Hemodynamic Impact of Stenting on Carotid Bifurcation: A Potential Role in the Stented Segment and External Carotid Artery

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Hemodynamic impact of stenting on carotid bifurcation: a potential role in the stented segment and external carotid artery

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Abstract

Carotid stenting near the bifurcation carina is associated with adverse events, especially in-stent restenosis, in-stent thrombosis, and side branch occlusion in clinical data. This study aims to determine the potential biomechanical mechanisms for these adverse events after carotid stenting. The patient-specific carotid models were constructed with different stenting scenarios to study the flow distribution and hemodynamic parameters, such as wall shear stress (WSS), flow velocity, relative residence time (RRT), and oscillating shear index (OSI) in the carotid bifurcation. The results suggested that existing stent obviously reduced blood flow to external carotid artery (ECA) but enhanced local flow disturbance both in ECA and stented internal carotid artery (ICA), and the inner-posterior wall of stented ICA and the outer-posterior wall of ECA might endure a relatively low level of WSS and remarkably elevated OSI and RRT. In addition, the implanted stent leads to more ECA adverse flow than stented ICA. While disturbed flow in the vicinity of strut increased as stent length increased, blood flow and areas of local flow disturbance in ECA slightly decreased as stent length increased. In conclusion, the results revealed that ECA might be in relatively high levels of abnormal local hemodynamics after stenting, followed by stented ICA, leading to potential adverse events after interventions.

Keywords: Carotid Bifurcation, Stent, Hemodynamics, Restenosis, Occlusion

1 Introduction
The carotid bifurcation consists of external carotid artery (ECA), internal carotid artery (ICA), and common carotid artery (CCA). Early clinical studies demonstrated that atherosclerotic lesions in the carotid bifurcations usually developed at the distal CCA and the proximal ICA [1-3]. The intervention, a breakthrough treatment for occlusive vascular disease, becomes an effective and widely used therapy, especially for carotid bifurcation lesions. However, this treatment may account for clinical events during follow-up. The disadvantages of this treatment are clinically evidenced by a relatively high risk of in-stent recurrent stenosis and fatal complication of in-stent thrombosis [4-6]. In-stent restenosis (ISR) after stenting in carotid has been stated to ranges from 1% to 50%, with worse patient outcomes in the long run due to postoperative complications [1, 4-6]. Moreover, intervention in the carotid bifurcations is an independent predictor for occlusion of branches without stenting. The implanted stent usually covers the segment of ICA or CCA because of atherosclerotic lesions. Interestingly, ipsilateral ECA after stenting in the carotid bifurcation presents a high risk of occlusive disease [1-3]. The trial included 312 patients in Netherlands found that more than 50% of stenosis in ipsilateral ECA emerged after carotid stenting [7]. These clinical data suggested that the carotid bifurcation intervention technique caused clinical events at the stented segment and had adverse effects on the branches without stents. Both of these impacts of stenting on the host artery may lead this treatment to compromised clinical benefits.

Despite complicated and multifactorial reasons for these adverse events, the changed hemodynamics caused by stenting has been shown to have an essential role in the
procession of adverse in-stent events and lateral branch occlusion [8-10]. The implanted stent certainly disturbs the local blood flow in the host artery and cause flow separation and stagnation flow around the stent struts, manifested by high relative residence time (RRT) and oscillating shear stress index (OSI), but low wall shear stress (WSS) [11-13], which are evidenced to contribute the vascular injury and ISR and stent thrombosis [8-10]. Since little information is available both on the stented vessel and other branches in bifurcations after stenting, we herein aimed to investigate a potential role of intervention in ECA and stented ICA, based on images of in vivo human patient-specific carotid bifurcation. As non-Newtonian and pulsatile behaviors of blood flow, this work analyzed the local hemodynamic characteristics of carotid bifurcation after ICA stenting in terms of velocity field, flow distribution, WSS, OSI, and RRT. The impact of stenting scenarios (long, medium, and short stenting) on the hemodynamic performance in the treated carotid bifurcation was also addressed.

2 Methods

2.1. Image-based computational model after carotid stenting

The patient-specific carotid bifurcation with stenosis (Fig. 1(A)) was constructed based on angiographic images at some point of the cardiac cycle. The carotid bifurcation images in this study included internal carotid (ICA), external carotid (ECA), and common carotid (CCA). As shown in Fig. 1(A), ICA and CCA were 68 mm and 71 mm at least in length, and eccentric stenosis was observed, and the rate of the narrowest luminal stenosis of ICA was 78.5%.
Fig. 1 (A) Geometry of carotid bifurcation model with stenosis. Figs (B)-(D) are carotid models with a short (13.2 mm), medium (17.7 mm) and long stent (22 mm). The locations of Slices 1-4 are indicated in Fig (D), taken as example. (E) views for the flow presentation. (F) is the inlet fluid velocity waveform [18] applied in this numerical simulations.

The lumen boundaries of carotid bifurcation were manually segmented by Mimics (Materialise N.V.) to develop the carotid model, while the centerline of carotid was simultaneously exacted. This three-dimensional model was subsequently smoothed to make it similar to a true artery in vivo and suitable for calculation. This study was carried out following Beijing Anzhen Hospital regulations, and all volunteers approved this study and written informed consent.

The commercial carotid stent, whose structure resembles ViVEXX, was constructed in Pro/E (Parametric Technology Corporation). Strut thickness and an external diameter of stent are 81 μm and 6.5 mm. Extensive details about geometrical parameters of stent can be found in early works [14].

A stent was finally assembled in the diameter reduction region along the lumen centerline, while the stenosis was removed from carotid. The stent should at least cover all lesion regions. Since clinical evidences suggested that long stent was significantly
related to restenosis [15], stent length effects on hemodynamics after stenting was carried out in the present study. Carotid models (Figs. 1(B)-(D)) were investigated numerically with short (13.2 mm), medium (17.7 mm) and long (22 mm) stenting [16, 17].

2.2 Numerical Approaches

Assumptions. We assumed that blood was a kind of non-Newtonian and homogeneous fluid [18, 19].

Governing equations. Numerical simulations for blood flow were carried out based on Navier-Stokes equations [18, 19].

\[
\rho \left( \frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right) = -\nabla p + \nabla \cdot \boldsymbol{\tau} \tag{2}
\]

\[\nabla \cdot \mathbf{u} = 0 \tag{3}\]

where \(\rho\) is the density of this flow (\(\rho=1050 \text{ kg/m}^3\)), \(\mathbf{u}\) and \(p\) stand for the fluid velocity vector and the pressure, respectively, and \(\boldsymbol{\tau}\) is the tension tensor which is described as:

\[\boldsymbol{\tau} = 2\eta(\dot{\gamma})T \tag{4}\]

where \(\dot{\gamma}\) and \(T\) stand for the shear rate and deformation tensor, respectively, and the viscosity of blood regulated by the shear rate which is indicted by \(\eta\). The Carreau model is used to get the viscosity of this flow.

\[\eta(\dot{\gamma}) = \eta_\infty + (\eta_0 - \eta_\infty) \left[1 + (\dot{\gamma}/\lambda)^2\right]^{(n-1)/2} \tag{5}\]

where \(\lambda=3.313 \text{ s}, n=0.3568 [20], \eta_\infty = 3.45 \times 10^{-3} \text{ kg/(m s)}\), \(\eta_0 = 5.6 \times 10^{-2} \text{ kg/(m s)}\).

Boundary conditions. In this work, the boundary are as follows [21-24]:

Inlet: the pulsatile velocity and parabolic flow velocity profile as shown in Fig. 1(F) was applied at the inlet [21];
Outlet: the traction-free outflow was set at the both outlets;

Walls: the arterial wall was treated as nonslip rigid.

Computation procedures.

The numerical simulation was conducted using the commercially available CFX (ANSYS, Inc., Canonsburg, PA, USA). Velocity-pressure coupling method was used for pressure, and the momentum equations were discretized by a pressure-based solver. Computational meshes of models in this study were obtained by ANSYS ICEM CFD (ANSYS Inc., Canonsburg, PA). Three models after stenting were meshed with tetrahedral and hexahedral elements, and near wall was with high quality hexahedral cells. The results in this work were mesh independent with different mesh densities. In order to ensure the time-independent results, the 5th cardiac cycle results were presented in this article. Convergence criterion was $10^{-6}$ for velocity residuals and $10^{-5}$ for continuity.

Statistical analysis.

To quantitative present the spatial distribution of WSS, the time-average of WSS (TAWSS) during a pulsatile cycle was calculated for the data analysis, and it was defined as [25]:

$$\text{TAWSS} = \frac{1}{T} \int_0^T \text{WSS} (s, t) dt$$

where $t$ is the time, $T$ stands for the time duration of a pulsatile cycle, $s$ is the position on the arterial wall, and WSS stands for wall shear stress vector at $t$. 
Oscillating shear index (OSI) is a value to evaluate variation of the WSS in the direction during a cardiac cycle. OSI values range from 0 to 0.5, with higher value indicating disturbance flow, and they were described as [26, 27]:

$$\text{OSI} = \frac{1}{2} \left[ 1 - \left( \frac{\int_0^t WSS(s,t) \cdot dt}{\int_0^t |WSS(s,t)| dt} \right) \right]$$

Relative residence time (RRT) is a useful parameter to measure the resident time of the blood flow indicating the regions in oscillating and low WSS. It was calculated by [26, 27]:

$$\text{RRT} = \frac{1}{(1 - 2 \cdot \text{OSI}) \cdot \text{TAWSS}}$$

The flow ratio is defined as the peak flow of ECA to ICA during the cardiac cycle, and it was quantified as:

$$\text{Flow ratio} = \frac{Q_{\text{max,ECA}}}{Q_{\text{max,ICA}}}$$

where $Q_{\text{max,ECA}}$ is the peak flow rate of ECA, and $Q_{\text{max,ICA}}$ is the peak flow rate of ICA.

3 Results

3.1 Flow patterns

The flow patterns in the carotid were visualized by instantaneous streamlines and contours of velocity, which were colored by the blood flow velocity magnitude (Fig. 2). The blood flow in the model with stenosis was characterized by significantly higher speed than other models after stenting, especially in ICA and ECA downstream. The narrow section had the highest velocity compared to other regions because of eccentric stenosis, and the blood flow kept the skewed path trajectory after the stenosis. The
stented models were with evident lower flow velocity in ECA and ICA. As blood moved to ICA, the flow was still skewed toward the outer-anterior wall, forming axial velocity with crescent-shaped distributions. The blood flow velocity in IAC was lower at inner-posterior wall than in others. The blood flow in ECA became less and in lower velocity, emerging evidently disturbed flow at the proximal ECA, and these were more obvious for the model with a longer stent. In addition, disturbed flow was observed at the distal CCA after stenting relative to the model with stenosis.

Fig. 2 Velocity streamlines and four representative contours of velocity in carotid at 0.35s.

3.2 Flow distribution

To facilitate analysis of blood flow distribution after carotid stenting, the flow ratios of peak blood flow in stented ECA to peak blood flow in ICA were computed. As shown in Table 1, the blood flow to ECA decreased sharply after intervention, particularly as
stent length increased. When a long stent is implanted, the carotid bifurcation has a flow ratio of 0.14458, less than the media and a short one.

**Table 1** Effect of stenting on the ratio of peak ECA flow to ICA.

|           | Long stent | Media stent | Short stent | Without stent |
|-----------|------------|-------------|-------------|---------------|
| The flow ratio | 0.1415     | 0.1419      | 0.1425      | 0.6689        |

3.3 WSS distribution

The impact of carotid stenting on TAWSS distribution and magnitude was assessed. As displayed in Fig. 3, TAWSS magnitude decreased remarkably at the stenting segment, particularly for the regions near struts. Moreover, the inner-posterior wall of stented ICA endured abnormally low TAWSS, and the lowest value was located at the proximal stent end, while TAWSS level was considerably elevated at the downstream of stented segment. The proximal ECA and distal CCA also experienced severely reduced TAWSS, and the lowest value for each of the models was located at the outer wall of bifurcation.

![Fig. 3 Distributions of TAWSS on carotid surface after intervention.](image)
To facilitate observation of TAWSS change in the carotid, the histogram presented the area of low TAWSS level (<0.26) in Fig. 4(A). As the stent was implanted, more areas with low TAWSS emerged in ICA, particularly as stent length increased. After a long stent implanted, low TAWSS area was 1.45 times larger than the short one. Interestingly, the blood flow area was markedly greater in low-level TAWSS at ECA than in-stent ICA, and this range was slightly elevated as stent length increased.

**Fig. 4**
(A) represents area of TASS<0.26. (B) Distributions of OSI on carotid bifurcation with a stent. (C) represents the surface area of OSI>0.31 in ICA and ECA

3.4 OSI distribution

Fig. 4(B) displayed a comparison in terms of OSI on the three models after stenting. The proximal ECA could be clearly observed at relatively high OSI values. In more detail, the maximum values of OSI were located on the outer-posterior wall of ECA, and this value was 0.491, 0.490, 0.481, respectively. In addition, the inner-posterior wall of stented ICA was also in low-level OSI value, particularly at the proximal end of stent.
To assess effect of stenting on the carotid bifurcation, we analyzed the area of high OSI (Fig. 4(C)) statistically. The area of high OSI on the wall increased as the length of stent at ICA increased but decreased at ECA. Moreover, the area on ECA surface is at least 11 times larger than on ICA surface.

3.5 RRT distribution

As for RRT in Fig. 5(A), it was greatly enhanced after stenting and more evident near the stent struts and bifurcation. The inner-posterior wall of ICA with stent was also in a relatively low-level value of RRT, particularly at the proximal stent end. The maximum values of RRT in models were located in the vicinity of the proximal end of ECA, and the values were 134.01, 117.806, and 67.06.

The area of high RRT, displayed in the Fig. 5(B), suggested that the implanted stent enhanced this value at stented ICA and ECA. Although there was a little impact on the host artery, implanted stent would induce more high RRT region on the luminal surface of ECA than ICA. The statistical results of high RRT area on ECA wall showed that it was over 2.31 times larger than ICA.

Fig. 5 (A) Distributions of RRT on carotid surface with a stent. (B) represent area of RRT>8.95 in ICA and ECA.

4 Discussion
Emerged as a therapeutic alternative for the severe stenosis, carotid stenting is still controversial due to high rate of adverse events during follow-up. It has been evidenced that in-stent restenosis and thrombosis are the main drawbacks of this treatment [1, 4-6]. Moreover, clinical reports indicated that, in the case of carotid artery bifurcation, the implanted stent was attributed to significant stenosis that occurred in the external carotid artery after stenting [1-3, 7]. Although previous investigations provided extensive insight into the adverse events in the stented segment, they failed to quantitatively analyze the impact of stenting on the blood flow in the carotid bifurcation. This work was conducted to study the local hemodynamic characteristics of carotid stenting, exploring the potential role for adverse events after intervention.

This study found that stenting led to abnormal blood flow in stented ICA, and the regions near stent struts were characterized by observably decreased WSS but increased OSI and RRT, especially in the inner-posterior of artery wall and the proximal end of stent. These adverse mechanical parameters might explain the underlying mechanisms for clinical events, and these regions might be the primary sites to develop in-stent restenosis and stent thrombosis in clinic [1, 4-6].

Moreover, our simulation results showed that the mechanical environment of stented vessel was dependent not only on the presence of stent struts but also on the geometry of host artery after intervention. In other words, the bifurcation geometry after intervention should be given full consideration, which would probably be also a key factor for the alternation of local blood flow besides the design and deployment of stents.
In addition, stenting might be an alternative way to adjust the configure and geometry of bifurcation for improved local flow patterns.

Our numerical results also demonstrated that implanted stent significantly reduced blood perfusion to ECA with quick restoration of ICA, and there was increased flow turbulence (low WSS, high OSI, and RRT) in ECA after stenting. Moreover, the area of disturbed flow in ECA was evidently larger than ICA after IAC stenting, inducing more harmful flow to ECA than stented ICA. This might severely damage ECA and significantly increase ECA occlusion after carotid stenting in clinical data [1-3, 7]. Therefore, ECA patency after carotid stenting, like recurrent stenosis and thrombosis in vessels with stents, was an important factor affecting the postoperative outcomes after intervention. These may also indicate the importance of bifurcation angles and geometry after intervention on ECA patency.

This study also confirmed a linear relationship between abnormal flow and stent length, and longer stenting would result in a larger area of low WSS, high OSI, and RRT than the shorter one. This was in agreement with clinical conclusions, which showed that risk of in-stent recurrent stenosis and thrombosis increased with a longer stent [17, 28]. This study also indicated that a longer stent slightly relieved the adverse local hemodynamic environment at ECA, implying that longer stenting to some degree may be safer than shorter one for ECA interventions in clinic.

The local turbulence of blood flow induced by drug eluting-stent is a critical factor for drug transport. Our numerical results also revealed that intervention in branching model was complex and distributed more non-uniformly (Fig. 6) drug than the straight one,
and the inner-posterior wall near the distal of drug stent was in an obviously high level of drug concentration [29, 30]. This would seriously damage the endothelium and induce adverse events in clinic, and the optimized performance of stent should be designed individually for the complex artery, like branching stenting.

![Drug concentration distribution](image)

**Fig. 6** Distribution of drug concentration on the branching model after stenting.

The limitation of this study was the simplified artery and the rigid wall after stent implantation [22]. In addition, more patients’ images should be obtained from clinical data, and in vitro mechanical tests should be performed to verify our conclusion in future. Despite these limitations, the numerical results presented here entirely agreed with the clinical data.

5 Conclusions
The implanted stent may induce an unfavorable hemodynamic environment both at the stented segment and the other branches without stenting and hence leading to the occurrence and evolution of in-stent events and branch occlusion. Moreover, our results indicated that carotid bifurcation angles and geometry after intervention should be essential for postoperative outcomes.

**Declarations**

**Abbreviations**

WSS: wall shear stress; RRT: relative residence time; OSI: oscillating shear index; ECA: external carotid artery; ICA: internal carotid artery; CCA: common carotid artery; ISR: in-stent restenosis.

**Authors' contributions**

Zhenmin Fan, Xiao Liu and Xiaoyan Deng. conceived the idea; Zhenmin Fan and Yingying Zhang conducted the analyses; Zhenmin Fan and Nan zhang provided the data; Zhenmin Fan and Xia Ye wrote the paper; all authors contributed to the writing and revisions.

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Ethics approval and consent to participate

Not applicable.

Consent for publication

All authors have given consent for publication of this paper.

Availability of data and materials

All data generated or analyzed during the present work are available from the corresponding author.

Competing interests

The authors declare that they have no competing interests.

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