

MISINTERPRETATION OF STENOSIS SEVERITY IN THE PRESENCE OF SERIAL CORONARY STENOSES

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ABSTRACT

Diagnosis of the functional severity of an epicardial coronary stenosis using parameters like Fractional Flow Reserve, FFR (ratio of distal to proximal pressure of a stenotic region), might be affected in the presence of an additional downstream stenosis. In order to assess this effect, we have performed an *in-vitro* experiment which is used to validate a computational study. Three combinations of serial stenoses were tested: 80%-64%, 80%-80% and 80%-90% area stenosis (AS). The physiological mean hyperemic flow (flow at maximal arterial dilatation) values were obtained using an *in-vitro* experimental set-up. These flow rates were used as *steady flow* inputs by time-averaging the spatially averaged flow pulse over two cardiac cycles for the computational study. FFR values were calculated at hyperemic flow using both the experimental and numerical pressure data. As the downstream severity increased from 64% AS to 80% AS, hyperemic coronary flow decreased from 136.4 ml/min to 126.4 ml/min. Flow decreased further to 90.7 ml/min with a downstream severity of 90% AS. FFR of the intermediate stenosis increased from 0.76 to 0.79 and further to 0.88 as the downstream stenosis increased from 64% to 80% with a final severity of 90% AS. Similarly, numerically obtained FFR values increased to 0.83, 0.80 and 0.92 for the corresponding cases indicating an error within 7% of the experimental values. These results indicate that the presence of a downstream stenosis might lead to a clinical misinterpretation of the upstream stenosis severity.

INTRODUCTION

The severity of an epicardial coronary stenosis is commonly assessed using the pressure-derived Fractional Flow

Reserve, FFR. Multiple lesions within the same coronary vessel represent a complex unstable flow characterized by fluid acceleration and wall shear-layer separation. Individual FFR of stenoses in series may fail to account for the fluid dynamic interactions between the two and hence inaccurately quantify disease severity leading to possible misdiagnosis. In this study, we sought to quantify this effect using a computational model and validate the results with experimental values. We assessed the effect of various downstream stenoses on the physiologically relevant case of an intermediate (80% AS) upstream stenosis.

METHODS

Experimental Set-up: Bench-top tests for the multiple stenoses models were carried out using a previously designed setup [1]. Using the pressure-drop (Δp) and flow curves for each serial stenoses combination, the physiological hyperemic flow rates and the corresponding mean distal coronary pressures were determined from the coronary flow reserve (CFR: ratio of flow at maximal vasodilation to flow at rest) - distal perfusion pressure (CFR-*Prh*) curve [2] using the procedure outlined in [1]. Functional and hemodynamic parameters for the cases under study were then evaluated at hyperemic flow.

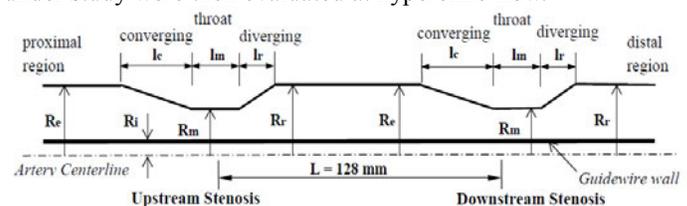


Figure 1: Test Section of multiple stenoses

Geometry and Mesh: A typical geometry representing multiple stenoses in a coronary artery with a 0.014” guidewire inserted through it is shown in Figure 1. Details of the model along with geometric dimensions of the individual stenosis can be found in [1]. Three geometries representing combinations of area stenosis of 80%-90%, 80%-80% and 80%-64% were constructed using DesignModeler (Ansys Inc., PA). Taking advantage of the axisymmetric geometry, a 3-D model was created and the flow was solved for a sector of 20°. A mesh comprising of around 200,000 hexahedron elements was generated for each case based on local mesh refinement.

Assumptions: Our present study assumes a steady flow condition and a rigid concentric arterial wall with a concentric guidewire placed across the stenoses.

Numerical Setup and Solution: Time-averaged hyperemic flow rates obtained from experiments were input as Poiseuille flow at the inlet, using a velocity profile defined for fully-developed annular flow to include the presence of the guidewire. A stress-free boundary was applied to the outlet of the flow domain. A no-slip boundary condition was specified at the artery wall and the guidewire surface. Symmetry was specified on the two fluid surfaces represented by the sides of the sector. The blood was modeled as Non-Newtonian Carreau and incompressible fluid, using the constants obtained from the experimental fluid viscosity data fit to the Carreau curve [1]. The commercial CFD code, CFX (Ansys Inc., PA) was used to solve for mass and momentum conservation using a laminar model.

RESULTS

Experimental hyperemic flow rates, Q_h , used for the steady-state simulations corresponding to the three cases are tabulated below in Table 1 along with a comparison of FFR values calculated using experimental and numerical pressures.

Stenosis Combination	Hyperemic Flow, Q_h (ml/min)	Upstream stenosis (80%) FFR		% Error
		Experimental	Numerical	
80%-64%	136.4	0.77	0.83	7%
80%-80%	126.4	0.79	0.80	1%
80%-90%	90.7	0.88	0.92	4%

Table 1: Comparison of functional parameters of an intermediate stenosis

As the downstream severity increased from 64% to 80% AS, the maximum flow across the 80% AS located upstream decreased from 136.4 ml/min to 126.4 ml/min. The hyperemic flow further decreased to 90.7 ml/min when a 90% AS was placed downstream. Diagnostic parameters evaluated at hyperemia would thus be affected by the limit in maximum flow in the coronary artery. This effect of multiple stenoses on the currently used diagnostic parameter, FFR, is highlighted in Figure 1. A clinical cut-off range of 0.75-0.8 has been defined for FFR below which intervention is recommended (shaded region, Figure 2).

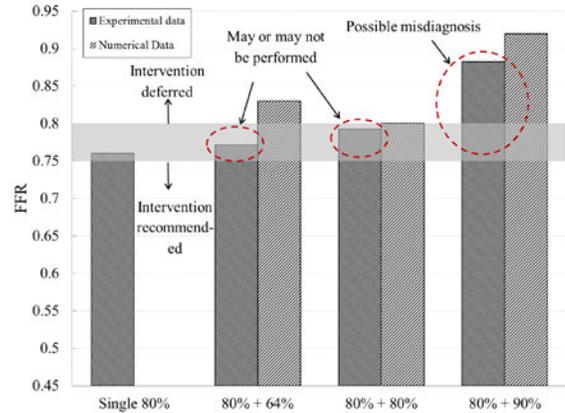


Figure 2: Bargraph showing the effect of a downstream stenosis on the FFR of an intermediate upstream stenosis

For a constant intermediate stenosis, in the presence of a 64% downstream stenosis, the FFR value increased from 0.76 [3] to 0.77. A comparable FFR value (7% error) of 0.83 was obtained numerically. Similarly, as the downstream severity increased to 80% and 90% AS, the FFR calculated experimentally increased to 0.79 and 0.88 respectively. The numerical FFR values for the corresponding cases were 0.80 and 0.92 (errors within 1% and 4% of experimental values) respectively.

Based on the above experimental and numerical FFR values, an intervention may or may not be performed for the 80% AS case when coupled with a downstream AS of 80% or 64%. However, the elevation of FFR with a downstream 90% AS above the cut-off value could lead to misinterpretation of the severity of the upstream intermediate stenosis and might even lead to clinical misdiagnosis.

DISCUSSION AND CONCLUSION

We therefore conclude that a varying downstream stenosis overestimates the FFR of a clinically relevant intermediate stenosis located upstream. This would lead to a misinterpretation in severity of the upstream stenosis and possible misdiagnosis of disease.

The complexity of flow through multiple stenoses may be accurately modeled computationally and this may provide for a better analysis of the effects of the two stenoses in series. We would like to extend the steady state flow conditions in this study to include the effect of flow pulsatility. We believe that the error between experimental and numerical results would lie in the range of 0.3%-20% [1].

REFERENCES

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