Hemodynamic effects of lesion length on competitive flow with internal mammary artery bypass

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Abstract

Background: The left internal mammary artery (LIMA) is the most selected vessel in coronary artery bypass graft, because of its long-term patency. But the influence of flow coming from incomplete stenosis of native coronary artery which is called competitive flow is an important factor for graft failure. There are many factors that affect the competitive flow such as the stenosis severity, the amount of myocardial tissue subtended by the stenosis, the length of lesion, as well as the afterload etc. This article is aimed to discuss the hemodynamic influence of different length of intermediate lesion to competitive flow.

Materials and Methods: A patient-special 3-dimensional model with internal mammary artery graft was constructed. The research made a 50% stenosis of six different lengths in the left anterior descending (LAD), including 3mm, 5mm,10mm,15mm,20mm,25mm. Geometric multiscale analysis method which couples the lumped parameter model(LPM) and three-dimensional (3D) model was used in the numerical simulations.

Results: From the results of numerical simulation, graft flow, coronary flow, wall shear stress(WSS) and the oscillatory shear index(OSI) of graft were extracted. With the increase of the lesion length, the mean graft flow and graft WSS increased, in addition, the coronary flow and graft OSI decreased, but when the stenosis reached 15 mm, these variables were stable and almost had no change.

Conclusion: Apart from the stenosis rate, competitive flow is also affected by the length of lesion. Because of the presence of competitive flow, it should be put more attention to choose bypass surgery for moderate stenosis. But below 15mm, with the increase of the length of stenosis, the hemodynamic environment in bypass surgery is becoming better. In summary, for moderate stenosis, stenosis length is a very important factor in the choice of treatment options.

Keywords: competitive flow; coronary artery; the lumped parameter model; WSS; OSI

Introduction

In anatomy, there is no significant correlation between coronary artery stenosis and

myocardial ischemia. Moderate severity of coronary artery disease may lead to ischemia and coronary heart disease. When LIMA is selected, the string sign is the most common phenomenon appearing in the early postoperative period. Most scholars believe that the string sign is caused by the not serious stenosis [1]-[5]. It's reported that the string sign which is described as diffuse distal narrowing of the graft and usually occurs early in the postoperative period has relationship with competitive flow [1][6][7]. As early as 1972, Bousvaros et al [8] proposed the competitive flow. Since then, many scholars studied the influence of competitive flow to graft patency. Nordgaard et al [9] defined the competitive flow as the flow competing each flow from the partially stenosed native coronary artery and from the arterial graft. Numerous studies have shown that the blood flow from native coronary artery reduces arterial graft flow and its long-term patency [10]-[13]. Thus, competitive flow is an important factor affecting early arterial graft patency. [14][15] Many researchers have found that competitive flow may lead to adverse hemodynamic environment, such as low WSS, high OSI which can induce the intimal hyperplasia and atherosclerosis [16]-[18]. Currently, there are a number of researchers dedicated to the competitive flow evaluation. For research of competitive flow, there are three kinds of common methods: statistical analysis of clinical data, animal experiment and numerical simulation analysis. Nakajima H et al [19] believe that a minimum of coronary artery stenosis can be used to measure the intensity of competitive flow. Joseph F.Sabik et al [20] found that the minimum diameter and the coronary artery graft patency has a good correlation. In addition, through clipping the target vessel, graft blood flow changes represent the intensity of the competitve flow [21]. Li lanlan et al [22] studied the hemodynamic effects of competitive flow at varying degree of stenosis. They found that a stenosis rate of less than 50% will cause bad hemodynamic effects, such as low WSS, high OSI. In addition, when the stenosis percentage reaches 50%, there will be inverse flow. The severity of native coronary artery stenosis is not the only factor affecting the hemodynamic parameters, the anastomotic configuration, morphometric parameters and afterload are other major factors affecting the hemodynamics. The stenosis length is also common.

The length is one of determinants of reclusion [23]. Brosh D [24] et al hold the view that lesion length has a significant impact on the physiological significance of intermedia-grade coronary lesions. Fractional Flow Reserve (FFR) is the "gold standard" which determines whether coronary artery stenosis causes myocardial ischemia. According to statistical analysis, it is found that the area of stenosis and lesion length are the most influential factors [25]. Other scholars hold the view that with the degree of moderate stenosis and lesion length increases, FFRCT value will gradually decline to 0.80 or less, indicating that moderate degree of disease and lesion length can also cause myocardial ischemia, which is consistent with clinical results. Even some scholars have shown that when the lesion length is greater than 10mm, there is a strong collection between FFRCT and lesion length [26]. Apart from the degree of lesion stenosis, lesion length is another considerable geometric parameter in the morphological assessment of coronary ischemia, the impact of lesion length on competitive flow has never been adequately assessed. The purpose of this study was to investigate the relationships between competitive flow and lesion length.

Methods

Reconstruction of 3D models

The patient's CT data obtained from a 55-year-old male. A 50% diameter stenosis with different length (3mm,5mm,10mm,15mm,20mm,25mm) was set in the LAD, respectively, by using ‘Freeform’ (software of the 3D modeling system) and ’PHANTOM DESKTOP’ (a kind of force feedback device). In addition, the LIMA was constructed in the process of 3D model establishment. One of the final 3D models are illustrated in Figure 1.

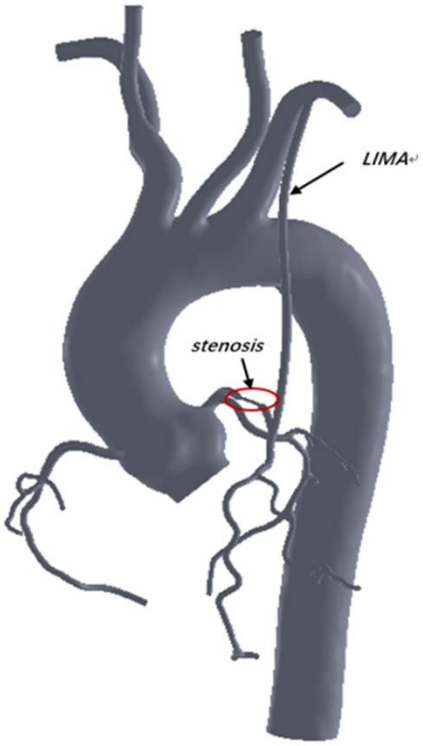

Figure 1. The 10mm stenosis 3D model with LIMA which was anastomosed to the LAD. Seven different length of stenosis were made by hands in the red mark location.

Meshing is the basis of numerical simulation of 3D model, high-quality meshing can guarantee the accuracy of simulation. The computational models were generated by meshing the 3D sub-models with hexahedral mesh. This process is done by the CFX module of commercial software ANSYS. The nodes and elements numbers of the 3D models are shown in Table 1.

Table1. The nodes and elements numbers of the 3D models

Lesion length	***3mm***	***5mm***	***10mm***	***15mm***	***20mm***	***25mm***
nodes	994196	999085	984951	1018705	977169	1017709
elements	1296410	1308740	1290611	1327942	1278619	1334527

Lumped parameter model

Construction of Lumped Parameter Model

Individualized Lumped parameter model can provide physiological boundary conditions for 3D simulation calculation, which cannot be obtained from clinical data such as MR and CT etc. The most common lumped parameter model is the Windkessel model, which simulates downstream resistance and compliance of vessel [27]. The three-element Windkessel model consists of proximal resistance(R_p), a capacitor(C), and a remote resistor(R_d), as shown in the following Figure 2.

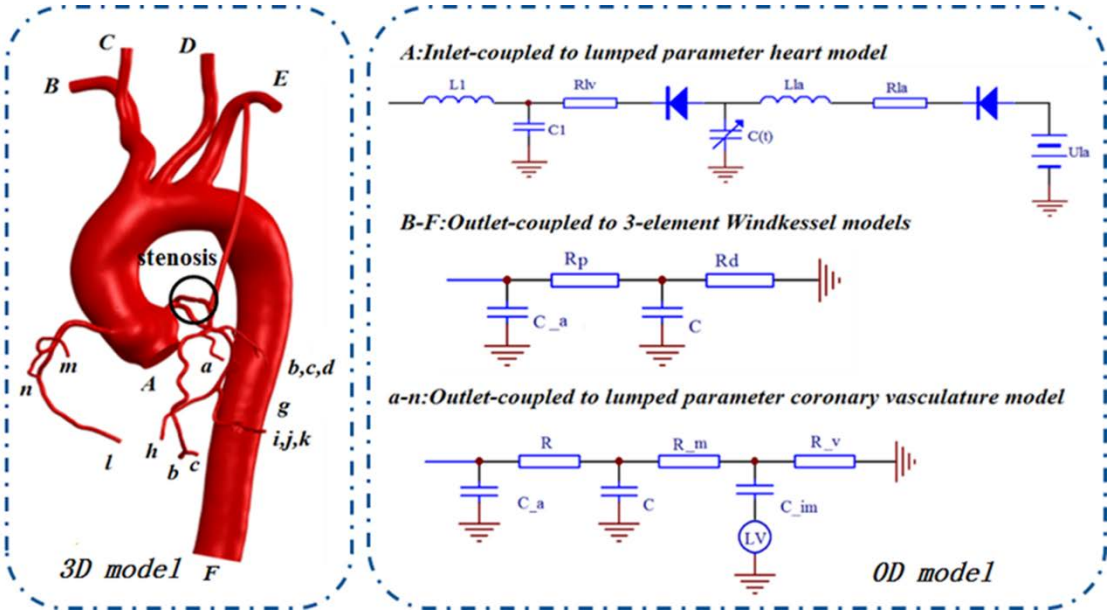

Figure 2. Part A which was coupled with the right aorta lumped parameter model is the inlet. Part B to F are the outlets, and they were coupled to the right middle 3-element Windkessel model. From a to n are also outlets, and they were coupled to the right lumped parameter coronary vasculature model

In this circuit model, the relationship between pressure and flow is shown as Eq.(1), where Q_t is the outlet flow and P_t is the outlet pressure.

$$\mathrm{P}(t) = \left[P(0) - R_p Q(0)\right] e^{-\frac{t}{R_d C}} + R_p Q(t) + \int_0^t \frac{-\frac{t-\tilde{t}}{R_d C}}{C} Q(\tilde{t}) d\tilde{t} \qquad (1)$$

The lumped parameter model of the heart is also shown in the following Figure 2. In the model, the heart valve has a diode to ensure its one-way flow, and the variable capacitance simulates the contraction and relaxation of the heart. Rlv and Rla represent left ventricular blood flow resistance and left atrium resistance, respectively. In the process of cardiac contraction, the coronary artery wall is squeezed, and blood flow decreased significantly, in the diastolic, coronary return to natural state. Based on this factor, a coronary lumped parameter model is created as shown Figure 2, where R, R_m, C, C_{im}, R_v, U_{lv} indicate the coronary artery resistance, microcirculation resistance, the compliance of the vessel, compliance of myocardial, coronary vein and its microcirculation resistance and myocardial pressure, respectively. The complete lumped parameter model is shown in Figure 3.

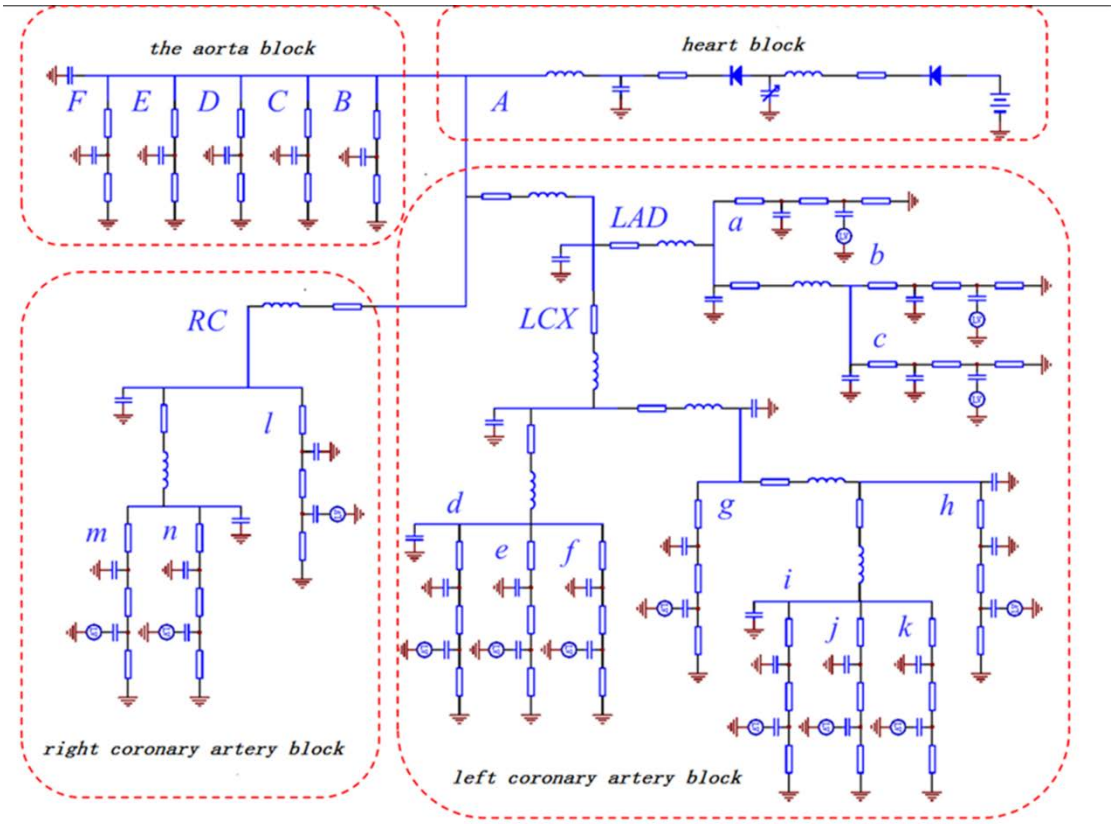

Figure 3. Lumped parameter cardiovascular system model

Parameter Determination of Lumped Parameter Model

In the compartment of the ventricle, the cardiac cycle of the left ventricles was demonstrated by the function of pressure-volume relationship which has been determined by several animal experiments (shown as Eq. (2))

$$\mathrm{E}(t) = \frac{P(t)}{V(t)-V_0} \tag{2}$$

where $\mathrm{E}(t)$ is the time-varying elastance $(mmHg/ml)$, $\mathrm{V}(t)$ and $\mathrm{P}(t)$ are the ventricle volume (ml) and pressure $(mmHg)$, respectively , with the reference volume (ml). Mathematically, the function is used as the approximation (shown as Eq. (3) and Eq. (4))

$$\mathrm{E}(t) = (E_{max} - E_{min}) \cdot E_n(t_n) + E_{min} \tag{3}$$

$$E_n(t_n) = 1.55\left[\frac{\left(\frac{t_n}{0.7}\right)^{1.9}}{1+\left(\frac{t_n}{0.7}\right)^{1.9}}\right]\left[\frac{1}{1+\left(\frac{t_n}{1.17}\right)^{21.9}}\right] \tag{4}$$

where $E_n(t_n)$ is the normalized time varying elastance and $t_n = t/t_{max}$, $t_{max} = 0.2 + 0.15tc$, and tc is one cardiac cycle interval(s). In this paper, we set $E_{max} = 2.0$, $E_{min} = 0.002458$ and $\mathrm{tc} = 0.8\mathrm{s}$.

E_{max} and E_{min}, respectively , are related to end of cardiac systole and end of diastole pressure and volume. Tayor et al [28] have shown that there is a certain relationship between flow distribution and vessel diameter. Based on this theory, by using the genetic algorithm, these values were adjusted to make sure that the cardiac output, the systolic pressures

matched the patient's data. (Table 2)

Table2. The list of model predictions compared against clinical data

	Model Predictions	***Clinical Data***
Systolic Pressure	147.69*mmHg*	147*mmHg*
Diastolic Pressure	103.48*mmHg*	103*mmHg*
Cardiac Output	4.58*L/min*	4.6*L/min*

0D/3D coupling calculations

The algorithm of coupling used in this study has been used in previous studies [29][30]. In the coupling process, the 0D model provides the outlet pressure and the inlet flow rate for the 3D model, and the 3D model provides the inlet pressure and the outlet flow for the 0D model. The coupling problem for each time step between the two dimensional models is calculated using the formula (5) (6). This cycle is calculated at each time step until the result is determined to be convergence.

$$\bar{P}_{3D,in} = \frac{1}{A_{3D,in}} \int_{\Gamma_{in}} P d\gamma = P_{0D,in} \tag{5}$$

$$Q_{3D,out} = \rho \int_{\Gamma_{out}} u \cdot n_i \, d\gamma = Q_{0D,out} \tag{6}$$

A_{3D}, Q_{3D}, Q_{0D} is the interface area, flow of 3D model and interface flow of 0D model, respectively whose unit is cm^2, ml/s, ml/. μ is the interface velocity and P is the average pressure at the interface with their units are cm/s, Pa. Γ_{in} and Γ_{out} is defined of the import and export interface of 0D and 3D.

The convergence judgment condition is as shown in Eq. (7) (8).

$$\left| P_{out}^{(k)} - P_{out}^{(k-T_k)} \right| \leq \varepsilon \tag{7}$$

$$\left| P_{in}^{(k)} - P_{in}^{(k-T_k)} \right| \leq \varepsilon \tag{8}$$

In the 3D simulation, the vessel is assumed to be rigid. The blood flow was treated as an incompressible viscous Newtonian fluid. The density of the blood flow was 1050 kg/m^3, the dynamic viscosity is 0.0035Pa.s.

Results

Graft flow

In coronary artery bypass surgery, the graft flow is a very important indicator that determines whether the operation is successful. The time-averaged graft flow of different stenosis length

in one cycle which were extracted from the middle of the graft are listed in Figure 4.

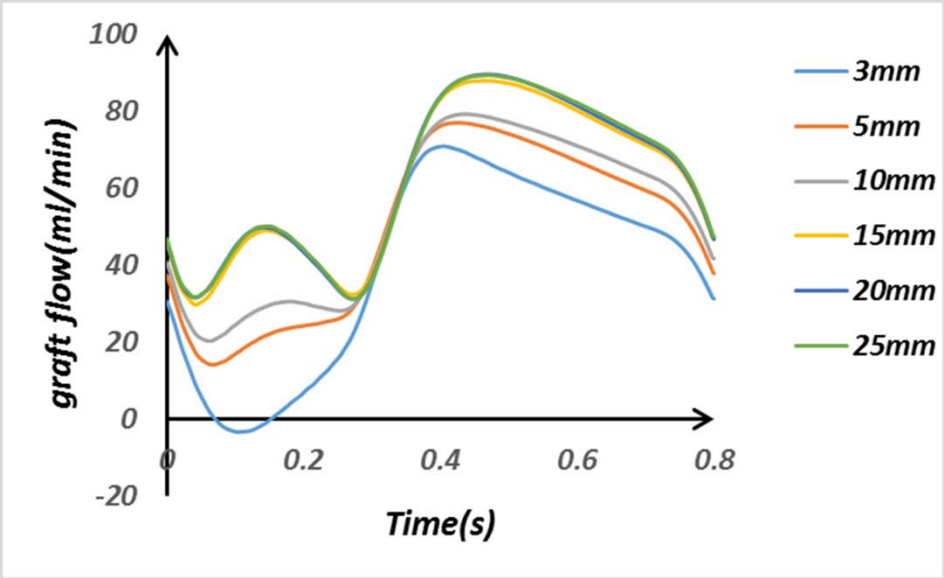

Figure 4. The flow of LIMA with different stenosis length in one cycle

The average flow of graft in one cycle varies with the length of stenosis as shown in Figure 6. It can be seen that the inverse flow appears during the systole in the 3mm stenosis. But with the increase of stenosis length, the inverse flow disappeared. In addition, as the degree of stenosis increases, the graft flow increases, but when the stenosis reaches 15mm, the flow becomes no longer change basically.

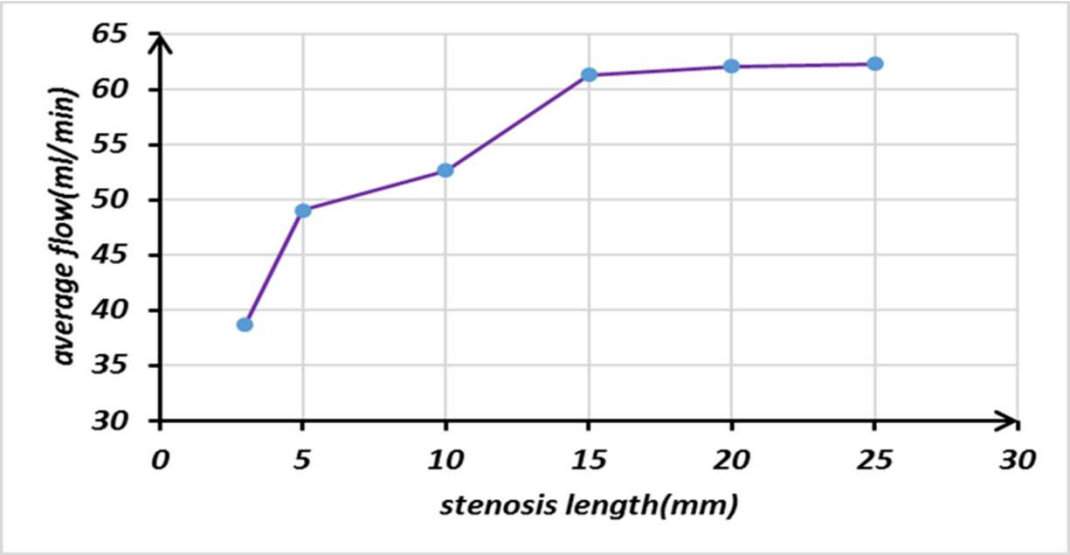

Figure 5. The changing trend of time-average graft flow with different length

Competitive flow

The average flow of the graft and stenosis are shown in the following Table 3. $R_{C/G}$ (Eq.9) is a quantity that characterizes the degree of the competitive flow. The trend is shown in Figure 6. At 3 mm, the graft flow is almost the same as that at the stenosis, indicating that the competitive flow is obvious. This situation is likely to result in the string sign, that is, the failure of the graft. With the increase of the stenosis length, the competitive flow declined,

Table 3. Time-average graft flow, coronary flow and $R_{C/G}$

Lesion length	*3mm*	*5mm*	*10mm*	*15mm*	*20mm*	*25mm*
Q_{LIMA} *(ml/min)*	38.729	49.039	52.633	61.333	62.061	62.289
Q_{LAD} *(ml/min)*	41.375	30.981	27.345	17.907	17.693	17.413
$R_{C/G}$	1.068	0.632	0.520	0.292	0.285	0.280

but when the length reaches 15mm, the competitive flow becomes basically no longer change.

$$R_{C/G} = \frac{Q_{LAD}}{Q_{LIMA}} \tag{9}$$

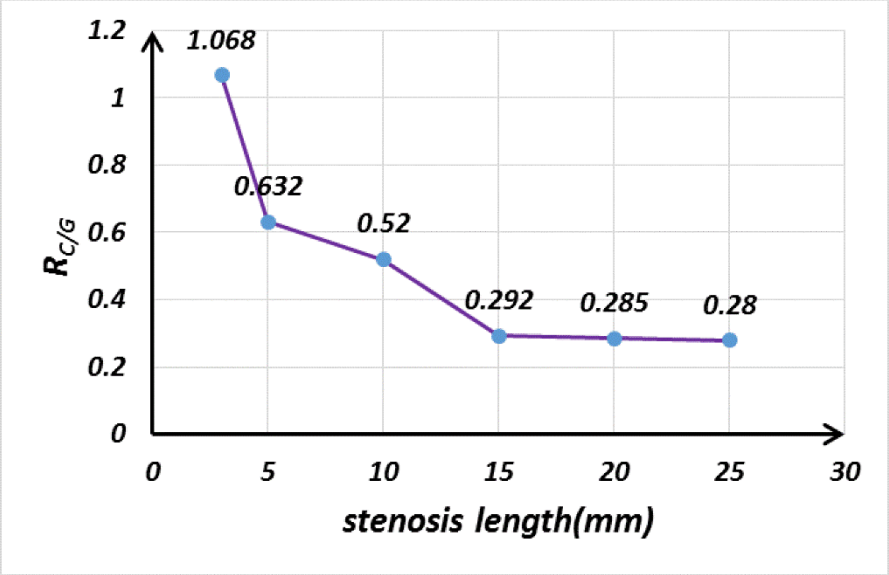

Figure 6. $R_{C/G}$ for LIMA in each model

Wall shear stress

Many studies have found that wall shear stress is an important factor that relates the blood flow to the localization of atherosclerosis which is characterized by localized plaques that form within the artery wall and the plaque rupture. According to the Poiseuille theory, WSS is proportional to blood viscosity and blood flow, inversely proportional to the diameter, the formula is as follows Eq. (10) and Eq. (11). The average wall shear stress for graft vessel in one cycle is shown below Figure 7. The wall shear stress contour at the peak systolic flow rate were extracted (Figure 8).

$$\text{wss} = \tau_{\omega} = -\mu \frac{du}{dr} \tag{10}$$

$$\text{wss} = -\mu \left[\frac{2Q}{\pi R^4} (-2r)|_{r=R} \right] = \frac{4\mu Q}{\pi R^3} \tag{11}$$

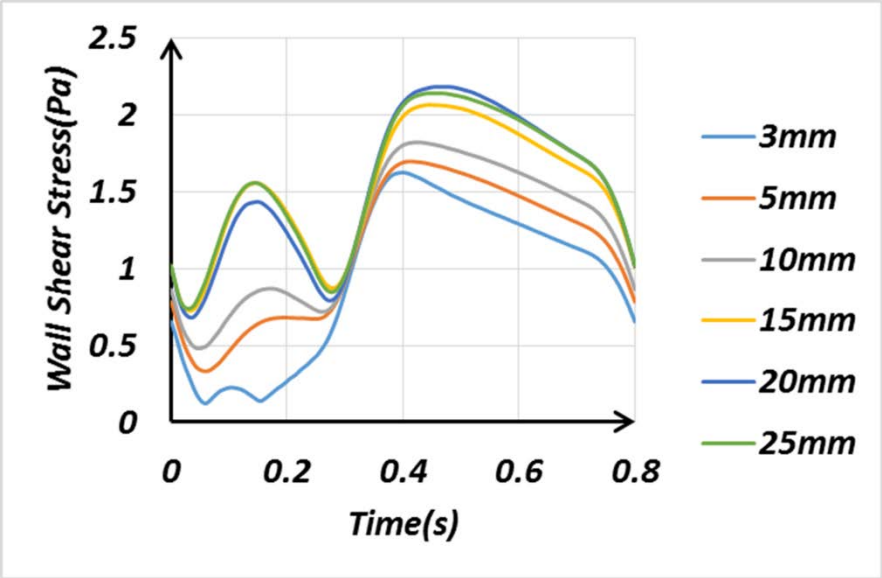

Figure 7. The graft WSS of different stenosis length in one cycle

Oscillatory shear index

The OSI is a known predictor of formation of atherosclerosis and vulnerability for plaque in coronary arteries. The OSI for the pulsatile low simulation is calculated as [29]

$$\mathrm{OSI} = 0.5\left(1 - \frac{\left|\int_0^T \overrightarrow{\tau_\omega} dt\right|}{\int_0^T \left|\overrightarrow{\tau_\omega}\right| dt}\right) \tag{12}$$

where $\overrightarrow{\tau_\omega}$ represents wall shear stress, dt means differential time, and T is upper limit of integral. Table 4 shows the average OSI value of the LIMA surface. It can be seen that when the stenosis length increases from 3mm to 25mm, the OSI decreases from 0.0190 to 0.0042. As the degree of stenosis increases, the OSI gradually decreases. When the stenosis reaches 15mm, OSI changes very little.

Table 4. The OSI values of the six grafts

Lesion length	***3mm***	***5mm***	***10mm***	***15mm***	***20mm***	***25mm***
OSI	***0.019***	***0.0076***	***0.0054***	***0.0045***	***0.0043***	***0.0042***

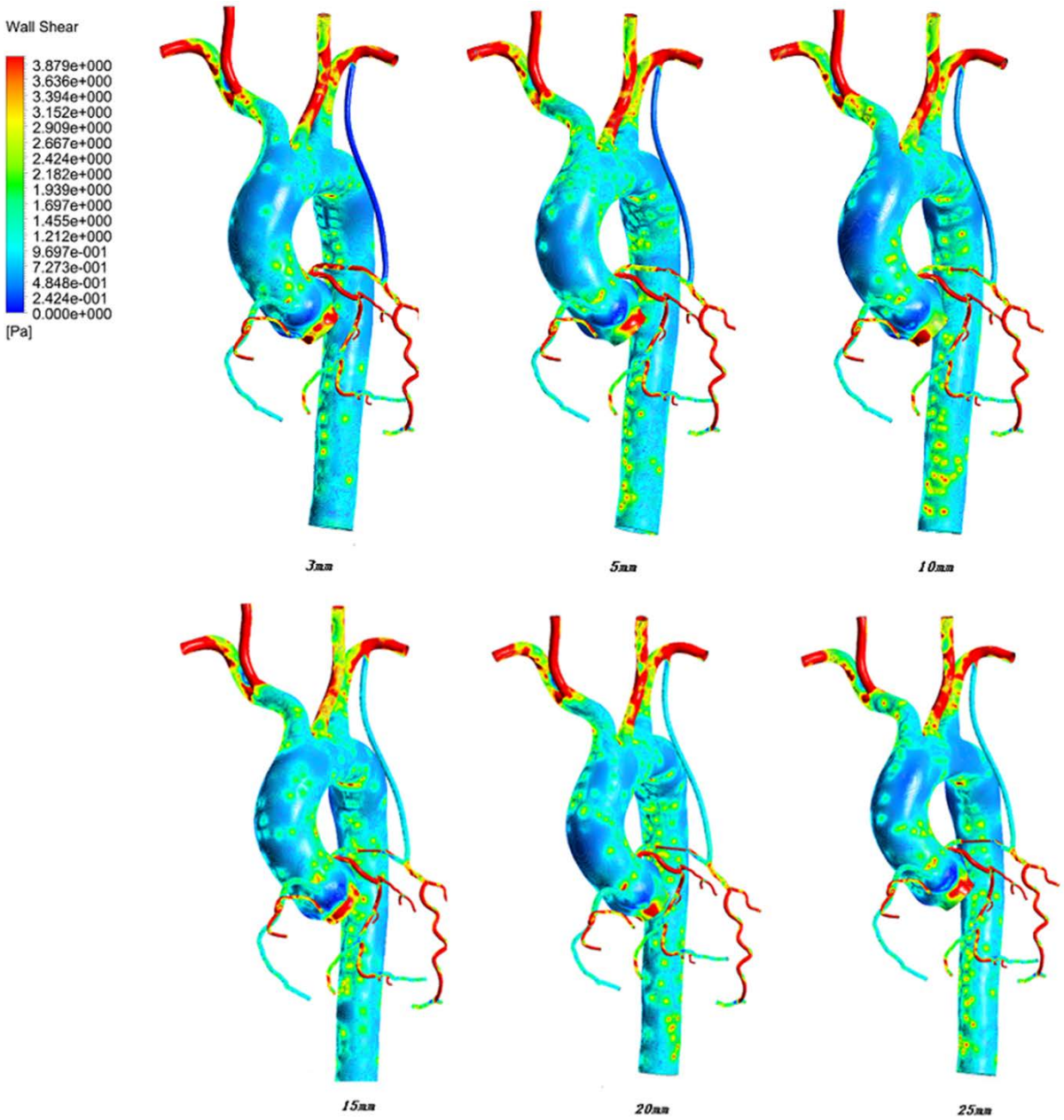

Figure 8. The WSS contours at the moment of maximum graft flow.

Discussion

Competitive flow

Inverse flow is a bad hemodynamic phenomenon that may lead to string sign. In clinical surgery, the severity of inverse flow is a factor for doctors to judge the surgical results. The inverse flow appeared in the 3mm stenosis, but in other lengths, the inverse flow disappeared. With the increase of the stenosis length, the average blood flow in the upstream of the anastomosis decreased continuously, but when the stenosis reached 15 mm, the blood flow remained at a steady state basically. Compared with the results of Li lanlan [22], when the lesion length reached 15mm, the graft flow is similar to the degree of 75% stenosis. In other words, when the lesion length increases to a certain value, it can also produce the same degree

of severe stenosis results. Because of the differences in the coronary of each individual, the correspondence between the lesion length and the degree of stenosis is also different in terms of the competitive flow. Therefore, facing with the treatment choice of moderate narrow, the narrow length is a decisive factor.

WSS&OSI

Zhao et al. hold the view that the high OSI might be the major hemodynamic characteristic leading to the string sign in an LIMA graft. In this study, we found that the wall shear stress has a peak in the systolic period. When the length is less than 15mm, the wall shear stress increases with the increase of the stenosis length, but it does not change after 15mm. So in a certain range of stenosis length, the longer the stenosis, the better the long-term patency of the graft. From the OSI point of view, when the lesion length reaches 15 mm, the OSI value does not change, but before 15mm, the longer the length, the graft OSI is smaller.

Limitation

The limitations of the article are mainly reflected in the following aspects. Firstly, for the boundary conditions of 3D model, there is a gap between model and the physical reality. For example, in order to reduce the calculation time, the vessel wall is set to be rigid, in fact, the properties of blood vessels is very complex, and fluid-structure interaction (FSI) was not considered due to the complex 3D models.

Conclusion

Except for the stenosis rate, the stenosis length is also an important factor influencing the competitive flow, but not linearly. As the lesion length increases, the competitive flow decreases, but when the narrow length reaches 15 mm, the competitive flow does not change.

Acknowledgements

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