Acta of Bioengineering and Biomechanics
Vol. 25, No. 1, 2023

Original paper
DOI: 10.37190/ABB-02207-2023-01

Hemodynamic impact of snoring on carotid artery after stent implantation: the role of oscillation

XIANGHAO ZHANG[1], ZHENMIN FAN[1]*, XIAO LIU[2], MINGYUAN LIU[3], XIA YE[1]*, XIAOYAN DENG[2]

[1] School of Mechanical Engineering, Jiangsu University of Technology, Jiangsu, China.
[2] Key Laboratory for Biomechanics and Mechanobiology of Ministry of Education, School of Biological Science and Medical Engineering, Beihang University, Beijing, China.
[3] Department of Vascular Surgery, Beijing Friendship Hospital, Capital Medical University, Beijing Center of Vascular Surgery, Beijing, China.

Snoring is common in overweight and elderly patients treated by endovascular stenting. Studies have proved a correlation between snoring and carotid stenosis, thus, snoring after carotid artery stenting (CAS) might promote or worsen clinical performance. This study tested this hypothesis by constructing a patient-specific carotid bifurcation model and numerically analyzing hemodynamic changes of the carotid artery under different snoring conditions. These conditions included small and large amplitude, low and high frequency, and different age groups. The results found that high amplitude snoring suppressed the disturbed flow at the stented segment while the downstream region of ICA became more chaotic, accounting for in-stent intimal restenosis and thrombosis. Furthermore, local blood flow patterns of elder groups with snoring symptoms were more likely to be changed due to low-speed flow, increasing the possibility of vascular remodeling and thrombosis. Besides, increased snoring frequency hardly influenced the local disturbed flow. Therefore, older adults should receive medical treatment actively after stenting for high-amplitude snoring as soon as possible to avoid potential adverse events.

Key words: *snoring, carotid artery, stent, hemodynamics, numerical study*

1. Introduction

Carotid atherosclerosis is an important risk factor for ischemic cerebrovascular diseases, seriously threatening the health of middle-aged and elderly adults. Carotid artery stenting (CAS) is a predominant clinical treatment for this disease. However, in-stent intimal restenosis (ISR) and thrombosis after the intervention are inevitable postoperative problems associated with adverse events, such as stroke and death [17], [41]. The prevalence of carotid artery restenosis ranges from 2.7 to 33% [11], [28]. Even though late stent thrombosis occurs in about 1% of cases, it accounts for more than 90% of disabilities or fatalities [35]. These outcomes occur due to the discounting of the effects, eventually causing the failure of CAS.

Physiological and non-physiological activities in patient's life might affect postoperative manifestations after CAS. Patients experience various normal physiological activities such as breathing, swallowing, head head-turning. A previous study has confirmed that such activities can contribute to carotid artery deformation [3], [33]. These deformations induced by physiological activities change the biomechanical environment of the host artery. In addition, abnormal physiological activities such as snoring have a close relationship with adverse cardiovascular outcomes, such as stroke, hypertension, and myocardial infarction [9], [24]. Evidences shows that snorers have a high risk of carotid stenosis than non-snoring [12]. Therefore, abnormal physiological activities might enhance the risk of adverse events after CAS. Moreover, typical non-physiological activities such as daily exercise may adversely

* Corresponding authors: Zhenmin Fan, Ye Xia, School of Mechanical Engineering, Jiangsu University of Technology, Changzhou Jiangsu, China. Phone: 86-519-86953201, fax: 86-519-86953201, e-mail: fanzhenmin2009@163.com, yx_laser0@163.com
Received: March 1st, 2023
Accepted for publication: May 18th, 2023

affect the outcomes following stenting. Vigorous exercises increase the risk of stent fracture in the superficial femoral artery [16] and are closely related to late stent thrombosis [34], [44]. Therefore, physiological and non-physiological activities might be associated with adverse events after CAS caused by hemodynamics changes in the host artery.

Hemodynamics plays a crucial role in the presence of adverse events after CAS. For one thing, stenting changes the local hemodynamic environment, directly influencing endothelial shear stress. It is considered a principal contributor to restenosis and thrombosis [5], [13]. Adverse or disturbed local blood flow associated with these adverse events is featured by separation and low oscillatory wall shear stress (WSS) flow around protruding struts. WSS, relative residence time (RRT) and oscillating shear stress index (OSI) are the quantitative evaluation indicators to describe the unfavorable flow [36], [43]. A low WSS and high RRT and OSI can lead to disturbed local mechanical conditions contributing to adverse events after stent implantation. Moreover, local disturbed flow caused by stenting increases the residence time and the deposition of atherogenic particles and inflammatory cells, contributing to the adverse event after stenting [6], [40]. Unsuccessful stent implantation and inappropriate designs also increase the risk of postoperative complication. Stent under expansion, stent malapposition, and thicker and no-streamlined stent designs result in abnormal shear stress concentration on stent struts edges, which may increase the risk of adverse events after the intervention [20], [32].

Snoring might alter the hemodynamic environment of the host's carotid artery after the intervention. A 10--year study found that habitual snoring is significantly related to increased risks of ischemic stroke, total cardiovascular diseases and ischemic heart disease [42]. Researches has proven that snoring is strongly associated with the intima–media thickness of carotid bifurcation [1], [18], [25]. Besides, there might be a close connection between snoring and high-risk plaque formation [19]. Overweight/obese people and middle-aged adults with snoring symptoms have a higher possibility of vascular remodeling than non-snoring [39]. Moreover, several studies have investigated how snoring influences morphology and biomechanical properties of the carotid artery. The vibratory energy or acoustic of snoring induces endothelial damage and endothelial dysfunction nearby. The surface acoustic wave improves binding kinetics and enhances low-density lipoprotein receptor-mediated endocytosis pathways [21]. The continuous peri-carotid tissue oscillation study displays an endothelial dysfunction, indicating a plausible direct mechanism linking heavy snoring and atherosclerosis development [7]. Cho et al. [8] found that loud snores decreased carotid peak systolic blood flow and wall shear stress. *In vitro* snoring experiments in rabbits showed that snoring in the carotid tissues accompanied high-frequency oscillations and flow limitation on the flow trace [31]. Previous research has built a connection between cardiovascular disease and snoring, discussing how snoring alters the biomedical environment of the host artery. However, there is limited research on snoring's influence on the hemodynamic environment of the stented carotid artery. Based on the existing research, this study hypothesized that snoring promotes or worsens the hemodynamics of the host artery after stenting. Therefore, a carotid bifurcation model was constructed based on patient-specific carotid images and numerically-analyzed hemodynamic changes of the stented carotid artery under different snoring conditions. The effects of different snoring amplitudes, frequencies, and ages on the local hemodynamic environment were also discussed.

2. Method

2.1. Computational model

Carotid artery

To reconstruct carotid geometry, consecutive carotid artery sections were taken using an imager (Siemens Medical Solutions, Forchheim, Germany). Carotid bifurcation images in this study included three branches (the external carotid, internal carotid and common carotid, ECA, ICA and CCA), as illustrated in Fig. 1a. The lengths of the CCA and ICA were 71 and 68 mm, respectively. Subsequently, Materialise interactive medical image control system was manually utilized to segment lumen boundaries to create the carotid model while simultaneously exacting the carotid centerline. The original carotid model was processed by Geomagic Studio (Geomagic, Inc., Morrisville, the United States) to ensure the smoothness of the surface. The participant gave written informed consent and approved the study, which was carried out in compliance with Beijing Friendship Hospital regulations.

Stent

Pro/Engineer (Parametric Technology Corporation) was applied to construct the model of carotid stent, and it was similar to the commercially available one. Strut had a rectangular cross-section, width of 0.087 mm and thickness of 0.188 mm. Additional geometrical features of the stent in the present study has been described in previous work [4]. The stent was placed along the centerline of the carotid artery at the area with the largest degree of stenosis. Because diameters from different carotid arteries varied, the ratio of stent diameter to artery was 1 : 1 – 1.1 : 1, and ratio 1.1:1 was assumed in this study.

Governing equation

Studies have proven that non-Newtonian blood flow models helps to improve the computational fidelity of WSS [26]. Therefore, blood was assumed as an incompressible non-Newtonian fluid in this study. The governing equations are the continuity Eq. (2) and incompressible Navier–Stokes Eq. (1) [29].

$$\rho(u \cdot \nabla)u + \nabla p - \mu \Delta u = 0\,, \tag{1}$$

$$\nabla \cdot u = 0\,, \tag{2}$$

where u stands for the fluid velocity vector and ρ (ρ = 1060 kg/m^3) is the constant density of blood [30], p represents the pressure.

$$\boldsymbol{\tau} = 2\mu(\dot{\gamma})\mathbf{S}\,, \tag{3}$$

where **S** and stand $\dot{\gamma}$, respectively, stand for the rate of deformation tensor and the shear rate (Eq. (3)). The blood flow viscosity is described by Carreau model (Eq. (4)) [38].

$$\mu(\dot{\gamma}) = \mu_\infty + (\mu_0 - \mu_\infty)[1 + (\lambda\dot{\gamma})^2]^{\frac{n-1}{2}}\,, \tag{4}$$

where μ_∞ and μ_0 represent respectively the viscosity at infinite shear rate (μ_∞ = 0.00345 kg/ms) and at zero shear rate (μ_0 = 0.056 kg/ms), λ stands for the time constant (λ = 3.31 s) and n stands for the power law index (n = 0.36) [29].

Flow velocity waveform at inlet of CCA [2] from different aged groups shown in Fig. 1c was applied at the CCA of the carotid artery. The outlet of ICA and ECA were set as no surface traction outflow. In this simulation, the vessel wall and stent region were considered as rigid with no-slip boundary condition.

Snoring simulation

Previous research showed that snoring can induce high frequency oscillations on the blood flow in carotid tissues [31]. Based on these findings, we simplified the oscillations of carotid flow as sine waves, and oscillation frequency was assumed as 2.5 Hz. Amplitude of oscillation velocity was set as 0.04 m/s in accordance with previous works [3], [31]. Therefore, snoring oscillation curve of the carotid flow field was set as:

$$V = 0.4 * \sin(15.7 * t)\,, \tag{5}$$

where V stands for the oscillation velocity of carotid artery and t represents different moments of the cardiac cycle. The sinusoidal velocity was applied on the whole carotid fluid domain to characterize the effect of snoring oscillation on the carotid flow field, and the oscillating velocity was along Y-axis in YZ plane as shown in Fig. 1a.

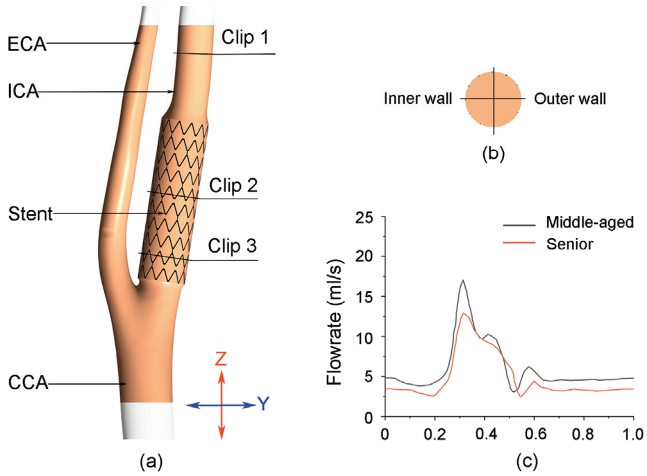

Fig. 1. (a) computational model of stented carotid bifurcation, (b) view of carotid cross-section, (c) carotid inlet velocity waveform of middle-aged and elderly groups

To figure out the effect of oscillation amplitude and frequency on carotid artery, different computational models were investigated.

The Normal model (***Normal***) represents conditions without snoring. The models with snoring amplitude of 0.04 m/s and 0.08 m/s were symbolled by ***SA0.04*** and ***SA0.08*** while ***SA0.04TF*** represents snoring amplitude equal to 0.04 m/s with the double frequency.

Computation procedures

The CFD analysis was performed using commercial software Fluent 18.0 (Ansys, Inc., Canonsburg, the United States). Hexahedral dominated meshes were generated by ICEM CFD 18.0 (Ansys, Inc., Canonsburg, the United States). Stented regions were meshed with high-quality tetrahedral elements using a maximum size of 0.05 mm and segments without stent were meshed with high-quality hexahedral cells. Mesh density is a factor that can influence the computational results, so results have undergone mesh-independent studies with 5 different mesh densities. Changes of hemodynamic parameters based on WSS (area-averaged value of TAWSS, OSI, and RRT) was observed by

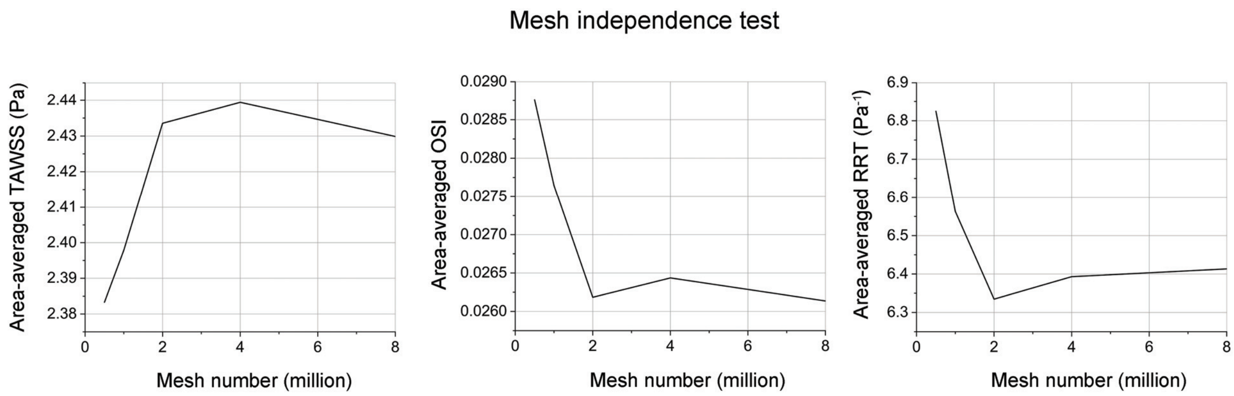

Fig. 2. Mesh independence analysis involving mesh number of 0.5, 1, 2, 4, and 8 million

increasing number of meshes from 0.5 million to 8 million, and number of meshes was doubled each time. As shown in Fig. 2, it can be found that three interested paraments become stable after mesh number reached 2 million, and relative difference between two adjacent sets of meshes was below 3%. Therefore, to reduce calculation cost and ensure calculation accuracy, mesh number of 2 million was adopted in this study. To get a convergent solution, velocity-pressure coupling method was used and the coupled second order upwind method was used for the discretize the momentum equation. In order to eliminate the influence of initialization effects on results and ensure the convergence of calculation, the hemodynamic results of this study are exported from the 3rd cardiac cycle singly.

2.2. Statistical analysis

Reverse flow volume was applied to calculate flow volume opposite to the direction of normal blood flow (along positive *Z*-axis) at different times, it can be used to characterize disturbed flow [27]. Large reverse flow volume indicates that there is more disturbed flow in local flow field.

TAWSS was calculated by integrating the size of the WSS of carotid wall during the cardiac cycle, and low TAWSS values have closely connection with expression of proatherogenic genes, and it was defined as:

$$\mathrm{TAWSS} = \frac{1}{T}\int_0^T |\,\mathrm{WSS}(s,t)\,| \cdot dt\,, \tag{6}$$

where T represents overall interval of the cardiac cycle, s is the position on the arterial wall, t stands for the time, and WSS is the wall shear stress vector at t.

OSI is used to identify areas of the blood vessel wall that are affected by high oscillating WSS values during the cardiac cycle. High OSI value indicates regions where disturbed flow exists and it is defined as:

$$\mathrm{OSI} = \frac{1}{2}\left[1 - \left(\frac{\left|\int_0^T \mathrm{WSS}(s,t)\cdot dt\right|}{\int_0^T |\,\mathrm{WSS}(s,t)\,|\cdot dt}\right)\right]. \tag{7}$$

RRT reveals the residence time of the atherogenic particles at the arterial wall. High RRT values are considered to increase the risk of in-stent restenosis, and it is defined as

$$\mathrm{RRT} = \frac{1}{(1-2\cdot\mathrm{OSI})\cdot\mathrm{TAWSS}}\,. \tag{8}$$

Previous research have proven that abnormal hemodynamic parameters may increase the risk of vascular disease, vessel wall exposed to low TAWSS (<0.26 Pa), high OSI (>0.31) and high RRT (>8.95 Pa^{-1}) are particularly prone to lesions [22], [23]. Therefore, these thresholds are used in this study to quantitatively describe the disturbed flow.

3. Results

3.1. Effect of snoring amplitude

The velocity streamlines during snoring at different moments showed that snoring altered the hemodynamic environment of the carotid bifurcation significantly (Fig. 3). Snoring increased the upstream blood flow located at the inner surface of the wall of ICA (Fig. 3a). In addition, the flow disturbance at the outer surface of the wall of the stented segment was slightly suppressed at 0.4 seconds. However, snoring can induce significant disturbed flow at the downstream regions of ICA. When the snoring amplitude increased to 0.04 m/s, a small amount of disturbed flow appeared in the downstream area of ICA. In contrast, when the snoring amplitude increased to 0.08 m/s, the level of disturbance increased significantly. Nevertheless, snoring under different amplitudes did not significantly change the hemodynamic environment in the stented segment at 0.6 seconds (Fig. 3b), but significantly changed the streamlines at the downstream regions of ICA. As the snoring amplitude increased to 0.04 m/s, a small amount of local disturbed flow downstream of ICA occurred. In contrast, when the snoring amplitude increased to 0.08 m/s, the level of disturbance increased significantly, much greater than the same amplitude at 0.4 seconds. By comparing different moments, it was found that snoring could slightly disturb the systolic blood flow of the stented segment. However, the downstream areas of ICA were disturbed when snoring at different moments, and it was more serious at high amplitudes of snoring.

This study also calculated the reverse flow of snoring under different conditions to quantitatively analyze the changes of flow field in stented segment and downstream areas of ICA. As shown in bar graphs of Figs. 3a, b, reverse volume of stented segment was much larger than that in downstream regions of ICA at 0.4 seconds. The increased snoring amplitude slightly increased the reverse flow volume of stented segment at 0.4 seconds, and the maximum snoring amplitude (0.08 m/s) increased the reverse flow volume by about 4% compared to non-snorers. While the reverse flow volume in downstream areas of ICA was increased dramatically from 3.44×10^{-10} m^3 to 2.28×10^{-9} m^3, increasing by 563%. Compared to phenomenon that stented segment had more reverse flow at 0.4 seconds, downstream areas of ICA existed more reverse flow volumes at 0.6 seconds. Reverse volume ratio of downstream areas of ICA to stented segment was 5.74 when snoring amplitude was 0.04 m/s, and this ratio increased to 452 when snoring amplitude increased to 0.08 m/s. Besides, reverse flow volume of downstream regions of ICA was almost 0 m^3 when snoring amplitude was below 0.08 m/s at 0.6 seconds. As snoring amplitude increased, maximum snoring amplitude (0.08 m/s) caused reverse flow volume to be 3157 times larger than normal condition in downstream regions of ICA.

The TAWSS, OSI, and RRT distributions under snoring (Fig. 4) showed that low TAWSS regions were mainly distributed in the stented segment and the end bifurcation of CCA. In contrast, high levels of OSI and RRT regions were distributed in the outer surface wall of the stented segment and the distal ICA. Snoring resulted in a slight decrease in low TAWSS in the downstream regions of the stented segment. The stented segment was over the entire low TAWSS region at no or low snoring. When the snoring amplitude increased to 0.08 m/s, the low TAWSS region in the downstream regions of the stented segment was significantly reduced. This study quantitatively analyzed the changes in the regions with low TAWSS (TAWSS < 0.26 Pa). It was found that the area of low TAWSS in the stented segment decreased by about 22% when the snoring amplitude increased to 0.08 m/s. In addition, snoring increased the OSI in the stented segment slightly, but caused significantly high OSI distribution in the downstream areas of ICA. The high OSI region was hardly observed in the downstream region of ICA, with no snoring. However, as the snoring amplitude increased to 0.04 m/s, the high OSI region in the downstream region of ICA increased significantly. When the snoring amplitude was 0.08 m/s, the high OSI region in the downstream regions of ICA further increased and expanded towards the stented segment. This study quantitatively analyzed changes in high OSI regions (OSI > 0.31). The results showed that with the increase of snoring amplitude, the stented segments and downstream regions of the ICA

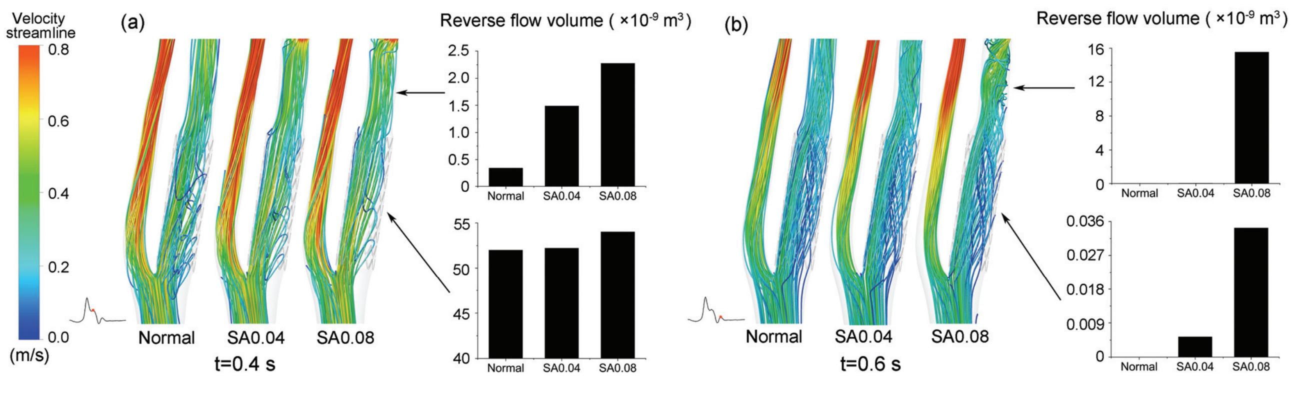

Fig. 3. (a) velocity streamlines in the stented carotid bifurcation under snoring at 0.4 s, (b) velocity streamlines in the stented carotid bifurcation under snoring at 0.6 s. Bar charts are the volumes of reverse flow in stented segment and downstream regions of ICA at 0.4 s and 0.6 s

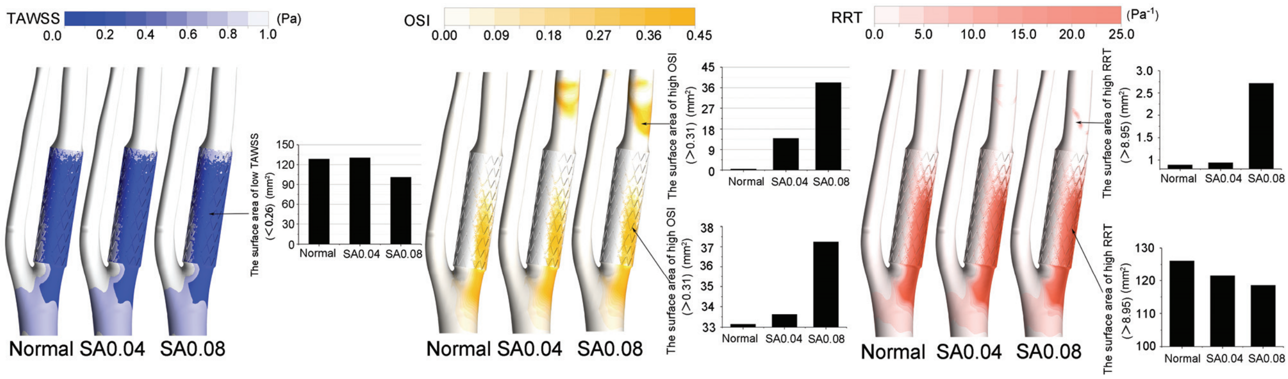

Fig. 4. TAWSS, OSI and RRT distributions under different snoring amplitudes.
The bar charts show low TAWSS (<0.26 Pa), high OSI (>0.31) and high RRT (>8.95 Pa^{-1}) area

high OSI area significantly increased. The high OSI area in the stented segment increased by about 12% from no snoring state to maximum snoring amplitude (0.08 m/s), and OSI at the downstream regions of ICA increased by about 175%.

The stented segment distribution of RRT (Fig. 4) at different states showed little difference. However, degrees of snoring caused differences in downstream regions of ICA. In the absence of snoring, almost no high RRT area was observed downstream of ICA, but when the snoring amplitude increased to 0.04 m/s, a small amount of high RRT areas appeared in the downstream regions of ICA. When the snoring amplitude increased to 0.08 m/s, the high RRT area slightly increased downstream of the ICA. This research quantitatively analyzed the changes in regions with high RRT (RRT > 8.95 Pa^{-1}). The results showed that heavy snoring slightly inhibited the high RRT area in the stented segment, but it caused the higher RRT areas at downstream regions of ICA. The high RRT area downstream of ICA with high amplitude snoring was thrice that of the control group. In addition, the RRT area of stented segment height was much greater than that of ICA in each group of models.

3.2. Effect of inlet velocity

The velocity streamline of different groups under the snoring amplitude of 0.04 m/s (Fig. 5) showed that the disturbed flow in the elderly group was more significant than that in the middle-aged group. The area of disturbed flow with low velocity appeared at the outer wall of the carotid stent segment in both groups at 0.4 seconds (Fig. 5a, b), and the lower flow velocity was observed in the elderly group. Besides, normal streamline in ICA still concentrated closely to the inner wall in both two models at 0.6 seconds, but the disturbed flow close to outer wall in the elderly group was more significant than that in the middle-aged group (Fig. 5a, b). Moreover, the elderly people displayed significant disturbance characteristics in downstream regions of ICA at this time.

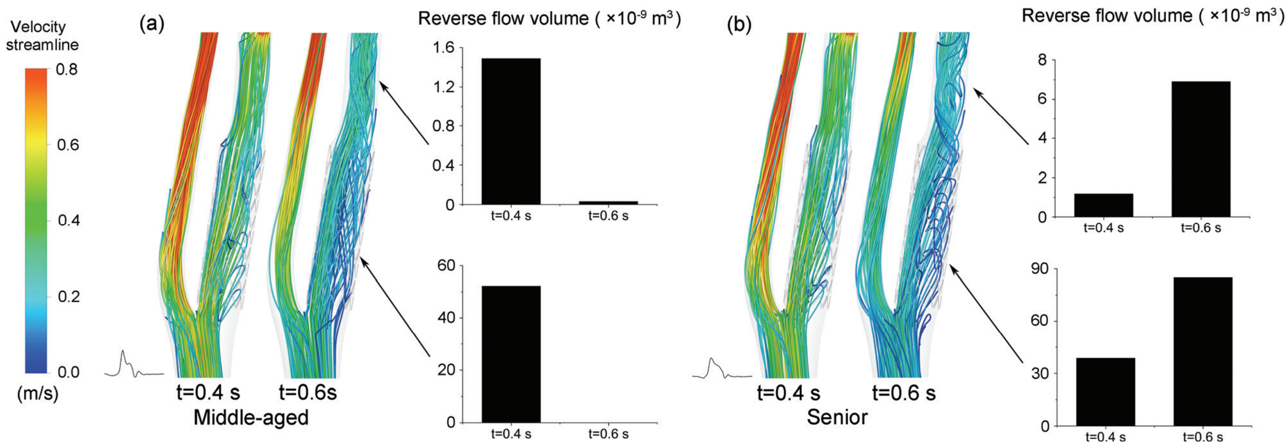

Fig. 5. (a) and (b) show the velocity streamlines of the middle-aged and the elderly groups.
Bar charts are the volumes of reverse flow in stented segment and downstream regions of ICA of the mid-aged and the elderly

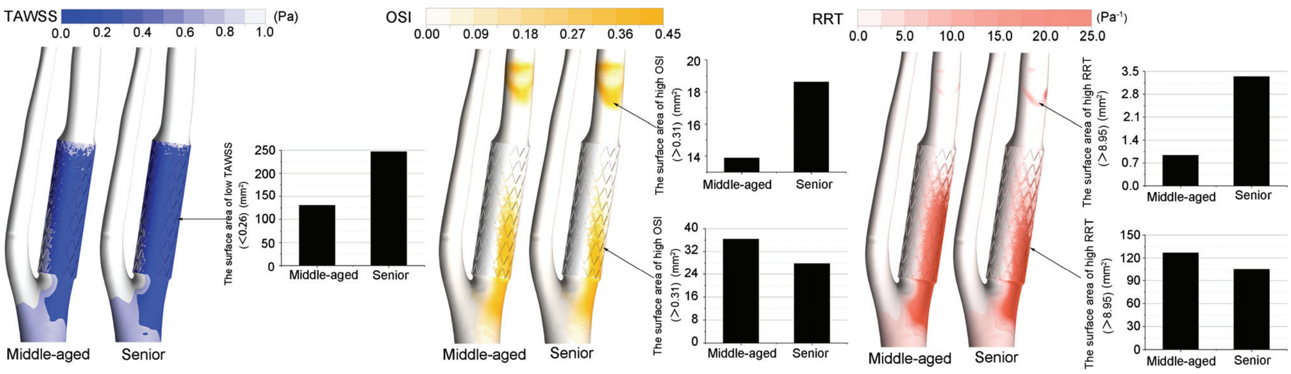

Fig. 6. TAWSS, OSI and RRT distributions of middle-aged and elderly people.
The bar charts show low TAWSS (<0.26 Pa), high OSI (>0.31) and high RRT (>8.95 Pa^{-1}) area

This research quantitatively analyzed the changes in the blood flow of the middle-aged and the elderly under the same snoring condition and the volume of reverse flow of different groups. Results showed that reverse flow volume of stented segment at different times was much larger than that in downstream regions of ICA in both groups. Moreover, reverse flow volume of middle-aged people was 1.35 times and 1.27 times larger than that of elderly groups in stented segments and downstream areas of ICA. It can be observed that reverse flow volume of middle-aged people was almost 0 m^3 in the whole ICA at 0.6 seconds. However, reverse flow volume of elderly people was up to 8.49×10^{-8} m^3 in stented segment and 6.91×10^{-9} m^3 in downstream regions of ICA at 0.6 seconds.

The TAWSS, OSI and RRT distributions of middle-aged and elderly people under a snoring amplitude of 0.04 m/s are shown in Fig. 6. Both stented segments had low TAWSS and high OSI and RRT values, concentrated at the ends of CCA and ICA. The elderly had lower TAWSS distribution in ICA bifurcation, but the OSI and RRT in the stented segment were slightly decreased. Moreover, compared with middle-aged people, elderly people had higher OSI and RRT distributions in the ICA downstream regions.

This study quantitatively analyzed the influence of age by studying the low TAWSS, high OSI, and high RRT areas of different aged groups. The results showed that low TAWSS area in the stented segment of the elderly was larger than that of the middle-aged people, and the value of the low TAWSS area was about 1.88 times that in the middle-aged people. The high OSI regions of the stent segment were 0.74 times less in the elderly than in the middle-aged. However, the high OSI areas downstream regions of ICA in the elderly were about 1.34 times that in the middle-aged. Similarly, the high RRT areas of the stented segment in the elderly were slightly lower than that in the middle-aged, about 0.82 times that in the middle-aged. Nevertheless, the RRT areas downstream of ICA of elderly people were much higher than that for middle-aged people, and the high RRT area was about 3.5 times that of middle-aged people.

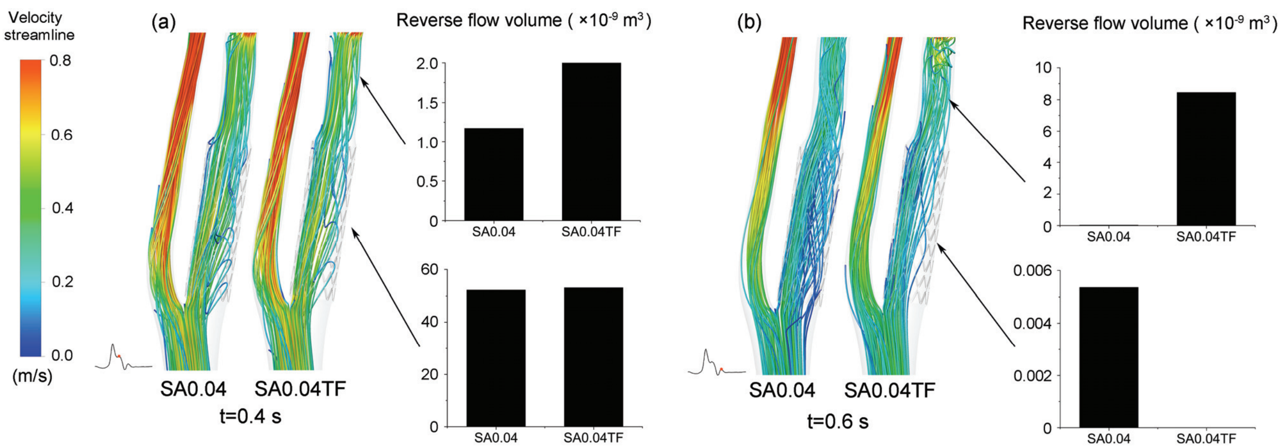

Fig. 7. (a) and (b) show the velocity streamlines of middle-aged people under different snoring frequencies.
Bar charts are the volumes of reverse flow in stented segment and downstream regions of ICA under different snoring frequencies

3.3. Effect of snoring frequency

The velocity streamlines of middle-aged people under different snoring frequencies (Fig. 7) showed that high snoring frequency slightly reduced the disturbed flow in the outer wall of the ICA stent segment. However, the streamline close to the vessels' inner wall became more obvious. Under high snoring frequency, there was no significant change in the disturbed flow between the stented segments and downstream regions of ICA at 0.4 seconds. However, the disturbed flow became more chaotic on these areas at 0.6 seconds.

This research quantitatively investigated the influence of snoring frequency on the carotid flow field by analyzing the volume of reverse flow in the host artery under different frequencies. It was found that the volume of reverse flow at stent segments was similar at 0.4 seconds, while higher frequency caused reverse flow volume increase to 1.34 times than normal frequency in downstream regions of ICA. Furthermore, reverse flow volume was almost 0 m^3 in downstream regions of ICA under normal snoring frequency at 0.6 seconds, while increasing of frequency led to 8.46×10^{-9} m^3 reverse flow volume in downstream regions of ICA. However, opposite phenomenon can be observed in stented segment that normal snoring frequency caused more reverse flow while almost no reverse flow was generated under higher frequency.

The TAWSS, OSI and RRT distributions in vessels under different snoring frequencies are shown in Fig. 8. The increase in snoring frequency slightly increased the values of low TAWSS, high OSI, and high RRT areas in the stented segments but decreased the values of high OSI and RRT areas downstream of ICA. Quantitative analysis of the stent segment showed that the low TAWSS area of the stent segment was almost unchanged. The increase in frequency resulted in a 3% increase in the high OSI area in the stent segments but led to a 32% decrease in the high OSI area downstream of ICA. The effect of snoring on RRT was smaller. High frequency increased the area of high RRT by about 0.4% and decreased it by about 2.8% downstream of ICA.

4. Discussion

As a treatment for carotid stenosis, the reliability of CAS in postponing problems such as in-stent restenosis and thrombosis has been widely studied [17], [41]. Since clinic reports have proven the relationship between snoring and cardiovascular diseases [9], [42], snoring might increase the possibility of carotid stenosis [12], [24]. Moreover, studies have established that snoring might be associated with intima-media thickness and high-risk plaque [19], [25]. Much work has investigated whether snoring could be an induced factor of cardiovascular. However, limited research focused on stented carotid artery's hemodynamic changes during snoring. A carotid model based on patient images was constructed to assess the changes in the hemodynamic environment after stent implantation during snoring. In addition, numerical simulations were run to investigate how different snoring characteristics influence the local flow field of the host artery. The effects of different snoring amplitudes, snoring frequencies, and inlet velocity on the local hemodynamic environment were discussed.

This study revealed that snoring influenced the hemodynamic environment of the host carotid artery, especially in the case of high snoring amplitude. Snor-

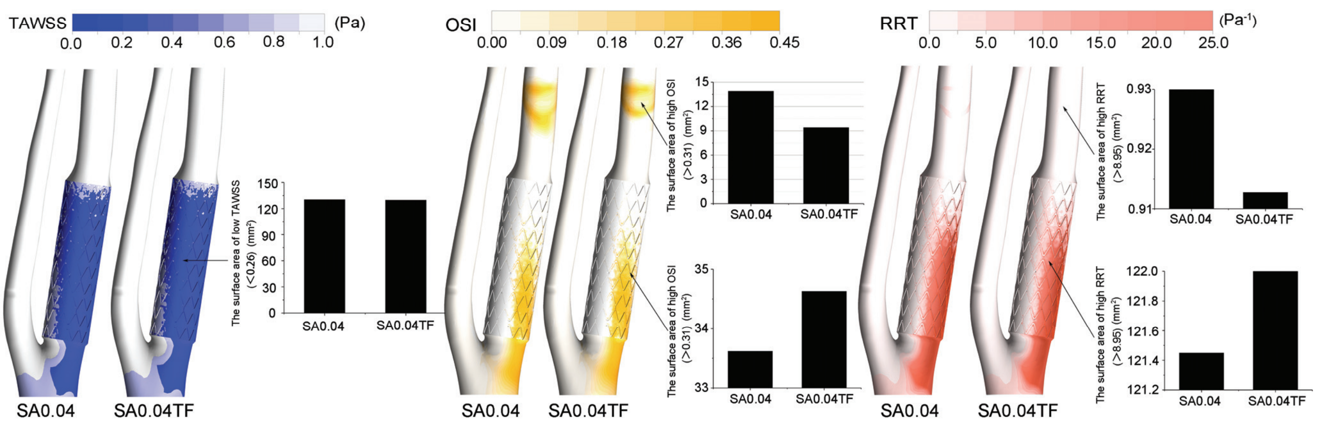

Fig. 8. TAWSS, OSI and RRT distributions of middle-aged people under different snoring frequencies. The bar chart shows low TAWSS (<0.26 Pa) high OSI (>0.31) and high RRT (>8.95 Pa^{-1}) area

ing offset the blood flow significantly at the proximal end of ICA to the inner wall of ICA, suppressing flow disturbance at the outer wall of the stented segment. Moreover, snoring suppressed the stented segment's low TAWSS and high RRT areas slightly, decreasing the possibility of proatherogenic endothelial phenotype and thrombosis [20]. In contrast, the high OSI area of the stented segment increased with increased amplitude snoring. These regions of high OSI (OSI > 0.1) demonstrated a significant relationship with the risk of neointimal hyperplasia in the stented artery [14]. However, snoring induced significantly disturbed flow downstream of ICA, and the area and degree of disturbed flow were increased acutely with the snoring amplitude. Furthermore, areas of high OSI and RRT increased dramatically with the increasing snoring amplitude in that region, indicating that thrombosis was more likely to form at the downstream regions of ICA. The disturbance of stented segments and downstream regions of ICA might be due to inertial force direction of blood flow being perpendicular to the direction of snoring oscillation. It synthesized a new velocity, deviating the blood flow and exacerbating the disturbance phenomenon. The results showed that snoring could relieve high RRT and low TAWSS distributions. However, this study could not prove that snoring induced positive effects in contrast to the adverse effects of increasing flow disturbance of stented segments and downstream regions of ICA on the local hemodynamic environment. Oscillating shear stress was associated with arterial wall remodeling, affecting smooth muscle cell intimal hyperplasia and in-stent restenosis [10]. Besides, increasing high OSI and high RRT contributed to adverse effects on downstream regions of ICA, increasing the risk of intima hyperplasia and thrombosis formation [14]. Therefore, patients with heavy snoring amplitude should not ignore their snoring, and patients who underwent snoring after CAS should receive a relevant diagnosis as soon as possible.

This research also indicated that snoring might cause more serious effects on senior-aged groups. The disturbed flow in the elderly group was more significant than that in the middle-aged group in the stented segment and downstream regions of ICA. The flow disturbances that occurred naturally might be an induced factor of neointimal hyperplasia or thrombosis [6]. The elderly had lower TAWSS distribution in ICA bifurcation. However, the OSI and RRT in the stented segment were slightly decreased, indicating that elder groups had an increased risk of in-stent restenosis [15]. Moreover, compared with middle-aged people, elderly people had higher OSI and RRT distributions downstream of ICA, increasing the risk of intima hyperplasia and thrombosis formation [37]. Higher turbulence was observed in elderly groups, possibly because the component of blood flow velocity along the *Z*-axis was perpendicular to velocity of oscillation along the *Y*-axis, thus generating a new velocity offset from the positive *Z*-axis to the positive *Y*-axis according to parallelogram law, causing the streamline to be offset. Moreover, due to the elderly's slower blood velocity, generating a larger offset velocity was easier. Therefore, elderly groups should pay more attention to snoring symptoms and take effective action to relieve snoring symptoms.

Numerical results showed that the growth of snoring frequency hardly influenced the blood flow. High snoring frequency reduced the disturbed flow easily in the outer wall of the ICA stent segment, indicating that higher frequency might not worsen the blood flow. The increase of snoring frequency slightly increased the areas of low TAWSS, high OSI and high RRT values in the stented segment but decreased the areas of high OSI and RRT values downstream of ICA. Therefore, increasing the snoring frequency might not cause adverse effects on the endothelial shear stress, and higher frequencies might not significantly influence the disturbed flow.

Limitations

There are some limitations in this study. The arterial wall was assumed as no-slip rigid, neglecting artery wall and stent movement, therefore, fluid-structure interaction research will be carried out in the future to figure out biomechanical changes of host artery under the influence of oscillation caused by snoring. Besides, the amplitude–frequency characteristic of carotid artery oscillation snoring state is difficult to capture and more complex, so this study simplified the oscillation of carotid artery during snoring. Moreover, for the geometric characteristics of carotid artery and the direction of human jumping will affect the local flow field of carotid artery, further study will be carried out in future to verify the influence of different oscillation characteristics on the host blood vessels.

5. Conclusions

The study numerically investigated the relationship between snoring and hemodynamic changes in the carotid artery after CAS. The results showed that high-amplitude snoring suppressed the disturbed flow of the stented segment. In contrast, the downstream region of ICA became more chaotic, which might be connected with adverse events. Moreover, the local blood flow of elderly people with snoring symptoms was more likely to be disturbed by the low inlet velocity waveform, increasing the possibility of vascular remodeling and thrombosis. In addition, increasing of snoring frequency slightly influenced the local disturbed flow. Consequently, oscillation caused by snoring suppressed the disturbed flow slightly and promoted a hemodynamic environment in the stented segment, but it contributed to an increased risk of abnormal blood flow at downstream regions of ICA. Therefore, this study cannot comprehensively comment on snoring affects the carotid artery's hemodynamic changes. However, it might be a reliable suggestion for old people with snoring symptoms to receive prompt medical treatment.

The ethical approval statement

This study was approved by the Ethics Committee of Beijing Friendship Hospital, Capital Medical University (approval No. 2022-P2-210-01). The study conformed to provisions of the Declaration of Helsinki (as revised in 2013).

Authors' contributions

Zhenmin Fan, Xia Ye and Xianghao Zhang conceived the idea. Zhenmin Fan, Xianghao Zhang and Xiao Liu conducted the analyses. Zhenmin Fan, Xianghao Zhang, and Mingyuan Liu provided the data. Zhenmin Fan, Xia Ye and Xiaoyan Deng wrote the paper. All authors contributed to the writing and revisions.

Declaration of conflicting interests

All authors declare no competing interests.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Acknowledgements

This work is supported by the National Natural Science Research Foundation of China (No. 12272153, 11902126), Social Development Science and Technology Support Project of Changzhou (No. G2023014038), and startup foundation of Jiangsu University of Technology (No. KYY16028), Postgraduate Research & Practice Innovation Program of Jiangsu University of Technology (No. XSJCX22_15), Zhongwu young innovative talents projection from Jiangsu Institute of Technology. Beijing Municipal Hospital Scientific Research Training Program Foundation (PX2021002), Science and Technology Project of Beijing Education Committee (KM202110025016), Beijing Hospitals Authority Youth Program (QML20210103), Capital's Funds for Health Improvement and Research (CFH 2022-4-20217).

References

[1] APAYDIN M., AYIK S.O., AKHAN G., PEKER S., ULUC E., *Carotid intima-media thickness increase in patients with habitual simple snoring and obstructive sleep apnea syndrome is associated with metabolic syndrome*, J. Clin. Ultrasound., 2013, 41, 290–296.

[2] AZHIM A., KATAI M., AKUTAGAWA M., HIRAO Y., YOSHIZAKI K., OBARA S. et al., *Blood flow velocities in common carotid artery changes with age and exercise study by using of telemetry method*, 2006 International Conference on Biomedical and Pharmaceutical Engineering, IEEE, 2006, 523–530.

[3] BOUSSEL L., HERIGAULT G., DE LA VEGA A., NONENT M., DOUEK P.C., SERFATY J.M., *Swallowing, arterial pulsation, and breathing induce motion artifacts in carotid artery MRI*, J. Magn. Reson. Imaging., 2006, 23, 413–415.

[4] CARNELLI D., PENNATI G., VILLA T., BAGLIONI L., REIMERS B., MIGLIAVACCA F., *Mechanical properties of open-cell, self-expandable shape memory alloy carotid stents*, Artif. Organs, 2011, 35, 74–80.

[5] CHIU J.-J., CHIEN S., *Effects of disturbed flow on vascular endothelium: pathophysiological basis and clinical perspectives*, Physiological Reviews, 2011, 91, 327–387.

[6] CHIU J.J., CHIEN S., *Effects of disturbed flow on vascular endothelium: pathophysiological basis and clinical perspectives*, Physiol. Rev., 2011, 91, 327–387.

[7] CHO J.-G., WITTING P.K., VERMA M., WU B.J., SHANU A., KAIRAITIS K. et al., *Tissue vibration induces carotid artery endothelial dysfunction: a mechanism linking snoring and carotid atherosclerosis?*, Sleep, 2011, 34, 751–757.

[8] CHO J.G., VERMA M., LARCOS G., AMIS T., WHEATLEY J., *Loud Snores Reduce Carotid Peak Systolic Blood Velocity and Arterial Wall Shear Stress*, A73 Sleep Disordered Breathing and Cardiovascular Impairment, American Thoracic Society, 2011, A2221-A.

[9] CHO J.G., WHEATLEY J.R., *The association of carotid artery disease with snoring and obstructive sleep apnoea: definitions, pathogenesis and treatment*, Australasian Journal of Ultrasound in Medicine, 2010, 13, 27.

[10] CUNNINGHAM K.S., GOTLIEB A.I., *The role of shear stress in the pathogenesis of atherosclerosis*, Lab. Invest., 2005, 85, 9–23.

[11] DAI Z., XU G., *Restenosis after carotid artery stenting*, Vascular, 2017, 25, 576–586.

[12] DEEB R., SMEDS M.R., BATH J., PETERSON E., ROBERTS M., BECKMAN N. et al., *Snoring and carotid artery disease: A new risk factor emerges*, Laryngoscope, 2019, 129, 265–268.

[13] DURAISWAMY N., JAYACHANDRAN B., BYRNE J., MOORE J.E., SCHOEPHOERSTER R.T., *Spatial distribution of platelet deposition in stented arterial models under physiologic flow*, Annals of Biomedical Engineering, 2005, 33, 1767–1777.

[14] HIMBURG H.A., GRZYBOWSKI D.M., HAZEL A.L., LAMACK J.A., LI X.M., FRIEDMAN M.H., *Spatial comparison between wall shear stress measures and porcine arterial endothelial per-*

meability, American Journal of Physiology Heart and Circulatory Physiology, 2004, 286, H1916-22.

[15] HOI Y., ZHOU Y.-Q., ZHANG X., HENKELMAN R.M., STEINMAN D.A., *Correlation Between Local Hemodynamics and Lesion Distribution in a Novel Aortic Regurgitation Murine Model of Atherosclerosis*, Annals of Biomedical Engineering, 2011, 39, 1414–1422.

[16] IIDA O., NANTO S., UEMATSU M., MOROZUMI T., KOTANI J., AWATA M. et al., *Effect of exercise on frequency of stent fracture in the superficial femoral artery*, Am. J. Cardiol., 2006, 98, 272–274.

[17] INOUE T., CROCE K., MOROOKA T., SAKUMA M., NODE K., SIMON D.I., *Vascular inflammation and repair: implications for re-endothelialization, restenosis, and stent thrombosis*, JACC Cardiovasc. Interv., 2011, 4, 1057–1066.

[18] KIM J., PACK A.I., RIEGEL B.J., CHIRINOS J.A., HANLON A., LEE S.K. et al., *Objective snoring time and carotid intima-media thickness in non-apneic female snorers*, J. Sleep Res., 2017, 26, 147–150.

[19] KIRKHAM E.M., HATSUKAMI T.S., HECKBERT S.R., SUN J., CANTON G., YUAN C. et al., *Association between Snoring and High-Risk Carotid Plaque Features*, Otolaryngol. Head Neck Surg., 2017, 157, 336–344.

[20] KOSKINAS K.C., CHATZIZISIS Y.S., ANTONIADIS A.P., GIANNOGLOU G.D., *Role of endothelial shear stress in stent restenosis and thrombosis: pathophysiologic mechanisms and implications for clinical translation*, J. Am. Coll. Cardiol., 2012, 59, 1337–1349.

[21] LEE G.S., LEE L.A., WANG C.Y., CHEN N.H., FANG T.J., HUANG C.G. et al., *The Frequency and Energy of Snoring Sounds Are Associated with Common Carotid Artery Intima-Media Thickness in Obstructive Sleep Apnea Patients*, Sci. Rep., 2016, 6, 30559.

[22] LEE S.-W., ANTIGA L., SPENCE J.D., STEINMAN D.A., *Geometry of the carotid bifurcation predicts its exposure to disturbed flow*, Stroke, 2008, 39, 2341–2347.

[23] LEE S.-W., ANTIGA L., STEINMAN D.A., *Correlations among indicators of disturbed flow at the normal carotid bifurcation*, 2009.

[24] LEE S.A., AMIS T.C., BYTH K., LARCOS G., KAIRAITIS K., ROBINSON T.D. et al., *Heavy Snoring as a Cause of Carotid Artery Atherosclerosis*, Sleep, 2008.

[25] LI Y., LIU J., WANG W., YONG Q., ZHOU G., WANG M. et al., *Association of self-reported snoring with carotid artery intima-media thickness and plaque*, J. Sleep Res., 2012, 21, 87–93.

[26] LIU X., FAN Y., DENG X., ZHAN F., *Effect of non-Newtonian and pulsatile blood flow on mass transport in the human aorta*, J. Biomech., 2011, 44, 1123–1131.

[27] LONG Q., XU X.Y., ARIFF B., THOM S.A., HUGHES A.D., STANTON A.V., *Reconstruction of blood flow patterns in a human carotid bifurcation: A combined CFD and MRI study*, Journal of Magnetic Resonance Imaging, 2000, 11, 299–311.

[28] MEGALY M., ALANI F., CHENG C.I., RAGINA N., *Risk Factors for the Development of Carotid Artery In-Stent Restenosis: Multivariable Analysis*, Cardiovasc. Revasc. Med., 2021, 24, 65–69.

[29] MORBIDUCCI U., GALLO D., MASSAI D., PONZINI R., DERIU M.A., ANTIGA L. et al., *On the importance of blood rheology for bulk flow in hemodynamic models of the carotid bifurcation*, J. Biomech., 2011, 44, 2427–2438.

[30] MORBIDUCCI U., GALLO D., PONZINI R., MASSAI D., ANTIGA L., MONTEVECCHI F.M. et al., *Quantitative analysis of bulk flow in image-based hemodynamic models of the carotid bifurcation: the influence of outflow conditions as test case*, Ann. Biomed. Eng., 2010, 38, 3688–3705.

[31] NARAYAN J., AMATOURY J., CHO J.G., VERMA M., KAIRAITIS K., WHEATLEY J. et al., *Snoring effects on the baroreflex: an animal model*, Respir. Physiol. Neurobiol., 2012, 180, 342–351.

[32] NG J., BOURANTAS C.V., TORII R., ANG H.Y., TENEKECIOGLU E., SERRUYS P.W. et al., *Local Hemodynamic Forces After Stenting: Implications on Restenosis and Thrombosis*, Arterioscler. Thromb. Vasc. Biol., 2017, 37, 2231–2242.

[33] ROBERTSON S.W., CHENG C.P., RAZAVI M.K., *Biomechanical response of stented carotid arteries to swallowing and neck motion*, Journal of Endovascular Therapy, 2008, 15, 663–671.

[34] SIMSEK Z., ARSLAN S., GUNDOGDU F., *Late stent thrombosis associated with heavy exercise*, Texas Heart Institute Journal, 2009, 36, 154.

[35] STONE G.W., ELLIS S.G., COLOMBO A., DAWKINS K.D., GRUBE E., CUTLIP D.E. et al., *Offsetting impact of thrombosis and restenosis on the occurrence of death and myocardial infarction after paclitaxel-eluting and bare metal stent implantation*, Circulation, 2007, 115, 2842–2847.

[36] STONE P.H., COSKUN A.U., KINLAY S., CLARK M.E., SONKA M., WAHLE A. et al., *Effect of endothelial shear stress on the progression of coronary artery disease, vascular remodeling, and in-stent restenosis in humans: in vivo 6-month follow-up study*, Circulation, 2003, 108, 438–444.

[37] SUH G.-Y., LES A.S., TENFORDE A.S., SHADDEN S.C., SPILKER R.L., YEUNG J.J. et al., *Hemodynamic Changes Quantified in Abdominal Aortic Aneurysms with Increasing Exercise Intensity Using MR Exercise Imaging and Image-Based Computational Fluid Dynamics*, Annals of Biomedical Engineering, 2011, 39, 2186–2202.

[38] TADA Y., WADA K., SHIMADA K., MAKINO H., LIANG E.I., MURAKAMI S. et al., *Roles of hypertension in the rupture of intracranial aneurysms*, Stroke, 2014, 45, 579–586.

[39] TAYLOR C., KLINE C.E., RICE T.B., DUAN C., NEWMAN A.B., BARINAS-MITCHELL E., *Snoring severity is associated with carotid vascular remodeling in young adults with overweight and obesity*, Sleep Health, 2021, 7, 161–167.

[40] TOMASZEWSKI M., SYBILSKI K., MAŁACHOWSKI J., WOLAŃSKI W., BUSZMAN P.P., *Numerical and experimental analysis of balloon angioplasty impact on flow hemodynamics improvement*, Acta Bioeng. Biomech., 2020, 22.

[41] WASSER K., SCHNAUDIGEL S., WOHLFAHRT J., PSYCHOGIOS M.N., KNAUTH M., GROSCHEL K., *Inflammation and in-stent restenosis: the role of serum markers and stent characteristics in carotid artery stenting*, PLoS One, 2011, 6, e22683.

[42] WEI Y., LV J., GUO Y., BIAN Z., FAN J., DU H. et al., *Age-Specific Associations Between Habitual Snoring and Cardiovascular Diseases in China: A 10-Year Cohort Study*, Chest., 2021, 160, 1053–1063.

[43] ZHONGYOU L., CHONG C., YU C., ZHENZE W., WENTAO J., XIAOBAO T., *Numerical insights into the determinants of stent performance for the management of aneurysm with a visceral vessel attached*, Acta Bioeng. Biomech., 2021, 23.

[44] ZWART B., VAN KERKVOORDE T.C., VAN WERKUM J.W., BREET N.J., TEN BERG J.M., VAN'T HOF A.W., *Vigorous exercise as a triggering mechanism for late stent thrombosis: A description of three cases*, Platelets, 2010, 21, 72–76.