Numerical Simulation of Instantaneous Wave-Free Ratio of Stenosed Coronary Artery

†Wenxin Wang[1], Boyan Mao[1], Bao Li[1], *Youjun Liu[1], Jinshseng Xie[2]

1 College of Life Science and Bioengineering, Beijing University of Technology, Beijing, China
2 Beijing AnZhen Hospital Affiliated to Capital Medical University, Beijing, China

*Presenting author: wangwenxin@emails.bjut.edu.cn
†Corresponding author: lyjlma@bjut.edu.cn

Abstract

Instantaneous wave-free ratio (iFR), an invasive index of coronary artery tree, can evaluate the functional performance of vascular stenosis without pharmacological vasodilators. The non-invasive assessment of diameter stenosis (DS) obtained from coronary computed tomography angiography (CTA) has high false positive rate in contrast to iFR. The aim of this study was to developed a numerical simulation method that predicts the iFR and non-invasive assess the myocardial ischemia. Based on the CTA images, a patient-specific 3 dimensional model of the aorta and coronary arteries were reconstructed. A stenosis was created in the left anterior descending artery (LAD) by reducing the DS of geometric model (40%, 50%, 60%, 75% and 90%). The patient-specific LPM boundary condition were set up to compute iFRct value during the wave-free period at the resting condition. The computed pressure and flow of coronary artery were realistic as compared to literature data. The iFR of the numerical simulation results (iFRct) has very significant positive correlation with the mean flow rate of LAD, which means that iFRct was a functional index of coronary stenosis and was consistent with the clinical significance. In contrast to invasive iFR, the iFRct can make a cost-benefit balance in terms of clinical cost and patient's health.

Keywords: Computational fluid dynamics (CFD), Coronary artery, Instantaneous wave-free ratio (iFR)

Introduction

Coronary artery disease is caused by coronary stenosis, which reduces the myocardial perfusion, results in ischemia, infarction, and even death. Stenosis is only an anatomic description of coronary artery disease. In clinic, in order to treat coronary artery disease, it is important to know whether the physiological or hemodynamic significance of a coronary stenosis could cause the coronary ischemia or not. Coronary stenosis severity has no absolute correlation with myocardial ischemia.

In recent years, instantaneous wave-free ratio (iFR), an important index of coronary stenosis, isolates a specific period in diastole, which called the wave-free period (WFP), and uses the ratio of distal coronary pressure (Pd) to the pressure observed in the aortic (Pa) [1]. In this period, the competing forces (waves) that affect coronary flow are quiescent meaning pressure and flow are linearly related as compared to the rest of the cardiac cycle [2]. During the WFP, the coronary flow rate is higher and the pressure is lower, which leads to coronary microcirculation resistance the most stable and the lowest. At the same time, the pressure and flow of coronary artery are linearly related as compared with the rest of cardiac cycle. The WFP begins 25% into diastole and ends 5ms before the end of diastole [3]. The concept of iFR was originally came from the wave intensity analysis using both coronary pressure and flow rate values [4]. Fractional flow reserve (FFR) is the gold standard for determining whether a coronary artery stenosis causes ischemia [5][6]. Sen S et al. [2] studied that there was a good correlation between iFR and FFR. FFR and iFR can only be measured using invasive coronary artery catheterization, however, which limits its widespread use in clinical practice. The data have shown that the clinical application rate of FFR is less than 6% in America [7], and that of iFR is even less.

On the other hand, computational fluid dynamics (CFD) has been applied to simulate the blood flow and pressure in patient-specific coronary artery models, which are coupled the lumped parameter model and the 3D model reconstructed from coronary computed tomography angiography (CTA) [8]. The multicenter and prospective clinical trials of DISCOVER-FLOW [9][10], DeFACTO [11] and NXT[12], which predicted the FFRct value through combining patient-specific CTTA images and CFD simulations, have improved diagnostic accuracy than CTA alone to evaluate the ischemic and non-ischemic stenosis. Therefore, iFRct derived from non-invasively through combining CTTA images and CFD can improved diagnostic accuracy as same as FFRct. We just need to simulate at the resting state, without the hyperemia state. In this way, it can avoid the mistake causing by simulating the hyperemia state.

In this study, we developed a numerical simulation method, which could simulate the pressure and flow of coronary artery at the resting (baseline) condition and predict the iFR value (iFRct) from CTA images using 0D/3D coupled method. The 0D/3D coupled method was used in this study to perform a numerical simulation by coupling the lumped parameter model (LPM; 0D sub-model) and 3D vascular sub-models. This method has been used in our previous hemodynamic research and proven useful in studying cardiovascular system [13][14]. The iFRct method can non-invasively assess the level of myocardial ischemia and avoid the deviations when simulate the coronary vascular beds were maximally dilated (hyperemia) condition.

Method

Study Design

The main purpose of this study was to develop a numerical simulation method which could predict the iFRct derived from CTA images and non-invasive assess the myocardial ischemia. The Ethics approval and consent to participate are not applicable, as it is a retrospect study. The patient's records or information have been anonymized prior to analysis. The patient didn't have a cardiac event and/or PCI in CTA examination in this study.

The patient-specific three-dimensional (3D) anatomic geometry was reconstructed, as illustrated in Fig.1. A moderate stenosis (DS≈50%) was applied to left anterior descending (LAD) in patient-specific model. In order to verify the feasibility and correctness of the computational simulation method, the other four 3D stenosis models were built by reducing the local diameter of the geometric model (including 40%, 60%, 75% and 90%) at LAD.

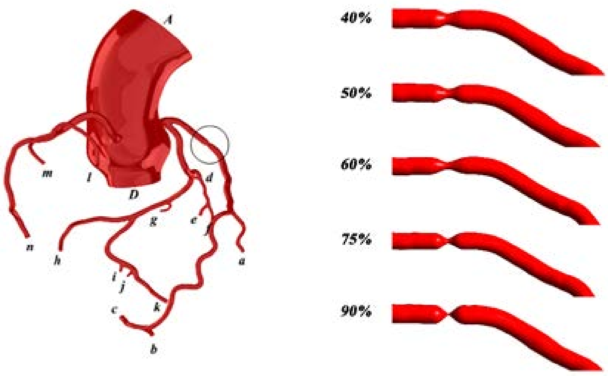


Fig 1. The reconstructed 3D geometry and LAD with different diameter reduction

Imaging acquisition

In this study, CTA images of the patient were provided by Beijing An Zhen Hospital in China. The 3D geometry of coronary arteries was reconstructed from CTA images with a slice thickness of 1mm. The simultaneous acquisition of multi-slice enabled the images of coronary and aorta in a single breath hold. The initial data window was positioned at 70% of the R–R interval. The cardiac output of the patient measured was 5.4 L/min. Four hundred and sixty slices of CTA images with 512×512 pixels were used for 3D reconstruction.

Geometrical models and computational models

Similar to our previous studies, the patient-specific 3D anatomic geometry was reconstructed through both the threshold segmentation and manual segmentation using the software MIMICS [13]-[16]. Based on these data, a moderate stenosis (stenosis degree ≈ 50%) was applied to the LAD artery. A hexahedral mesh was generated mainly by using the ANSYS-CFX (ANSYSTM). A steady state grid sensitivity analysis was conducted to make sure that the relative error in two consecutive mesh refinements < 1% for the maximum velocity.

In order to verify the correctness of the numerical simulation method, other four models with different stenosis in the LAD artery were constructed, reducing the local diameter of the geometric model by 40%, 60%, 75% and 90% respectively. Table 1 provides the geometric characteristics of stenosis LAD. The number of nodes and elements in these five models are within the same order of magnitude.

Similar to our previous study [14][15][17][18], the lumped parameter models were used in this study. On the basis of the 3D vascular models and the LPMs, 0D/3D coupled models were constructed, as illustrated in Fig.2. The boundary conditions of the 3D part were supplied by the 0D calculation and the forcing terms of the 0D part were calculated by the 3D simulation. Five 3D models shared the same 0D part since the patient's peripheral vascular structure was not changed with different stenosis. The algorithm of 0D/3D coupling method used in this study was also applied in our previous study. The difference was that we modified the lumped parameter model of right coronary which was not subjected to the pressure of the left ventricle (Plv). In addition, the coronary venous microcirculation compliance was eliminated from the original model in order to simplify the numerical simulation [8].

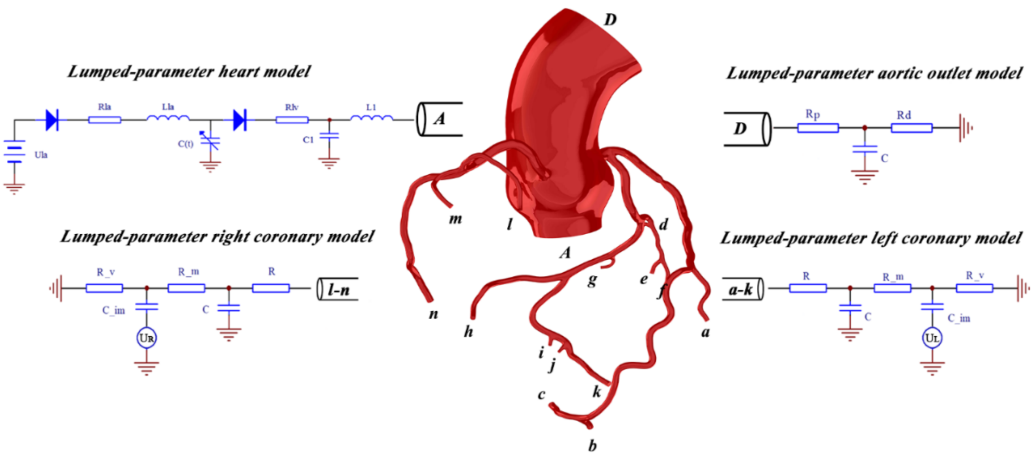


Fig 2. The 0D/3D coupled model

The 0D/3D coupled model

Similar to our previous study [13][14], governing equations were formulated for aorta and coronary arteries. In the 3D model, it was assumed that the vessel walls were rigid. The blood flow was treated as an incompressible viscous Newtonian fluid. The density of the blood flow was 1050 kg/m3 and the dynamic viscosity was 0.0035 Pa s. Navier-Stokes and continuity equations were solved using the commercial software solver ANSYS-CFX. Similar to previous studies [13][14], four cardiac cycles were set to implement convergence for transient analysis. The explicit Euler method was used and the constant time step was set in per cardiac cycle (=0.8s). In the 3D model, the time step was 0.0025s, while that was 0.0001s in 0D model. The boundary conditions of the 3D part were supplied by the 0D calculation and the forcing terms of the 0D part were calculated by the 3D simulation. All the 3D models shared the same 0D part since the patient's peripheral vascular structure did not change with surgery. Therefore, the variation of simulation results can be considered that only caused by the differences of 3D models. In each block of coronary branch, the resistance (R) was used to simulate the flow resistance, the capacitance (C) was used to simulate the compliance of the vessel, and the inductance (L) was used to simulate the inertia of the blood flow.
In the compartment of the ventricle, the function of pressure-volume relationship was applied to demonstrate the cardiac cycle of the left and right ventricle.

$$E(t) = \frac{P(t)}{V(t) - V_0} \tag{1}$$

Where $E(t)$ is the time-varying elastance (mmHg/ml).   and   are the ventricle volume (ml) and pressure (mmHg) respectively.   is the reference volume (ml). Mathematically, the function was used as the approximation.

$$E(t) = (E_{\max} - E_{\min}) \cdot E_n(t_n) + E_{\min} \tag{2}$$

where $E_n(t_n)$ is the normalized time-varying elastance.

$$E_n(t_n) = 1.55 \left[\frac{\left(\frac{t_n}{0.7}\right)^{1.9}}{1 + \left(\frac{t_n}{0.7}\right)^{1.9}} \right] \left[\frac{1}{1 + \left(\frac{t_n}{1.17}\right)^{21.9}} \right] \tag{3}$$

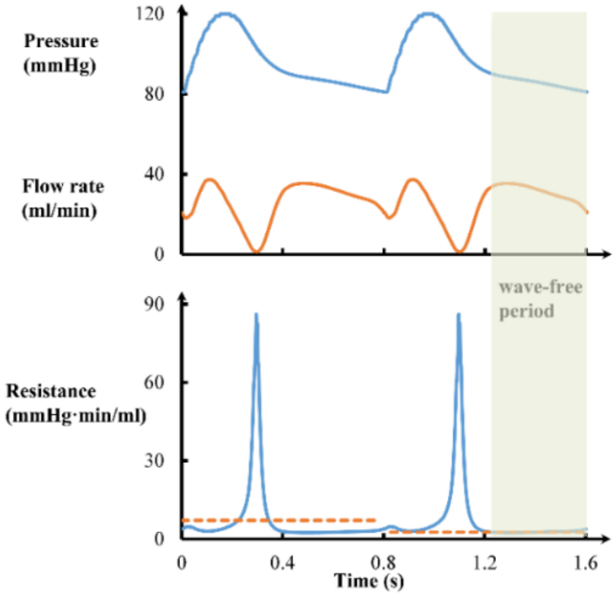
tc is the cardiac cycle interval (s). In this paper, we set $E_{\max} = 2.0$, $E_{\min} = 0.002458$ and $tc = 0.8s$.
The value of the parameters in the 0D network of coupled models were based on data from research into the modeling of coronary arteries [8]. The genetic algorithm was used to tune the parameters of the LPM model. In this way, the systolic pressure, the diastolic pressure and the cardiac output was matched the patient’s data.

Results

The iFRct values has been proposed as a new index of stenosis severity that is independent of hyperemia. It used the ratio of distal coronary pressure (Pd) to the pressure observed in the aortic (Pa) over this period.

$$iFR = \frac{Pd}{Pa} \tag{4}$$

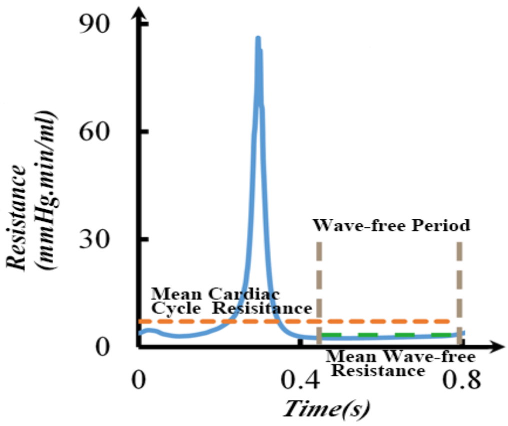
Not only the pressure, flow rate and the resistant of the section, but also the WFP is illustrated



in Fig.3.

Fig 3. Definition of the wave-free period

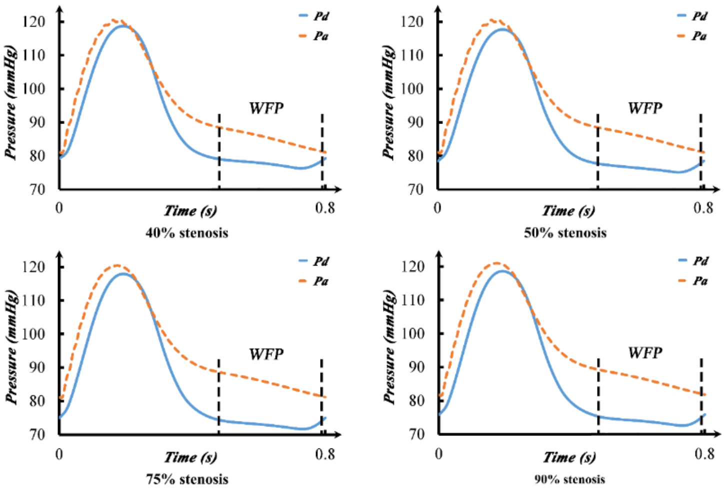
Moreover, the mean resistant of cardiac cycle and wave-free period are illustrated in Fig.4. The orange line and green line represent the resistance of the whole cardiac cycle and WTP,



respectively. Compared with the resistance of cardiac cycle, the resistance of WTP decreases 51.25%.

Fig 4. Mean resistance in whole cardiac cycle and wave-free period

The aortic pressure is used as Pa in the equation (4), while the coronary pressure distal to the stenosis in the 3D model is used as Pd. For every different stenosis model, the Pd and Pa in



cardiac cycle are plotted in Fig.5.

Fig 5. The Pd and Pa of five different stenosis model

During the WFP, the contours of iFRct in different stenosis models are illustrated in Fig.5. With the increase of the degree of the stenosis (DS), the iFRct value gradually reduces.

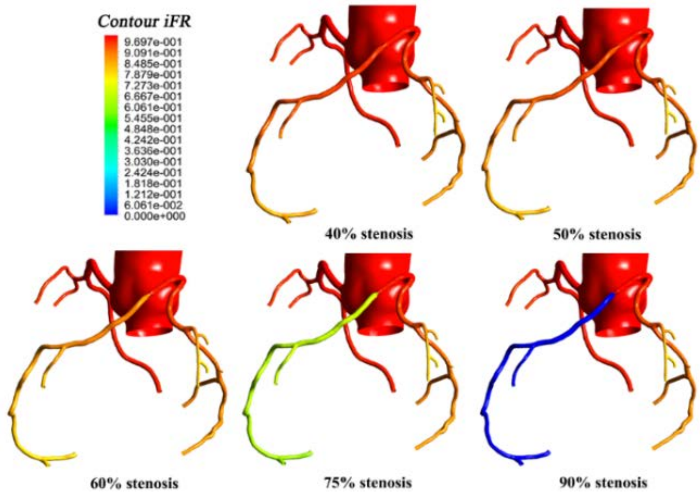


Fig 6. The iFRct contour of different stenosis models

The iFRct value of Model 1 is 0.965. And the iFRct of other four models are listed in Table 1. With the increase of the degree of stenosis, the mean flow rate of LAD is gradually decreased as followed: 81.18 ml/min, 79.64 ml/min, 77.47 ml/min, 64.22 ml/min and 12.79 ml/min. The iFRct contour of different stenosis models are plotted in Fig.7.

Table 1. The iFRct values of different stenosis models

Model	DS (%)	AS (%)	Flow Rate	iFRct
1	40	64.00	81.18	0.965
2	50	75.00	79.64	0.948
3	60	84.00	77.47	0.907
4	75	93.75	64.22	0.680

5	90	99.00	12.79	0.060

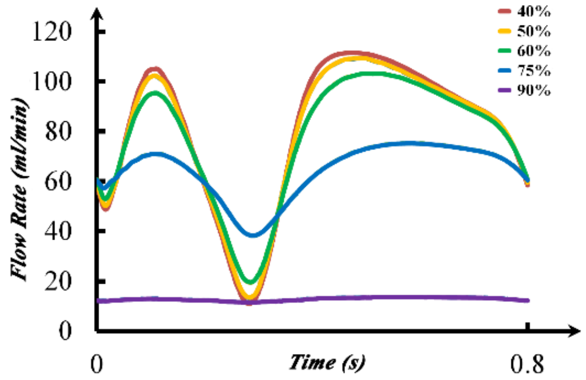


Fig. 7 The flow rate of different stenosis models

Discussion

In order to investigate the numerical simulation method of iFRct of stenosed coronary artery, multi-scale studies were conducted based on patient-specific model with different stenosis.

Similar to some study of Taylor, the inflow boundary condition was used, which coupled the lumped parameter heart model and a lumped parameter coronary model. We have successfully developed a numerical simulation method that coupled the 0D and 3D coronary model to calculate the iFRct. Noninvasive evaluation of the functional significance of coronary stenosis is possible using numerical simulation method based iFR from CTA data.

When the degree of stenosis was more than 75%, iFR was less than 0.86 (the critical value of myocardial ischemia). The DS was negatively correlated with iFR and the mean flow rate of LAD in low level of significance. The iFR had very significant positive correlation with the mean flow rate of LAD. So using iFRct was more accurate, to assess the myocardial blood supply. The iFR was a functional index of coronary stenosis in clinical application, and was consistent with the numerical simulation results. At the same time, it was proved the numerical simulation method could calculate the iFR.

This promising simulation method provided a combined anatomic-physiology-functional evaluation of coronary artery disease with the aim of improving clinical diagnostic accuracy while avoid the vasodilators, invasive pressure wire techniques and the unnecessary costs.

Future Work and Limitation

This paper developed a noninvasive method to assess myocardial ischemia. In the future, the physiologic realism of the boundary conditions can be improved even further in the simulation by the closed-loop lumped parameter network model which may consider the interactions between the heart and arterial system, and the models with different patients (have different afterload) to assess competitive flow is necessary.
Our model just considered the LAD artery with the only one stenosis, since the incidence of atherosclerotic lesions in the LAD artery was the highest and the stenosis was severe. The results and conclusion might be different when the coronary artery with two or more stenoses.

Conclusion

We have successfully developed a numerical simulation method to predict the iFR and non-invasive assess the myocardial ischemia. In anatomical, there is not absolutely correlation between sever stenosis of coronary artery and myocardial ischemia. Therefore, it is necessary to non-invasive assessment of myocardial ischemia by simulating iFRct.

FFR and iFR are both a functional evaluation indicators of coronary artery, however, the numerical calculation of iFRct requires only simulating the resting state without the hyperemia state. Some hypotheses must be set to simulate the hyperemia state of coronary artery, which may cause deviation with real physiological situation and may impair the accuracy of the assessment.

The iFR of the numerical simulation results (iFRct) have very significant positive correlation with the mean flow rate of LAD, which means that iFRct is a functional index of coronary stenosis and is consistent with the clinical significance. In contrast to invasive iFR, the iFRct can make a cost-benefit balance in terms of clinical cost and patient’s health.

Competing interests

The authors have declared that no competing interests exist.

Acknowledgement

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