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Biophysical modeling of cerebral ischemia: the impact of arterial stenosis and plaque morphology on blood flow and stroke outcomes

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Abstract: Objective: To analyze the impact of arterial stenosis and plaque morphology on cerebral hemodynamics and stroke outcomes, and to provide quantitative data support for ischemic stroke risk assessment using a biophysical model. **Methods:** Based on clinical 3D-CTA imaging data, a three-dimensional configuration of the internal carotid artery and middle cerebral artery bifurcation region was constructed. Computational fluid dynamics (CFD) was used to simulate blood flow dynamics under various stenosis degrees (30%, 50%, 70%, and 90%) and plaque shapes (eccentric, concentric, and irregular). Parameters such as blood flow velocity, wall shear stress (WSS), and pressure gradient were thoroughly investigated. The predictive performance of the model was validated using data from 100 clinical cases. **Results:** When stenosis was ⩾70%, the peak flow velocity (PSV) at the stenosis site increased by more than 3.2 times compared with the control group, the mean wall shear stress (MWSS) reached over 5 Pa, and the downstream recirculation area was significantly enlarged. Irregular plaques caused the most significant local blood flow disturbance, with the oscillatory shear index (OSI) being 42%-58% higher than that of concentric plaques. The model parameters (percentage of abnormal WSS area + area of recirculation zone) predicted stroke with an AUC of 0.89, superior to the degree of stenosis

alone (AUC = 0.72). **Conclusion:** Modification of vascular stenosis and plaque morphology significantly impacts hemodynamic parameters and influences stroke risk. Biophysical modeling can accurately quantify this association, providing a theoretical framework for clinical intervention.

Keywords: cerebral ischemia, biophysical modeling, arterial stenosis, plaque morphology, hemodynamics, stroke outcome

Introduction

Ischemic stroke is one of the neurological diseases with the highest disability and mortality rates worldwide. It is the pathological center of brain tissue ischemia and hypoxia, and is caused by insufficient blood perfusion in the cerebral arteries[1]. Clinical data show that some cases of ischemic stroke are closely related to cerebral atherosclerosis, with arterial stenosis and plaque rupture as the two main causes[2]. Decreased cerebral blood flow is directly caused by arterial stenosis, and plaque morphology (such as uneven surface and eccentric distribution) affects blood flow stability, indirectly causing thrombosis and plaque detachment[3]. The combined effect of the two leads to the final pattern of stroke risk and prognosis. Vascular stenosis assessment indicators such as diameter stenosis rate face interpretation difficulties in explaining differences in patient prognosis. It is necessary to further explore the intrinsic relationship between plaque morphology and hemodynamics.

Biophysical modeling technology has opened up new avenues for the analysis of cerebral vascular hemodynamics. Numerical simulation of computational fluid dynamics (CFD) accurately quantifies flow parameters such as intravascular flow velocity, pressure and shear stress. Its application has revealed the intrinsic mechanism of the effect of arterial stenosis on blood flow[4]. Low wall shear stress is closely linked to the progression of atherosclerosis, and elevated wall shear stress may induce plaque rupture. There is no systematic study yet on the differential effects of different plaque morphologies (e.g., eccentric and irregular) on hemodynamics.[5] Current models often use idealized vascular morphology as a basis and have not been verified based on clinical data, which limits their application in stroke risk prediction.

This study used a cerebral artery hemodynamic model based on actual vascular anatomy. By controlling variables, we explored the intrinsic relationship between arterial

stenosis (30%-90%) and plaque morphology (eccentric, concentric, irregular) and hemodynamic parameters. By comparing the model parameters with clinical stroke outcomes, we validated the correlation between the model parameters and provided biophysical scientific support for risk assessment and treatment optimization for ischemic stroke patients.

1 Subjects and Methods

1.1 Subjects and Ethical Issue

This study enrolled 100 male patients with cerebral artery stenosis treated in the neurology department of a tertiary hospital between January 2022 and December 2024. Fifty-eight of the patients were male, ranging in age from 55 to 75 years. Three-dimensional CT angiography revealed stenosis at the ICA-MCA bifurcation. Detailed clinical data, including stroke incidence and plaque morphology, were collected. Twenty healthy adults with no history of cerebrovascular disease were also included as controls, using 3D-CTA data. This study has passed ethical review by the hospital's ethics committee: research project identifier 2021-034. All participating individuals have signed informed consent.

1.2 Construction of the Vascular Model

1.2.1 Geometric Modeling

Mimics 21.0 software was used to extract the vascular contours of 3D-CTA images, and a three-dimensional morphological model of the ICA-MCA bifurcation point was established. The vascular wall and lumen were incorporated into the model. The model was expanded with reference to the pathological section data, and three types of plaque morphologies were introduced [6]. Eccentric plaques are attached to one side of the vascular wall. In the stenotic area, the eccentricity index of the lumen (the ratio of the maximum diameter to the minimum diameter) must be 1.5 or above. Equidistantly arranged concentric rings with an eccentricity of less than 1.2 times. The irregular plaque surface has at least two depressions with a depth exceeding 0.5 mm, or is accompanied by calcified protrusions.

1.2.2 Meshing and boundary conditions

ANSYS ICEM was used to complete the meshing. The internal mesh construction adopted the tetrahedron unstructured method. The mesh was encrypted around the vascular wall with a first layer thickness of 0.1 mm to optimize the WSS calculation accuracy and establish boundary parameter specifications. Individual patient inlet flow waveforms, measured by ultrasound Doppler, showed peak systolic velocity between 1.2 and 1.8 meters per second, with a diastolic velocity threshold of 0.2 to 0.4 meters per second. The outlet design employed a three-element Windkessel model, with arterial compliance set at C = 0.5 ×

$10^{-9}m^4/Pa$, peripheral resistance R_1 at $1 \times 10^9 Pa \cdot s/m^3$, and distal resistance R_2 at $2 \times 10^9 Pa \cdot s/m^3$. The vessel wall was assumed to be rigid, with no slip.。

1.3 Hemodynamic simulation

1.3.1 Blood Properties and Governing Equations

Blood is classified as an incompressible Newtonian fluid. Its density is 1060 kg/m^3 and its viscosity is 0.004 Pa·s . The governing flow equations are implemented using the three-dimensional Navier-Stokes equations as follows:

$$\rho(\frac{\partial u}{\partial t}+u\cdot\nabla u)=-\nabla p+\mu\nabla^2 u \quad (1)$$

Where $\rho$is the density, uis the velocity vector, $p$is the pressure, $\mu$and is the dynamic viscosity.

1.3.2 Simulation plan

Twelve experimental scenarios were conducted, and the degree of stenosis was calculated using the formula (normal diameter minus the minimum diameter at the stenosis site) divided by the normal diameter, multiplied by 100%. Dynamic simulations were performed using ANSYS Fluent software, with a time step of 0.01 seconds and a simulation period of three cardiac cycles, totaling 1.8 seconds. Data from the third cycle were analyzed to eliminate the adverse effects of the initial disturbance.

1.4 Evaluation indicators and statistical analysis

The extracted parameters include: ① Blood flow velocity: peak flow velocity (PSV) and mean flow velocity (MFV) at the stenosis [7]. ② WSS parameters: mean flow velocity (MWSS) and oscillatory shear index (OSI， $OSI=0.5\times1-\frac{WSS\text{ Vector average}}{\text{/Time average }WSS}(2)$) . ③ Pressure gradient (PG): pressure difference 10 mm before and after stenosis. ④ Recirculation area: area of the area where blood flow reverses downstream of the stenosis.

SPSS 26.0 software was used for statistical operations. Data were expressed as mean ± standard deviation. One-way analysis of variance was performed between groups. Paired sample differences were tested using the least significant difference test. The predictive power of model parameters in stroke prediction was analyzed. A P value less than 0.05 was considered statistically significant.

2 Results

2.1 Effect of stenosis degree on hemodynamics

2.1.1 Flow rate and pressure changes

With the increase of stenosis degree, PSV and MFV at the stenosis site increased significantly (P<0.05), and the pressure gradient increased with the increase of stenosis degree (P<0.01) (Table 1).

Table 1 Effects of different stenosis degrees on key hemodynamic parameters (taking concentric plaques as an example, x ± s)

Stenosis	Peak flow velocity (PSV, m/s)	Mean wall shear stress (MWSS, Pa)	Oscillatory Shear Index (OSI)	Recirculation area (mm²)	Pressure gradient (PG, Pa)
control group	1.26±0.15	1.12±0.18	0.08±0.02	0.00±0.00	5.2±1.1
30%	1.78±0.21	1.85±0.25	0.12±0.03	3.2±0.5	12.5±2.3
50%	2.85±0.32	2.96±0.35	0.16±0.04	8.5±1.2	22.6±3.2
70%	4.68±0.45	5.22±0.55	0.22±0.05	16.2±2.1	40.2±4.2
90%	6.55±0.60	7.22±0.75	0.28±0.06	24.8±3.0	105±12

2.1.2 WSS changes

The MWSS at the stenosis site increased with the increase in the degree of stenosis. A low WSS area appeared downstream of the stenosis, and the OSI value increased significantly, indicating that the shear direction was disordered (Table 2).

Table 3 Differences in hemodynamic parameters of different plaque morphologies at the same stenosis degree (70%) (x±s)

Plaque morphology	Peak flow velocity (PSV, m/s)	Mean wall shear stress (MWSS, Pa)	Oscillatory Shear Index (OSI)	Recirculation area (mm²)	Pressure gradient (PG, Pa)
Concentric	4.68±0.45	5.22±0.55	0.22±0.05	16.2±2.1	40.2±4.2
Eccentric type	5.15±0.50	5.86±0.60	0.28±0.07	19.8±2.5	45.6±4.5
Irregular type	5.82±0.55	6.85±0.70	0.35±0.08	22.5±2.8	52.3±5.0

2.2 Effect of plaque morphology on hemodynamics

At the same degree of stenosis, plaque morphology significantly affected blood flow parameters (P < 0.05) . Irregular plaques had the highest PSV at the stenotic site; eccentric

plaques had blood flow biased toward the non-plaque side, leading to increased MWSS on the contralateral vessel wall; concentric plaques had the most uniform blood flow distribution and minimal fluctuations in various parameters (Table 3).

Table 3 Comparison of main hemodynamic parameters under different stenosis degrees and plaque morphologies (x±s)

Stenosis	Plaque morphology	Peak flow velocity (PSV, m/s)	Mean wall shear stress (MWSS, Pa)	Oscillatory Shear Index (OSI)	Recirculation area (mm^2)	Pressure gradient (PG, Pa)
control group	No plaque	1.26±0.15	1.12±0.18	0.08±0.02	0.00±0.00	5.2±1.1
30%	Concentric	1.78±0.21	1.85±0.25	0.12±0.03	3.2±0.5	12.5±2.3
30%	Eccentric type	1.95±0.23	2.12±0.28	0.15±0.04	4.6±0.7	14.2±2.5
30%	Irregular type	2.26±0.25	2.58±0.32	0.18±0.05	6.8±0.9	16.8±2.8
50%	Concentric	2.85±0.32	2.96±0.35	0.16±0.04	8.5±1.2	22.6±3.2
50%	Eccentric type	3.22±0.35	3.42±0.40	0.20±0.05	11.2±1.5	25.8±3.5
50%	Irregular type	3.86±0.40	3.98±0.45	0.25±0.06	14.5±1.8	29.5±3.8
70%	Concentric	4.68±0.45	5.22±0.55	0.22±0.05	16.2±2.1	40.2±4.2
70%	Eccentric type	5.15±0.50	5.86±0.60	0.28±0.07	19.8±2.5	45.6±4.5
70%	Irregular type	5.82±0.55	6.85±0.70	0.35±0.08	22.5±2.8	52.3±5.0
90%	Concentric	6.55±0.60	7.22±0.75	0.28±0.06	24.8±3.0	105±12
90%	Eccentric type	6.98±0.65	7.85±0.80	0.30±0.07	26.5±3.1	115±13

90%	Irregular type	7.25±0.70	8.56±0.85	0.38±0.09	28.6±3.2	125±15

2.3 Association between hemodynamic parameters and stroke outcomes

The stenosis and regurgitation areas in the stroke group were significantly larger than those in the non-stroke group ($P < 0.01$). The proportion of abnormal WSS area combined with the regurgitation area was significantly better at predicting stroke than the degree of stenosis alone (Table 4).

Table 4 Association between hemodynamic parameters and stroke outcomes (x±s)

3 Discussion

3.1 Mechanism of stenosis degree and hemodynamic abnormality This study found that a stenosis of more than 70% indicates a fundamental change in hemodynamic properties, with a sharp increase in PSV and a significant increase in pressure gradient, which is consistent with the clinical consensus on active intervention for severe stenosis [8]. The high WSS formed by high-speed blood flow in the stenotic area mechanically activates vascular endothelial cells, promotes the excretion of inflammatory factors (such as IL-6 and VCAM-1), and accelerates plaque fragmentation. In the downstream area, low WSS and high OSI value areas are prone to platelet aggregation and thrombosis. This mechanism may constitute the core element of the sharp increase in stroke risk in patients with severe stenosis. The increase in the area of the recirculation zone causes a prolonged blood retention period, forming a favorable foundation for thrombosis. The results of the study show that the association between hemodynamic abnormalities and stroke is further confirmed.

3.2 Differential effects of plaque morphology

Irregular plaques with uneven surfaces cause the destruction of the laminar flow state of blood flow, induce local disturbances, and cause the WSS peak and OSI value to rise to the highest level [9]. Research data revealed that patients with irregular plaques have a significant risk of stroke, with a stroke incidence rate as high as 48.3%, significantly exceeding the risk level of concentric plaques. The blood flow deviation caused by eccentric plaques can cause continuous impact on the contralateral blood vessel wall, giving rise to a new stage of atherosclerotic lesions. The damage of eccentric plaques to both blood vessel walls should be the focus of clinical attention. The blood flow distribution in concentric plaques is uniform, and stable shear stress may reduce the risk level of plaque rupture. The new theoretical perspective reveals the connection between plaque morphology and stroke risk.

3.3 Clinical Value of the Model

The biophysical model constructed in this study quantifies key parameters such as WSS and recirculation zone area, significantly improving stroke risk prediction and transcending the limitations of single stenosis assessment. Based on the model's analysis results, early treatment (stent implantation) is recommended for patients with high-risk stenosis (70% stenosis with irregular plaques). For patients with low-risk stenosis (50% stenosis with concentric plaques), conservative treatment is the appropriate option, enabling personalized management. This model can simulate the blood flow-improving effects of various treatment options (stent configurations) to guide optimal surgical approaches.

4 Conclusion

Cerebral artery stenosis and plaque morphology have a direct effect on stroke outcomes by changing hemodynamic parameters (flow velocity, WSS, recirculation area, etc.). If the vascular stenosis reaches 70% or above, hemodynamic abnormalities are obvious, irregular plaques aggravate blood flow fluctuations, and the risk of stroke increases significantly. CFD-based biophysical modeling can accurately quantify the above associations, and its predictive effect significantly exceeds traditional stenosis assessment, providing key biophysical support for ischemic stroke risk grading and clinical treatment.

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