Introduction
Deferring intervention in intermediate coronary lesions that are not functionally significant is associated with favorable long-term clinical outcomes. However, identifying which lesions are functionally significant and warrant revascularisation and which should be deferred is challenging in patients with diffuse disease or multiple sequential stenoses with intermediate severity. Nonetheless, selecting the appropriate target lesion(s) is critical to achieving optimal clinical outcomes in patients with serial or multiple stenoses. In those patients, fractional flow reserve (FFR) measurements with pullback pressure recording can be helpful in identifying lesions with functional significance.

Fractional Flow Reserve
FFR is the reference standard for the physiological assessment of coronary artery stenoses, particularly intermediate ones. FFR is defined as the ratio between mean distal coronary pressure and mean aortic pressure, both measured simultaneously at maximal hyperaemia. Coronary pressure is measured using a 0.014-inch sensor-tipped PressureWire™ FFR measurement system (St. Jude Medical, St. Paul, Minnesota). The pressure guidewire is introduced through a 6 or 7 F guiding catheter, equalised, and then advanced distal to the stenosis. The FFR value is checked after continuous intravenous infusion of adenosine* (140 μg/kg/min) to induce maximal hyperaemia. Then, the pressure guidewire is slowly pulled back to the ostium of the coronary artery under steady-state hyperaemia. An FFR value of 0.80 discriminates coronary stenoses responsible for ischaemia.

*Specific use of hyperaemic agents during FFR procedures is done at the discretion of the physician.

Fractional Flow Reserve in Serial Stenoses
The clinical application of FFR in vessels with multiple stenoses is not easy, as one stenosis influences the FFR of the others and complicates the determination of FFR of each individual stenosis. However, studies have demonstrated that FFR can be measured accurately in serial stenoses. In a prospective study performed at two centers in Korea, FFR-guided percutaneous coronary intervention (PCI) was performed in 131 patients with multiple intermediate stenoses within the same coronary artery (141 vessels and 298 lesions). In vessels with an FFR ≤ 0.80, the pressure guidewire was slowly pulled back to the ostium of the coronary artery under steady-state hyperaemia. The stenosis that caused the largest pressure step-up (primary target lesion) during pressure guidewire pullback was treated first. After stenting the primary target lesion, FFR was measured again to determine whether PCI in the other stenoses was necessary. The apparent and true FFR of non-primary target lesion were calculated. Using this protocol, a total of 116 stents (70 proximal and 46 distal) were implanted, and revascularisation was deferred in 61.1 % (182 of 298) of lesions (Figure 1). Two or more stents were implanted in 38.9 % of lesions (116 stents were implanted in 70 proximal and 46 distal lesions). A total of 182 lesions (61.1 %) were deferred without revascularisation.

Keywords
- Serial lesions
- Serial stenoses
- Coronary artery stenosis
- Fractional flow reserve (FFR)
- Pullback pressure recording

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implanted in only 26 vessels (18.4%). In 89 vessels with an FFR ≤ 0.8, FFR increased from 0.67 ± 0.09 at baseline to 0.84 ± 0.07 after stenting (p < 0.001).

In our study of 141 vessels with 298 intermediate lesions, 239 FFR measurements were required to perform the FFR-guided revascularisation strategy. However, there were no procedure-related complications, demonstrating that this approach is a safe and feasible method for physiological assessment of serial stenoses in a real-world clinical practice. The results confirm earlier studies which demonstrated that true FFR was lower than apparent FFR in both proximal and distal stenoses and that the pressure step-up in a non-primary target lesion increased after stenting the primary target lesion. Also of note, baseline angiographic and physiological characteristics were not predictive of functional significance after primary lesion stenting. All these findings emphasize the importance of repeated FFR measurement after the primary target lesion has been stented to accurately assess the functional significance of non-primary target lesions. Otherwise, functionally significant lesions can be left untreated.

### Practical Guide for Using Fractional Flow Reserve in Serial Stenoses

The following process can aid in treatment decisions about serial stenoses:

1. Insert a pressure guidewire past the most distal stenosis.
2. Measure the FFR of all stenoses together under maximal hyperaemia.
3. If FFR is insignificant (FFR > 0.80), defer revascularisation in the serial stenotic lesions and treat with optimal medical therapy.
4. If FFR is significant (FFR ≤ 0.80), perform a pressure pullback tracing under maximal hyperaemia.
5. Perform PCI in the lesion with the largest pressure step-up first. Do not miss anatomical considerations around the target lesion.
6. Repeat a pressure pullback tracing past the most distal stenosis.
7. Repeat the decision-making process for each stenosis in the series.

### Conclusions

FFR can be used to assess the functional significance of serial lesions through repetitive pullback pressure recordings. The procedure was safe and enabled identification of the proper target lesions for revascularisation. This strategy can reduce unnecessary intervention, minimise stent-related complications, and maximise the benefit of PCI in patients with multiple stenoses within one coronary artery.

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