Use of Fractional Flow Reserve in Bifurcation Lesions

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Introduction

Previous studies proved that fractional flow reserve (FFR)-guided decision-making in general coronary lesions can reduce unnecessary revascularisation and improve patient outcomes. Compared to non-bifurcation lesions, bifurcation lesions are associated with more complex procedures, less procedural success and worse clinical outcomes. It is clinically important to accurately assess the functional significance of bifurcation lesions and whether complex interventional procedures are required during the percutaneous coronary intervention (PCI). Therefore, understanding when and how to use FFR in complex bifurcation lesions is needed to reduce unnecessary complex procedures and to improve the outcomes for patients with bifurcation lesions.

The Need for Fractional Flow Reserve

It is well-known that the angiography has limitations in the assessment of coronary artery stenoses. These limitations become worse in bifurcation lesions due to complex geometry, vessel shortening and overlap. In a study, when angiographic severity was compared with FFR in all ostial lesions, only 20 % of lesions with angiographically severe stenosis (≥70 %) were functionally significant (FFR <0.75). In a recent study, best angiographic cut-off values to predict the functional significance of main and side branch ostial lesions were 53 % and 67 %, respectively. However, the positive predictive value of angiographic criteria was just 58 % in main branch ostial lesions and 38 % in side branch ostial lesions. Use of better imaging tools such as intravascular ultrasound (IVUS) or optical coherence tomography (OCT) cannot completely overcome these limitations. When IVUS parameters and FFR were compared in side branch ostial lesions, a statistically significant cut-off value of minimal lumen area could not be found in side branch ostial lesions. These results seem to be natural considering the high variability in size, and the amount of blood supplying myocardium in side branches. It is also reported that the pre-intervention IVUS measurements cannot reliably predict the functionally significant side branch compromised after main branch stent implantation.

Anatomical assessment of jailed side branch lesions is more complicated. One study reported high variability in visual and quantitative coronary angiographic assessment for jailed side branch lesions. When 20 jailed side branch lesions were assessed by three different quantitative coronary angiography (QCA) systems, mean minimal lumen diameter and percentage of diameter stenosis differed by up to 0.30 mm and 9.7 %, respectively. Moreover, it is well-known that angiographic percentage of diameter stenosis does not match well with the functional significance of jailed side branch lesions.

Why Fractional Flow Reserve for Assessing Bifurcation Lesions?

• FFR can be easily measured in bifurcation lesions before and during intervention.
• FFR can be safely used during the intervention of bifurcation lesions.
• Angiographic evaluation overestimates the functional severity of jailed side branch lesion.
• While angiography, intravascular ultrasound (IVUS) and optical coherence tomography (OCT) can provide accurate anatomical information, they have inherent weaknesses that limit their effectiveness in assessing bifurcation lesions.

Fractional Flow Reserve Before Intervention

For the main branch, the application of a pressure wire is the same as for non-bifurcation lesions. However, when the FFR is used for the side branches, the influence of a main branch plaque should always be considered. In cases of true bifurcation lesions, it is generally impossible to differentiate the physiological significance of main and side branch lesions. In case of Medina 001 bifurcation lesions (pure side branch ostial lesions), pressure pull back tracing under maximal hyperaemia should be performed when FFR is significant. As the flow to the side branch is relatively smaller than that to the main branch, side branch FFR is more easily influenced.
by the main branch lesions. Pre-intervention side branch FFR cannot reliably predict the functional significance of jailed side branches due to the influence of main branch stenosis and the dynamic geometric changes during percutaneous intervention.

**Fractional Flow Reserve After Main Branch Stent Implantation**

After main branch stent implantation, side branch jailing can occur by carina shift, plaque shift, dissection, spasm and thrombus. This complexity makes anatomical assessment of these lesions more difficult. In general, angiographic percentage of diameter stenosis overestimates the functional significance of a stenosis due to a carina shift. Therefore, FFR is very useful in the accurate assessment of jailed side branches in reducing unnecessary complex interventions. Side branch FFR measured just after main branch stent implantation is reported to be maintained during follow-up. As the profile of a current pressure wire is almost the same as a conventional wire, re-crossing of a side branch through the main branch strut is not difficult in most cases. However, the pressure wire itself should not be jailed by a stent.

When the pressure wire is used to assess the functional significance of jailed side branch lesions, it is important to evaluate the clinical relevance of the side branch before the FFR measurement. The measurement of FFR is not indicated in small side branches or the branches in which the revascularisation is clinically not needed. Moreover, in very tortuous or heavily calcified side branches or diffuse side branch lesions, the benefit of FFR is less, and the procedural risk is higher than in ostial side branch lesions.

**Fractional Flow Reserve After Side Branch Angioplasty**

FFR-guided side branch revascularisation strategy is feasible. When jailed side branch FFR is <0.75 (or 0.8), side branch angioplasty including kissing balloon inflation can be performed over the pressure wire. In a recent study kissing balloon inflation increased side branch FFR from 0.66 ± 0.08 to 0.86 ± 0.05. Moreover, this acute functional gain was maintained during a 6-month follow-up. In another study there was no significant change in mean side branch FFR during the follow-up period in the kissing balloon group (0.92 versus 0.91; p=0.80). However, it should be noted that the functional and the angiographic late loss depends on the amount of injury during the procedure. Measurement of FFR is clinically not indicated in cases of severe dissection or slow flow after side branch angioplasty.

**Fractional Flow Reserve After Side Branch Stenting**

FFR-guided side branch intervention is feasible even for complex two-stenting strategies. In a study by Ye et al., when side branch FFR was compared between the provisional side branch intervention group and double kissing (DK) crush stenting group, FFR was higher in the DK crush stenting group than in the provisional group (0.90 ± 0.08 versus 0.94 ± 0.03; p=0.028). Lee et al. measured side branch FFR before and after kissing balloon inflation in patients who underwent crush stenting. FFR values increased from 0.94 ± 0.04 to 0.97 ± 0.03 with kissing balloon inflation. However, it should be noted that even before the kissing balloon inflation, FFR was already high and it was >0.9 in 75 % of the patients. Therefore, side branch FFR after stenting may not always guarantee the acute and long-term procedural success of complex side branch stenting.

**Conclusion**

FFR can be useful in the assessment of complex bifurcation lesions throughout the PCI procedure. Adequate use of FFR can reduce unnecessary complex interventions and may improve the outcomes of patients with bifurcation lesions.