Therefore, unless only clinically relevant side branches are included, no study will be able to prove the true efficacy of a certain intervention strategy. Although the investigators of the present study tried to select large side branches, the reference vessel diameters of the side branches were 2.28 ± 0.29 mm and 2.23 ± 0.30 mm in the Angio group and FFR group, respectively. Furthermore, previous studies demonstrated that vessel size may not be a sufficient parameter to represent the clinical relevance of a side branch (8,9).

As expected, the FFR-guided strategy reduced the need for side-branch stenting compared with the angiography-guided strategy (38.1% vs. 25.9%, p = 0.01) in this study. However, as pointed out by the authors, upfront use of a pressure wire may not be cost-effective when used in all jailed side-branch lesions. The present study also highlights the importance of procedural experience and adequate lesion selection. In this study, the failure rate of side-branch FFR measurement was 9.4%, which is similar to that from a previous multicenter study (10). However, this rate was <5% in several single-center studies. Therefore, risk and benefit need to be assessed before the application of FFR in daily practice. Its use is most effective when used in large side branches with relatively short ostial lesions.

It is interesting to note that the restenosis rate at the distal main vessel was higher in the Angio group than in the FFR group (9.9% vs. 1.7%, p = 0.02) in this study. In the Angio group, distal main vessel restenosis occurred only in lesions with side-branch intervention. As side-branch intervention tends to result in unfavorable geometric changes in the main vessel, operators need to be careful to achieve procedural success for both branches in cases of side-branch intervention. The use of intravascular ultrasound (IVUS) can be very helpful to optimize the procedures.

In this study, the proportion of functionally significant jailed side branches was higher than in previous studies. As discussed by the authors, it is important to understand that jailed side-branch FFR is influenced not only by the angiographic percentage of diameter stenosis but also by lesion length, lesion morphology, vessel size, and additional upstream or downstream stenosis. Furthermore, angiographic assessment of a jailed side branch is difficult and is not free of subjectivity (11). As side-branch FFR is more vulnerable to the influence of main-branch stenosis, pressure pullback tracing under maximal hyperemia needs to be performed when side-branch FFR is low.

The investigators should be praised for performing this randomized study and reminding interventionalists of the important issues in bifurcation PCI. During PCI for bifurcation lesions, the clinically relevant question may not be whether FFR-guided side-branch intervention is better than angiography-guided intervention, but how to optimize the procedures without unnecessary intervention. Operators need to acknowledge when and how additional procedures such as FFR or IVUS are best used. Furthermore, angiographic evaluation should be more than a simple assessment for the angiographic percentage of diameter stenosis of jailed side branches. The importance of careful angiographic evaluation to assess the myocardial mass at risk, the risk and benefit of FFR use, and
the presence of upstream and/or downstream stenosis, which can influence measured side-branch FFR, cannot be overemphasized. We need to embrace a more physiological approach than the mere measured FFR value itself.

REFERENCES


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