

# Left main stenting induced flow disturbances on ascending aorta and aortic arch

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## ABSTRACT

**Background and Objectives:** Ostial LM stenting potentially induces turbulence in the aortic wall near the LM ostium, which might be correlated with aorta dilation and dissection. We investigated through a computational fluid dynamic analysis (CFD), the presence and potential consequences of flow turbulences both in the ascending aorta and arch after a stenting left main (LM) mid shaft or distal disease. **Methods:** The model of the ascending aorta and left coronary artery was reconstructed reviewing both angiographic and echocardiographic measurements of 80 consecutive patients (43 males, mean age  $75.1 \pm 6.2$  years) with significant LM mid shaft or distal disease treated in our institution. For stent simulation, a third-generation everolimus-eluting stent was reconstructed. Two stenting procedures (lesion 1:1 or ostial coverage) were investigated. **Results:** The net area averaged WSS of the model resulted higher when the stent covered the lesion 1:1 compared to the ostial coverage (3.68 vs. 2.06 Pa,  $P=0.01$  and 3.97 vs. 1.98 Pa,  $P < 0.001$ , respectively). LM ostial coverage generates more turbulences in the LM itself, in the aortic wall at ostium level, and at the sino-tubular junction compared with the stenting of the lesion 1:1. Conversely, in the ascending aorta, the WSS appears lower when stenting the lesion 1:1. **Conclusions:** Extending the stent coverage up to the ostium, when the ostial region is not diseased, might induce unfavorable alterations of flow; not only both at the level of the LM lesion and ostium sites, but also in the ascending aorta and aortic arch, potentially predisposing the aortic wall to long-term damage.

**Key words:** coronary stent, left main, physiology, interventional, computed fluid dynamic

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## INTRODUCTION

Effects of coronary stenting techniques are generally investigated regarding wall shear stress (WSS) or turbulence of flow at the lesion or bifurcation sites.<sup>[1-2]</sup> Recently, we speculated that ostial left main (LM) stenting potentially induces turbulence in the aortic wall near to the LM ostium.<sup>[3]</sup> Potential impact on the ascending aorta and arch have never been evaluated despite the fact that it would be logical that any turbulence induced outside the coronary tree can propagate at a certain distance within the aortic vasculature. Noticeably, higher WSS within the ascending aorta have been suspected to be involved in aortic aneurysm

and dissection.<sup>[4-5]</sup> The aim of our study is to investigate, by means of computation fluid dynamic analysis (CFD), the presence and potential impact of turbulences induced by ostial LM stenting, not only in the LM but also within the ascending aorta and arch.

## METHODS

### *Construction of the virtual model*

For the computational domain analysis, we reconstructed the ascending aortic arch from the plane of the aortic valve to the left subclavian artery. Both coronary ostia were also modelled, with particular attention to the left coronary stem. The model of ascending aorta and arch and LM was based

on the dimensions obtained after analyzing transthoracic echocardiography (TTE) and coronary angiography (CA) of 80 consecutive patients (mean age  $75.1 \pm 6.2$  years, 43 males) with significant ( $> 50\%$ ) luminal narrowing on quantitative coronary analysis (QCA) LM mid shaft or distal disease. These patients had no significant ascending aorta or aortic valve disease, and they had undergone percutaneous coronary intervention (PCI) between January 1<sup>st</sup>, 2015 and January 1<sup>st</sup>, 2017. The mean diameter of proximal LM, left anterior descending artery (LAD), and left circumflex (LCX), evaluated with QCA were  $4.32 \pm 0.82$  mm,  $3.21 \pm 0.65$  mm, and  $2.52 \pm 0.88$  mm, respectively. The mean LAD-LCX bifurcation angle, measured after the diagnostic angiography using an electronic goniometer was  $52.6 \pm 10.4^\circ$ , whereas the mean length of the LM was  $18.5 \pm 2.7$  mm. Mean diameter stenosis by QCA was  $88 \pm 7.6\%$ , while mean ascending aorta diameter measured, as previously suggested<sup>[6]</sup> at the sinotubular region and before the emergence of right anonymous trunk, was  $28.8 \pm 7.9$  mm and  $28.2 \pm 6.7$  mm, respectively. Following these measurements, the diameters of LCA and LCX were modelled as following: LM 4.5 mm, LAD 3.5 mm and LCX 2.75 mm, with bifurcation angle set up at  $55^\circ$ . A 12 mm length plaque inducing a stenosis of 90% was placed at the mid-shaft position (Figure 1). The height of the aortic take off (distance between the origin of the LM and the aortic valve plane) was set at 10 mm, while the diameter of ascending aorta just above the left coronary origin was set at 28 mm (Figure 2). The model was constructed using Rhinoceros v. 4.0 Evaluation (McNeel & Associates, Indianapolis, IN). The systemic pressure was assumed to be stable at 120/80 mmHg.

### Stent geometry reconstruction

For the stent simulation, we reconstructed the strut design and linkage pattern of a third-generation,

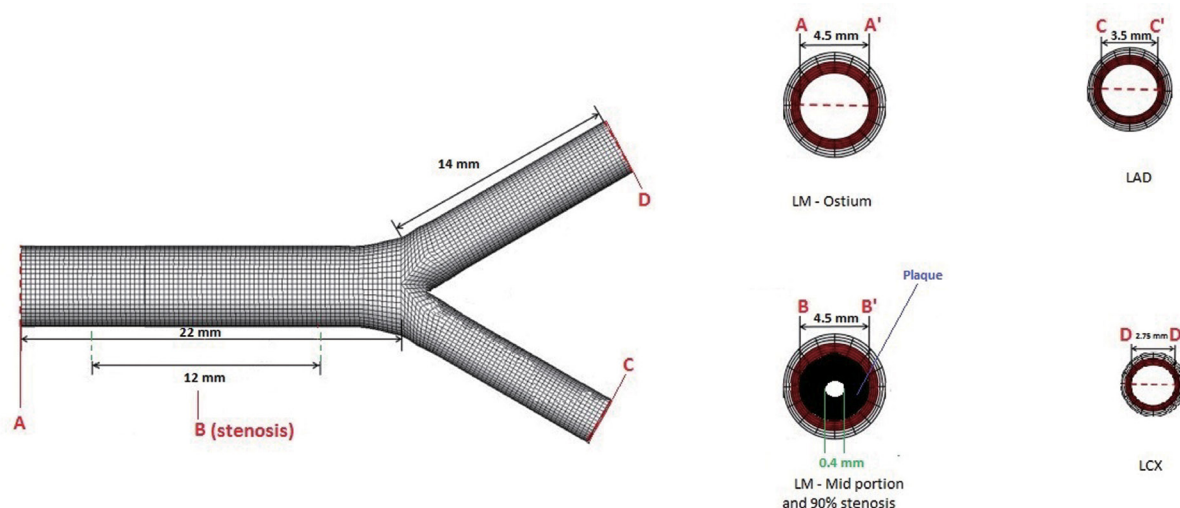
everolimus-eluting stent (ORSIRO stent, Biotronik IC, Bulack, Switzerland), commonly used in our institution. The strut thickness of this stent is characterized by a very ultrathin strut ( $60 \mu\text{m}$  up to 3.0 mm diameter stent and  $80 \mu\text{m}$  up to 4.0 mm stent, Figure 2). Computer Aided Design (CAD) software was used to reproduce the stented geometry as accurately as possible (SolidWorks 2009, Solidworks Corp, Concord, MA). In the first step, we created the solid model of the coronary artery bifurcation and then the expanded stent geometry. For this purpose, a hollow tube with outer diameter equal with both the nominal expanded diameter and thickness of the stent was created. Then, a 2-dimensional sketch with the stent strut was propagated and wrapped around the tube. Through a cut-out, the obtained ring of the stent was propagated axially to create the full-length expanded model.

### Virtual implantation

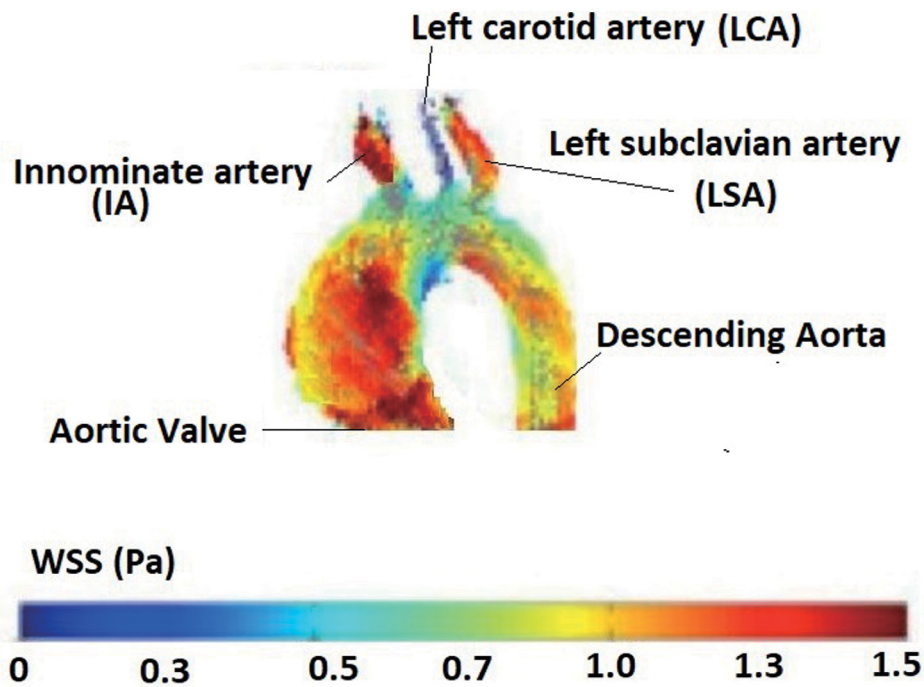
After placing the stent model in the correct position, the stenting procedure was performed following the real procedural steps in the following manner: lesion only or extending the stent coverage up to the ostium in order to assess the potential impact on ascending aorta fluid dynamic.

#### Lesion 1:1:

- Predilation with non-compliant Euphora (Medtronic Inc, USA) balloon  $3.0 \times 12$  mm at 16 atm
- Stent implantation: Orsiro  $4.0 \times 12$  mm at 18 atm covering the lesion 1:1
- Over-dilation with  $4.5 \times 12$  mm non-compliant Euphora (Medtronic Inc, USA) balloon at 20 atm



**Figure 1:** Left Coronary stem model details: diameters of the left circumflex and left anterior descending coronary artery were calculated following the Finet Law.



**Figure 2:** Computational fluid dynamic of the ascending aorta and aortic arch model at basal conditions before any stenting procedure.

### ***Ostial coverage:***

- Predilation with non-compliant Euphora (Medtronic Inc, USA) balloon  $3.0 \times 12$  mm at 16 atm
- Stent implantation: Orsiro  $4.0 \times 15$  mm at 18 atm placed from the lesion itself up to the ostium with no protrusion into the aorta
- Over-dilation with  $4.5 \times 15$  mm non-compliant Euphora (Medtronic Inc, USA) balloon at 20 atm

Using the Boolean operation, the modified solid model was subtracted from the bifurcation model to obtain the final geometry. We assumed that after stent deployment and implantation, there was no residual stenosis.

### ***Computational fluid dynamic analysis***

Blood was modelled as a non-Newtonian, viscous and incompressible fluid. Density was defined as  $1060 \text{ kg/m}^3$ , according to the standard values cited in the literature.<sup>[7-10]</sup> Blood was represented by the Navier-Stokes and continuity equations.

Instead, the Carreau model was applied for the viscosity of blood. Considering that coronary perfusion is mainly diastolic, we performed a steady flow simulation using a basal diastolic pressure of 80 mmHg (10665 Pa). In the

analysis, the static pressure (Pa), wall shear stress (WSS) (Pa) and Reynolds number were evaluated at the lesion site and ostium, whereas the velocity streamlines and the wall shear stress (WSS) (Pa) were evaluated along the ascending aorta and arch.

Static pressure in the vessel was evaluated in Pascal. From a pathophysiological point of view, low static pressure is generally related to increased vessel wall thickness.

WSS was defined as the force that is tangentially acting on the surface due to friction. As it is well known that low WSS are related to the development of greater plaque, higher neo-endothelization and necrotic core progression with a constrictive remodeling, whereas high WSS segments develop greater necrotic core and calcium progression with expansive remodeling.<sup>[11]</sup> The numeric grid was obtained with ANSYS Meshing 14.0 (Ansys, Inc., Canonsburg, PA), while the simulations were conducted using the commercial software ANSYS FLUENT 14.0 (Ansys, Inc., Canonsburg, PA).

### ***Statistical analysis***

Continuous variables were expressed as mean and standard deviation (SD) and compared with the Student's t-test, while differences of WSS were evaluated as delta between the mean WSS values at the same levels in the two models. All

statistical analyses were carried out using the SPSS statistical software version 19.0 (SPSS Inc, Chicago, IL, USA). A  $P$  value  $< 0.05$  was considered statistically significant.

## RESULTS

The net area averaged WSS of the model resulted higher when the stent covered the lesion 1:1 compared to the ostial coverage (3.68 *vs.* 2.06 Pa,  $P = 0.01$  and 3.97 *vs.* 1.98 Pa,  $P < 0.001$ , respectively). Similarly, the static pressure and the Reynolds number were significantly higher after the stent coverage of the ostium as shown in Table 1. LM stenting produced alterations of the fluid dynamic into the ascending aorta and arch. As a matter of fact, the LM ostial coverage induced more turbulence in the LM itself and in the aortic wall at the ostium level and at the sinotubular junction (Figure 3) compared with the stenting of lesion 1:1. In the ascending aorta, the WSS appeared to be lower when stenting lesion 1:1 but only at site 1 (Figure 4), whereas at site 2, the differences between WSS and areas of low WSS were not statistically significant between stenting up to the ostium and lesion 1:1 (Table 2). The differences in WSS were  $0.8 \pm 0.1$  Pa at site 1 and  $0.1 \pm 0.2$  Pa at site 2, with a difference in mean area average of  $0.31 \pm 0.3$  Pa.

## DISCUSSION

Our computational simulation suggested that LM stenting with ostial coverage, different from stenting only on the mid-shaft lesion, induced flow alteration not only at lesion and ostium sites but also in the ascending aorta and aortic arch regions, potentially causing an increase of WSS.

Stenting of LM requires a different strategy depending on whether the location of the lesion is the ostium, mid shaft,

distal or bifurcation. While percutaneous treatment of left main bifurcation disease is still problematic, stenting of ostial and mid-shaft disease is currently widely accepted as a safe alternative to surgery. When mid shaft lesions or distal lesions are to be treated, to extend the strut coverage up to the ostium, or to stent the lesion only is a matter of the operators' choice. Our study suggested that there are some reasons for preferential stenting of a lesion 1:1 over extending the stent up to the ostium.

As a matter of fact, in our study, at the lesion site, to extend the lesion coverage up to the ostium resulted in a decrease in WSS and increase in hydrostatic pressure and the Reynolds number of the models, potentially increasing the chance of restenosis and thrombosis, as suggested by LaDisa *et al.*,<sup>[12]</sup> Seo *et al.*,<sup>[13]</sup> and Koskinas *et al.*<sup>[14]</sup> On the contrary, at the ostium site, a high WSS caused an increase of flow turbulence, and similarly, into the ascending aorta and aortic arch compared to the stenting the lesion on a 1:1 fashion. A propagation to the ascending aorta seems to be an intuitive mechanism, and also, the straightness of the aortic wall section at the ostium caused by ostial stenting might contribute to regional increase of rigidity with subsequent increase in WSS.

As matter of fact, stent implantation at any site induces a flow separation and recirculation immediately downstream of the stents. In a steady flow, within straight vessels, the extent of flow disturbance downstream of the stent increases with both the Reynolds number and the stent wire thickness, but is relatively insensitive to stent interwire spacing.<sup>[12]</sup> These flow disturbances are probably caused by the stent properties and by vessel straightening the stent that conforms to the natural curvature of the artery and causes a reduction in the radius of curvature and subsequent increase in the stiffness

**Table 1: Computed fluid dynamic measurements of the considered parameters. Baseline refers to the model before stent implantation.**

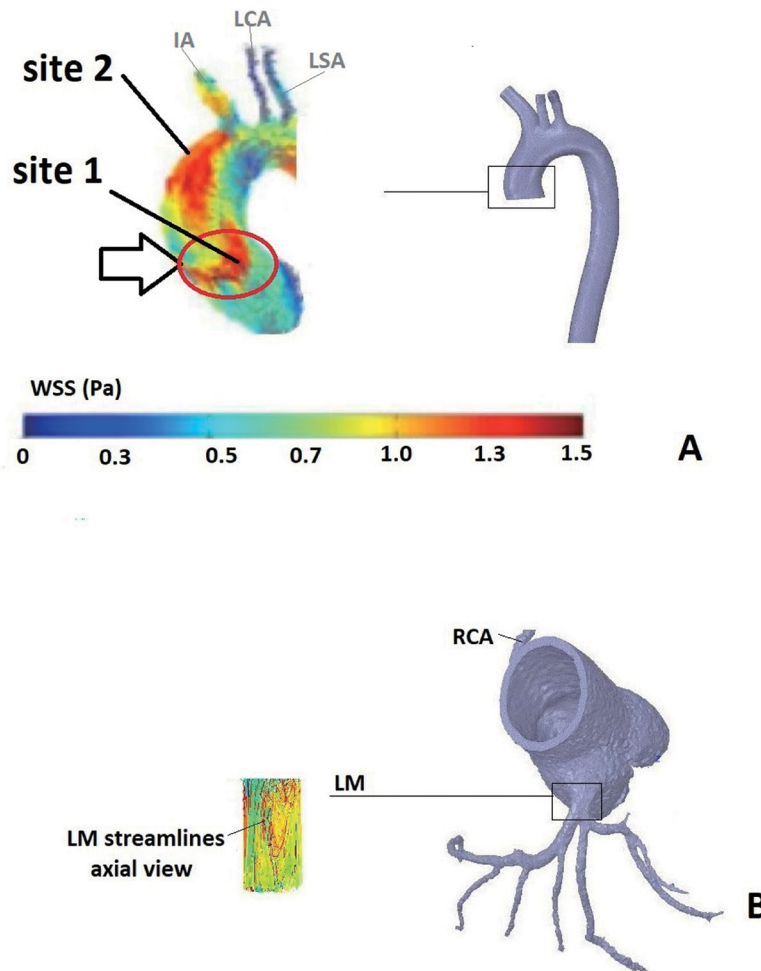
	Baseline	Lesion 1:1	Ostial coverage	$P$
<b>WSS</b>				
Mean WSS [Pa]	6.31	3.21	2.30	0.01
Mean area averaged WSS of the model [Pa]	6.33	3.70	2.12	0.01
<b>Static Pressure</b>				
Static pressure [Pa]	1060.25	10680.35	10740.24	0.01
Mean area averaged Static pressure of the model [Pa]	1052.20	1068.91	1090.52	0.01
<b>Reynolds Number</b>				
Reynolds number	3.30	6.160	2.980	$< 0.001$
Mean area averaged Reynolds Number of the model	3.30	6.230	10.630	0.01

**Table 2: Evaluation of WSS within the ascending aorta and arch**

	Lesion only	Ostial coverage	$P$
<b>WSS</b>			
Mean WSS at site 1[Pa]	$0.4 \pm 0.3$	$1.20 \pm 0.2$	$< 0.01$
Mean WSS at site 2 [Pa]	$1.2 \pm 1.1$	$1.3 \pm 0.9$	0.89
Mean area averaged WSS at site 1 [Pa]	$0.98 \pm 0.4$	$1.29 \pm 0.6$	0.58



## Ostial stenting



**Figure 3:** Computational fluid dynamic of the ascending aorta and aortic arch model after stenting of the Left Main with extension of the stent to the ostium. (A) WSS are severely regionally increased at the sino-tubular junction. (B) Similarly Left Main streamlines showed an increase of flow turbulences.

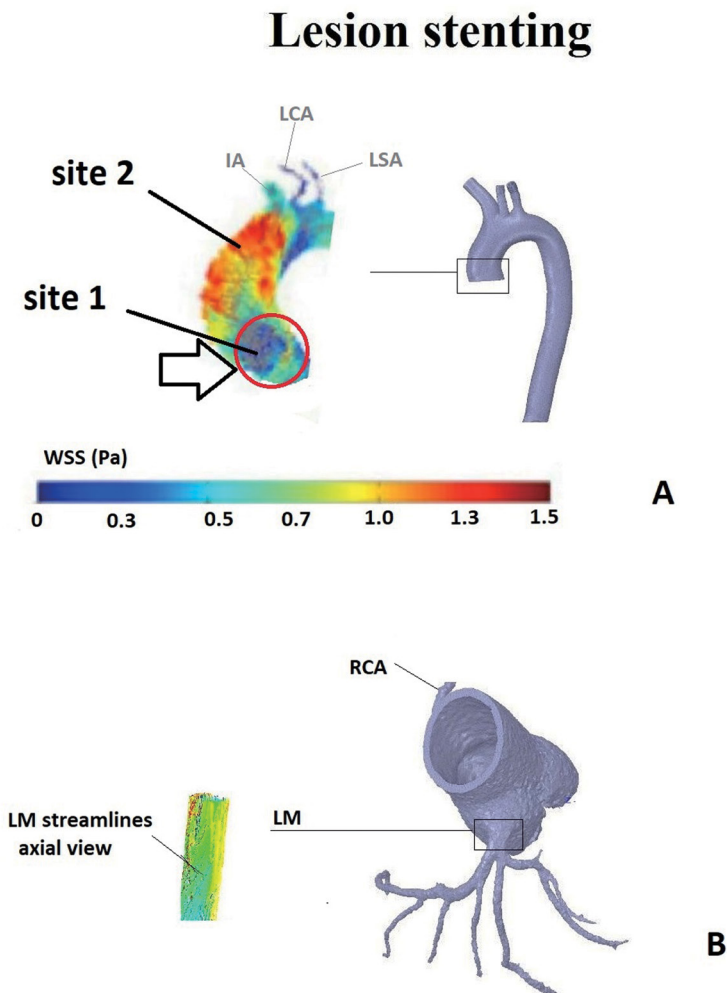
within the stented region. This straightening leads to modest skewing of the velocity profile at the inlet and outlet of the stented region where alterations in indices of WSS are most pronounced.<sup>[15]</sup>

Intuitively, the placement of a rigid stent within an elastic vessel produces wave reflection sites at the entrance to and exit from the stent. The net hemodynamic effects of these reflections depend critically on the degree of stiffness of the stent and on its length and position within the diseased vessel. In LM, stenting up to the ostium might result in an increase of rigidity also in the region of the ascending aorta near to the ostium.

Aldererson *et al.* showed that the presence of the stent within the larger diseased vessel has the effect of producing

higher pressure at the vessel entrance than that at exit.<sup>[16]</sup> This pressure difference, when superimposed on the underlying pressure distribution within the vessel, has the net effect of actually aiding rather than impeding the flow, but the extent of this depends on the length and position of the stent. Similar to the situation where LM is stented in the mild shaft only, a short stent placed near the entrance of the diseased vessel may be favored clinically for producing the least perturbation in the underlying hemodynamics, possibly avoiding an increase of aortic wall rigidity near the LM ostium.

Propagation of flow disturbances and increased WSS in the ascending aorta and aortic arch do not have the same effect of increasing WSS in any coronary vessel. In the latter, the high WSS seem to offer a protection against restenosis



**Figure 4:** Computational fluid dynamic of the ascending aorta and aortic arch model after stenting of the Left Main mid shaft lesion 1:1. (A) At sino-tubular junction WSS are much lower compared to stenting with ostium coverage. (B) Left Main streamlines showed a much less turbulent flow compared to stenting with ostium coverage.

and thrombosis; while in the former, the increased WSS recently have been correlated to propagation of retrograde aortic type B dissection<sup>[17]</sup> and the onset of aortic type A dissection.<sup>[4]</sup>

The increase of turbulence and flow alterations are well known phenomena associated with enlargement of aortic aneurysms,<sup>[18]</sup> and in general, it appears clear that an increase in the turbulence in the ascending aorta and aortic arch might cause damage of the aortic endothelium, leading to both dilation and atherosclerotic plaques, and thus, should be avoided. Dilation of the ascending aorta and alterations in the branching angles seem to be the key determinants of a high WSS and aortic dissection.<sup>[19]</sup> This recent evidence reinforced the suggestion to avoid stent extension to cover up the ostium of the LM when the ostium is not significantly diseased.

### Limitations

Our study considers virtual LM and ascending aorta and arch models. The vessels have been considered non-compliant, straight and with a steady diastolic blood flow in a virtual hemodynamically stable patient. However, coronary artery perfusion is mainly diastolic and previous studies have already demonstrated that myocardial motion has a negligible effect on blood flow distribution on the coronary tree. Our model considered an optimal stent deployment without residual stenosis despite the fact that in daily clinical practice, the different angles, the amount and circumferential extent of the calcium, the length of the respective lesion and many other parameters have an obvious impact on the implantation technique and outcomes. Other limitations of the study are that we did not evaluate the time averaged WSS, oscillatory index and the relative residence time, which had a recognized role in the development of arterial atherosclerosis.

## CONCLUSIONS

Our study confirmed the previous findings, and suggests that to a certain extent, stent coverage up to the ostium when the ostial region is not diseased might induce unfavorable alterations of blood flow not only at the LM lesion and ostium sites but also in the ascending aorta and aortic arch, potentially exposing the aortic wall to long-term damage. Further studies should be undertaken in order to establish if these findings translate into a clinical disadvantage.

## Conflicts of Interest

None declared

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