

MISINTERPRETATION OF STENOSIS SEVERITY IN THE PRESENCE OF SERIAL  
CORONARY STENOSES: AN IN-VITRO STUDY

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ABSTRACT

In patients with multiple stenoses in the same coronary artery, the severity of one stenosis influences the diagnosis of the serial stenosis. Currently used diagnostic end-point, Fractional Flow Reserve, FFR (ratio of distal to proximal pressure of a stenotic region), has a cut-off point of 0.75. A value of  $FFR < 0.75$  leads to a clinical intervention. However, FFR may fail to account for multiple stenoses interactions and might lead to clinical misinterpretation of one serial stenosis severity. In order to assess the effect of one stenosis on the other serial stenosis, we tested three combinations of serial stenoses: 80%-64%, 80%-80% and 80%-90% area stenosis (AS) respectively, using an *in-vitro* experimental setup. The hyperemic flow decreased from 136.4 ml/min to 126.4 ml/min and further to 90.7 ml/min as downstream stenosis severity increased from 64% AS to 80% AS and further to 90% AS, respectively. More importantly, the individual FFR values of the upstream stenosis (80% AS) increased from 0.76 to 0.79 and further to 0.88 as the downstream stenosis increased from 64% AS to 80% AS and further to 90% AS, respectively. On the contrary, the combined FFR across both the stenosis was below the threshold value of 0.75. These results indicate that the presence of a downstream stenosis might lead to a clinical misinterpretation of the upstream stenosis severity and also the combined stenosis severity.

INTRODUCTION

Multiple focal lesions within a single coronary vessel represent a complex clinical phenomenon and the fluid dynamic interaction between the two is difficult to quantify. Additional resistance offered by the downstream stenosis will reduce the hyperemic flow across the upstream stenosis, thus resulting in a lower pressure drop across it [1]. This would imply that the true severity of upstream lesion is masked by the presence of the downstream lesion [2]. Pressure-derived

Fractional Flow Reserve, FFR (ratio of distal to proximal pressure of a stenotic region), used to assess the functional severity of a stenosis. It has a threshold value of 0.75 for coronary stenosis below which percutaneous coronary intervention is recommended [3]. However, the *individual* FFR of stenoses in series may fail to account for interactions between multiple sequential stenoses and this might lead to clinical misdiagnosis. Therefore, in this study, using an *in-vitro* experimental setup, we assessed the effect of various downstream stenoses on the physiologically relevant case of an intermediate (80% AS) upstream stenosis.

METHODOLOGY

The experimental setup along with a schematic and the detailed procedure can be found in Banerjee *et al.* [4]. The single stenosis was replaced by a series of stenoses separated by a distance ( $L$ ) of 128 mm when measured between the mid-points of the throat regions.

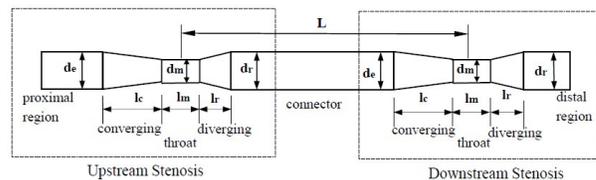
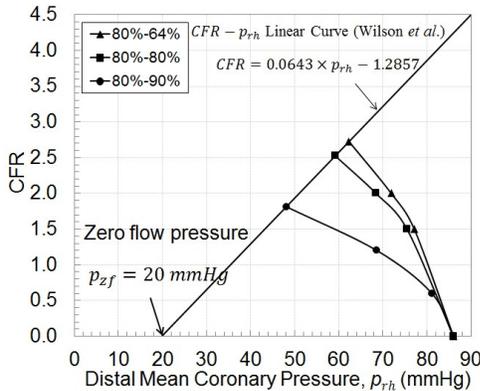


Figure 1: Test Section of multiple stenoses

Angiographic data from Wilson *et al.* was used to construct the test section geometries. Figure 1 shows typical test section geometry used to represent a multiple coronary stenosis *in-vitro*. The individual test sections were connected using a rigid connector fabricated from Plexiglas to form the serial stenoses combination. The dimensions of

the individual stenoses corresponding to the nomenclature used in Figure 1 are reported in [4]. Three cases of serial stenoses with upstream and downstream severities of 80%-64%, 80%-80% and 80%-90% area stenoses (AS) respectively were considered.

A 0.014" guidewire was placed with its tip distal to the second lesion in order to replicate a clinical scenario. Pressure values were obtained across both the stenoses at various flow rate values. Three data sets were taken and averaged. Using the pressure-drop ( $\Delta p$ ) and flow curves for each serial stenoses combination, the hyperemic flow rates and the corresponding mean distal coronary pressures were determined from coronary flow reserve (CFR: ratio of flow at maximal vasodilation to flow at rest) - distal perfusion pressure (Figure 2,  $CFR - p_{rh}$ ) curves. This graph is obtained using a data set of 32 patients undergoing angioplasty [5]. The relationship between CFR and mean distal perfusion pressure for the three cases is shown in Figure 2. An increase in the area reduction of the distal lesion reduces the combined CFR. The CFR values for 80%-64%, 80%-80% and 80%-90% cases were 2.7, 2.5 and 1.8 respectively. The distal perfusion pressures for the corresponding cases were 62.3, 59.2 and 48.1 mmHg.



**Figure 2:**  $CFR - p_{rh}$  curve for serial stenoses combinations with varying severities

The proximal pressure was kept constant at 86 mmHg for the three cases as indicated by Back and Denton [6]. A resting flow of 50 ml/min was based on the fact that the resting flow decreases only with an AS greater than 97% [7]. Measured  $\Delta p$  values at hyperemic flow rates were used to calculate the *individual* FFR of stenoses in series.

**RESULTS**

The hyperemic flow rates,  $Q_h$ , and calculated values of *individual* upstream stenosis and FFR for the serial stenoses combinations are reported in Table 1. For the same upstream stenosis severity of 80%, the  $Q_h$  was limited by the change in downstream stenosis. As the downstream stenosis severity increased from 64% to 80%, the value of  $Q_h$  decreased from 136.4 ml/min to 126.4 ml/min. As the downstream %AS increased further to 90%, the  $Q_h$  value further decreased to 90.7 ml/min. This decrease in  $Q_h$  is indicative of additional resistance offered by the downstream stenosis on the upstream stenosis.

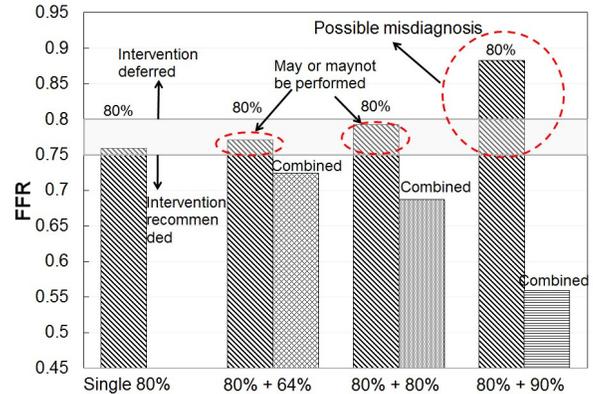
**Table 1:** Comparison of functional parameters of an intermediate stenosis with and without serial downstream stenosis

Stenosis combination	Hyperemic flow, $Q_h$ (ml/min)	Upstream stenosis (80%) FFR	Combined FFR
80%-64%	136.4	0.77	0.72
80%-80%	126.4	0.79	0.69
80%-90%	90.7	0.88	0.56

More importantly, in a clinical scenario, interventional decisions are taken based on the FFR value 0.75-0.80 (shaded region, Figure 3).

Due to additional flow limiting effect of downstream stenosis, the FFR values are also affected. This effect is summarized in the Figure 3.

With the upstream stenosis constant at 80% AS, in the presence of a serial stenosis downstream, the combined FFR values decreased from 0.72 for the 64% AS to 0.69 for the 80% AS and further to 0.56 as the downstream stenosis severity increases to 90% AS. *On the contrary, the FFR value of the upstream 80% AS increased as the downstream stenosis severity decreased.* When there is no serial stenosis present, the value of FFR for 80% AS is 0.76 [1]. In the presence of 64%AS downstream the value increased a little to 0.77. The value further increased to 0.79 in the presence of an 80%AS downstream. Based on the cut-off range of 0.75-0.80, an intervention may or may not be performed in these cases (Figure 3).



**Figure 3:** Bargraph showing the increase in FFR values of an intermediate stenosis as the downstream stenosis severity increases

However, the FFR value for the 80%AS in the presence of downstream 90%AS is 0.88. This elevation of FFR value above the interventional threshold of 0.75-0.80 might lead to *misinterpretation of the severity of the upstream 80%AS* and might even lead to a clinical *misdiagnosis*.

**DISCUSSION AND CONCLUSION**

From the results above, for the same 80%AS, the value of FFR increased from 0.76-0.88 as the downstream severity increased from 65%AS - 90%AS. This increase in the value of FFR for a clinically relevant stenosis of 80% in the presence of varying downstream stenosis, might lead to a misinterpretation of the stenosis severity and further lead to a misdiagnosis. Therefore, we conclude that in the presence of a downstream stenosis, the true severity of an intermediate stenosis located upstream is overestimated by FFR. Care should be taken about the interpretation of the FFR values in the presence of multiple stenoses.

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**REFERENCES**

- De Bruyne, B., et al., 2000, *Circulation*, 101:1840-1847
- Pijls, NHJ, et al., 2000, *Circulation*, 102:2371-2377
- Pijls, N.H.J., De Bruyne, B., Peels, K., et al., 1996, *Engl J Med*, Vol. 334, pp.1703.
- Banerjee, R.K., et al., 2008, *Biomed Eng Online*, 7:24.
- Wilson, R.F., et al., 1988, *Circulation*, 77, pp. 873-885.
- Gould KL, Lipscomb K, 1974, *The Am J of Cardiology*, Vol. 34.
- Back LH and Denton TA, *Adv Bioeng ASME BED 22*: 337-340, 1992.