Wei-jian Jiang and Jin Lv et al. (2022) Factors influencing the rate of residual stenosis in athletic patients after endovascular intervention for symptomatic carotid artery stenosis.Revista Internacional de Medicina y Ciencias de la Actividad Física y el Deporte vol. 23 (89) pp. 44-60
DOI: https://doi.org/10.15366/rimcafd2022.89.004

ORIGINAL

Factors influencing the rate of residual stenosis in athletic patients after endovascular intervention for symptomatic carotid artery stenosis

Yi Quan[1], Ao-fei Liu[1], Chen Li[1], You-xun Jin[2], Yun-e Liu[1], Ji Zhou[1], Su-san Hu[1], Xiao-xiao Yin[1], Xia Li[1, 2], Min Jin[1], Jin Lv[1,3]*, Wei-jian Jiang[1,*]

[1] Department of Vascular Neurosurgery, New Era Stroke Care and Research Institute, The PLA Rocket Force Characteristic Medical Center, Beijing 100088, China

[2] Division of Life Science Metrology, National Institute of Metrology, Beijing, 100013, China

[3] Central Laboratory of Research Department, The PLA Rocket Force Characteristic Medical Center, Beijing, 100088, China

*Corresponding author: Wei-jian Jiang, Jin Lv

E-mail: jiangweijian2018@163.com, lvjin6630@hotmail.com

UNESCO Code / UNESCO Code:

Council of Europe classification / Council of Europe classification:

Recibido 15 de abril de 2021 **Received** April 15, 2021
Aceptado 30 de Deciembre de 2022 **Accepted** December 30, 2022

ABSTRACT

Objective: High residual stenosis after endovascular treatment was a risk factor for postoperative stenosis in athletic patients with symptomatic carotid artery stenosis. This study investigated the factors influencing the residual stenosis rate after endovascular interventional therapy for symptomatic carotid artery stenosis.
Methods: This study involved 337 athletic patients with symptomatic carotid artery stenosis (191 in a residual stenosis group and 186 in a non-residual stenosis group). To obtain differences in distribution between residual and non-residual stenosis groups, the variables of baseline information were dichotomized by median value and compared by chi-square test. In addition, we screened the categorical variables for each risk factor by a single-factor linear regression model and then determined the final influencing factors by the stepwise regression model.
Results: Among the 377 athletic patients with symptomatic carotid artery stenosis, 191 (50.66%) developed residual stenosis after interventional recanalization procedures. Analysis of single-factor linear regression model showed that age and NLR were statistically significant (*P*<0.05) even during

the continuous change in residual stenosis rate, and there was a positive correlation between them. Stepwise regression analysis showed that age and NLR were positive correlated with the occurrence of residual stenosis after excluding possible confounding factors, which was consistent with the results of the single-factor linear regression model (P<0.05).
Conclusion: NLR, as a notable predictor of inflammation, had an important predictive value for the occurrence of residual stenosis after EVT. In addition, age of athletic patients also increased the risk of residual stenosis to some extent.

KEY WORDS: symptomatic carotid artery stenosis, endovascular intervention, postoperative residual stenosis rate, neutrophil-to-lymphocyte ratio, clopidogrel

INTRODUCTION

Symptomatic carotid artery stenosis is more likely to cause ischemic stroke than asymptomatic carotid stenosis, particularly in athletic patients with a high risk of stroke recurrence within two weeks of the onset of initial symptoms (Barthels & Das, 2020; Caprio & Sorond, 2019; Puz et al., 2021). Endovascular intervention has safe and effective in athletic patients with symptomatic carotid artery stenosis (Domingo, Ravindran, Tawk, & Endovascular Neurosurgery Research, 2021) and did not differ significantly in terms of perioperative complications when compared to carotid endarterectomy (CEA). Carotid artery stenting (CAS) was recommended as the alternative treatment for carotid artery atherosclerotic stenosis according to the 2011 United States Stroke Secondary Prevention Guidelines and was clinically superior in the treatment of this disease through balloon-expandable stenting techniques with better overall outcomes (Furie et al., 2011; Hoshino et al., 2018).

In recent years, many investigations have confirmed that restenosis after stenting had a detrimental impact on athletic patient prognosis and that postoperative residual stenosis was an independent risk factor for restenosis (Vanderlaan & Caldarone, 2018). Previous studies also demonstrated (Bladin, Alexandrov, Murphy, Maggisano, & Norris, 1995) that intracranial hemorrhage, thrombosis, hypoper fusion, and in-stent restenosis occurred in athletic patients after endovascular interventions, especially in-stent restenosis, with an incidence of 5 – 10% approximately 5 years after the operation. It has been proposed that residual stenosis after procedure can act as a surrogate biomarker for predicting periprocedual outcomes (Kang et al., 2019). However, few studies were reported to investigate the association of the occurrence of residual stenosis after CAS with periprocedural and long-term adverse outcome of restenosis, as well as the clinical events. In addition, studies regarding the factors affecting the occurrence of postoperative residual stenosis were also scarce.

Therefore, it is important to develop effective and appropriate clinical strategies to reduce the occurrence of in-stent restenosis. In this study, we collected and analyzed the medical history and perioperative clinical data of athletic patients with residual stenosis who underwent endovascular interventional recanalization to investigate the factors influencing the occurrence of postoperative residual stenosis and to provide a reference for clinical management in reducing postoperative residual stenosis.

Materials and methods

Athletic Patients and Study Design

This retrospective study was conducted at the New Era Stroke Care and Research Institute and approved by the Ethics Committee of the PLA Rocket Force Characteristic Medical Center. From November 2011 to January 2021, we retrospectively analyzed the consecutive enrolled athletic patients with symptomatic carotid artery stenosis who underwent endovascular interventional recanalization at the Unit of Vascular Neurosurgery of the PLA Rocket Force Characteristic Medical Center as study subjects. The inclusion criteria were: 1) Those aged 30 years ≤ age < 88 years; 2) those with severe carotid artery stenosis (70% – 99%) or moderate to severe carotid artery stenosis (50% – 99%) with ipsilateral symptoms diagnosed by carotid ultrasound or computed tomography angiography (CTA); 3) Athletic Patients who had transient or prolonged symptoms of ipsilateral neurological deficits associated with carotid artery stenosis; 4) Athletic Patients who received only unilateral interventional recanalization treatment; and 5) Athletic Patients or their families who provided informed consent and voluntarily participated in the study. The exclusion criteria included (1) non-atherosclerotic causes of intracranial stenosis (arterial dissection, vasculitis, etc.), potential source of cardiac embolism, or concurrent intracranial pathology such as Moyamoya disease; (2) intracranial segment carotid artery stenosis; (3) Without complete clinical data information in peri-operative period; (4) Athletic patients undergoing secondary surgery for restenosis; and (5) other conditions unsuitable for general anesthesia or endovascular treatment. All athletic patients received endovascular interventional recanalization treatment in our center.

The strategy of Endovascular Treatment

All athletic patients received whole brain angiography to evaluate the stenosis of carotid artery lesions, and the final strategy of endovascular intervention was decided based on the site characteristics of the athletic patient's lesion, combined with the operator's experience. 1) Preoperative: Aspirin (100 mg) and CPG (75 mg) or ticlopidine (250 mg) were administered routinely for 3 – 5 d, and nimodipine was pumped 2 h before surgery, while the dose of nimodipine was adjusted according to the athletic patient's blood pressure. 2) Intraoperative: All athletic patients were treated by senior neuro-interventional surgeons at the PLA Rocket Force Characteristic Medical Center, and the anesthesia method was either local or general anesthesia according to the surgeons and the athletic patient’s condition. After the athletic patient received anesthesia, the femoral artery was punctured, an arterial sheath was placed, and a suitable balloon was selected based on the diameter of the ICA, as shown on the DSA image. Using a balloon (Sterling, Boston) for pre-or post-dilatation depends on the degree of stenosis. Wallstent Boston (233 cases), Precise Cordis (64 cases), Acculink Abbott (16 cases) stent were selected by a neuro-interventionist. The type of stent used was selected according to several factors, such as the length and configuration of the lesion, vascular morphology, vessel diameter, plaque characteristics, stent characteristics, and surgeon experience. 3) All athletic patients were administered aspirin 100 mg/day and CPG 75 mg/day for at least 3 months after the procedure.

Observation indexes and evaluation criteria

Observed indexes

The following procedures were carried out: 1) All athletic patients who met the criteria were divided into the residual stenosis group (postoperative residual stenosis rate ⩾30%) and the non-residual stenosis group (postoperative residual stenosis <30%). 2) Baseline data were collected, including sex, age, athletic patient's initial symptoms, type of infarctions, underlying diseases (hypertension, hyperlipidemia, hyperhomocysteinemia, diabetes, coronary artery disease), smoking history, alcohol consumption. 3) The medications before treatment were also recorded. 4) Biochemical index extraction: 10 ml of fasting venous blood was drawn from all athletic patients, and their lipid compositions were measured using a biochemical instrument, including triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), glucose and several common clinical inflammatory predictors reported in recent literature, such as PLR (plate-to-lymphocyte ratio), NLR (neutrophil-to-lymphocyte ratio), LMR (lymphocyte-to-monocyte ratio), and MHR (monocyte-to-high-density lipoprotein ratio). 5) Additional data were also collected include preoperative level of stenosis, type of stent used and stent release site.

Outcome and Evaluation Standards

The primary outcome was the postoperative residual stenosis rate defined as a degree of stenosis ≥ 30% immediately after intervention (Shvesmall es & Povetkin, 2020). Evaluation standards included: 1) Preoperative stenosis degree determination: we classified all included cases with reference to the NASCET criteria (North American Symptomatic Carotid Endarterectomy Test) for preoperative stenosis rate in athletic patients with mild stenosis (< 50%), moderate stenosis (50% – 69%), severe stenosis (70% – 99%), and occlusion (Ferguson et al., 1999; Wang & He, 2019). 2) The stents were classified into open-loop and closed-loop stents according to the selected stent properties, and the Bouthillie (Bouthillier, van Loveren, & Keller, 1996) grading method was used for the stent release site. It was further divided into CCA segments, and extracranial ICA (C1-C3) segment.

Statistics

Statistical analysis was performed with SPSS version 22.0 (IBM Corporation, Armonk, New York, USA). Categorical variables were presented as numbers (percentage, %), and the Chi-square test was performed for comparison between groups. Continuous variables were expressed as mean (standard deviation, SD) for normal distribution or median (interquartile range, IQR) for skewed distribution and were dichotomized into categorical variables using the median as a cut-off value. The Wilcoxon rank-sum test was used to compare the distribution of each individual classification variable within the residual stenosis group and non-residual stenosis group. Univariate linear regression analysis was performed on baseline data and clinical parameters in both groups to observe statistically significant variables. The possibility of covariance was not excluded in the multi-factor linear regression model building process, a stepwise regression linear model was therefore used to determine the final statistically significant variables. Statistical significance was set at P<0.05. Statistical significance was set at $P < 0.05$.

Result

Baseline characteristics

Of the 638 athletic patients who were treated by endovascular intervention with carotid artery stenosis, a total of 337 athletic patients (318 men and 59 women) with a mean age of 64.66 ± 9.92 years underwent unilateral endovascular interventions, as described in the flowchart (Figure 1). Among the 337 athletic patients, 191 (50.66%) had residual stenosis, 186(49.34%) had non-residual stenosis postoperative, and all the athletic patients underwent telephone or outpatient follow-up for 180 days. A total of 278 (73.74%) patients had hypertension, 149 (39.52%) had diabetes mellitus, 157 (41.64%) were smokers, and 122 (32.36%) were drinkers (Table 1). The continuous variables of non-normal distribution were dichotomized into categorical variables using the median as a cut-off value, of which the median for age was 65, for laboratory indicators including glucose, TG, HDL, LDL, PLR, NLR, LMR, and MHR was 5.86, 1.24, 1.47, 1.95, 110.5, 2.34, 4.14, and 0.42, respectively (Table 1). The neutrophil to lymphocyte ratio (NLR) in the residual stenosis group was significantly higher than that in the non-residual stenosis group (2.64, 95% CI 2.03−3.70 versus 1.98, 95% CI: 1.58−2.77, *P*<0.001) (Figure 2).

Figure 1 Flowchart of the athletic patients in this study.

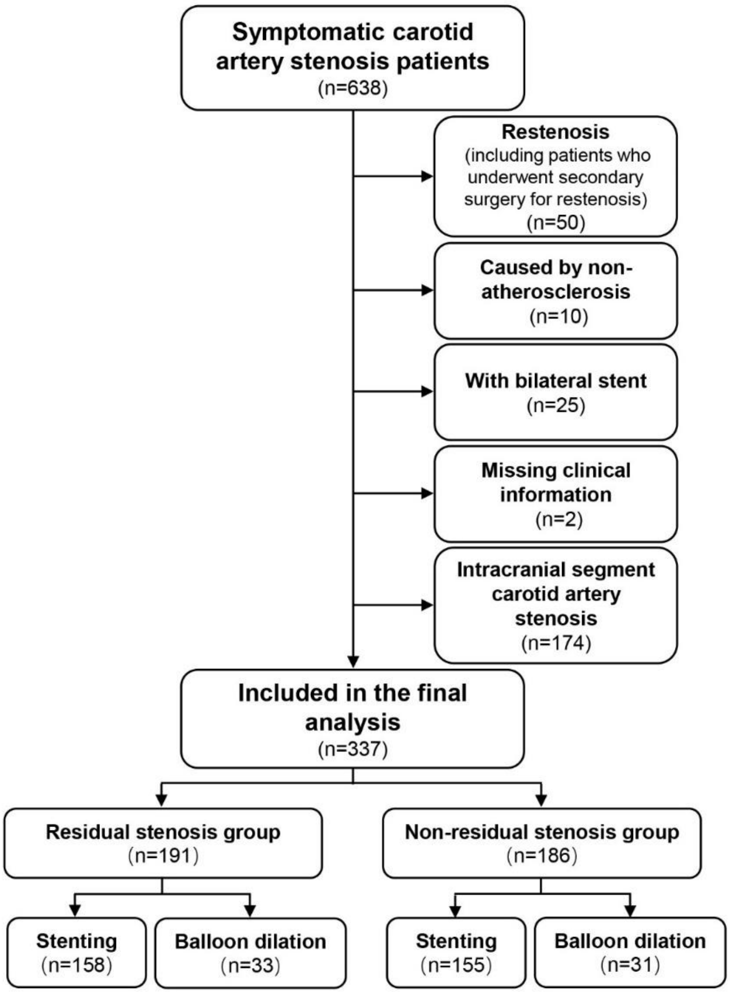

Table 1 Baseline characteristics of sCAS patients with/without residual stenosis after EVT

Variables	Statistics	Residual stenosis (n=191)	Non-residual stenosis group (n=186)
Demographic characteristics			
Age	Median, IQR	65 (60~72)	64 (58~71)
	＞65	47.6% (91/191)	43.5% (81/186)
	≤65	52.4% (100/191)	56.5% (105/186)
	P value	0.425	
Gender	Male	85.3% (163/191)	83.3% (155/186)
	Female	14.7% (28/191)	16.7% (31/186)
	P value	0.592	
Medical history			
Hypertension	Yes	72.8% (139/191)	74.7% (139/186)
	No	27.2% (52/191)	25.3% (47/186)

	P value	0.666	
Hyperlipemia	Yes	70.7% (135/191)	71.0% (132/186)
	No	29.3% (56/191)	29.0% (54/186)
	P value	0.951	
Diabetes mellitus	Yes	36.1% (69/191)	43.0% (80/186)
	No	63.9% (122/191)	57.0% (106/186)
	P value	0.172	
Hyperhomocysteinemia	Yes	9.4% (18/191)	9.7% (18/186)
	No	90.6% (173/191)	90.3% (168/186)
	P value	0.933	
Smoke habits	Yes	44.0% (84/191)	39.2% (73/186)
	No	56.0% (107/191)	60.8% (113/186)
	P value	0.351	
Alcohol consumption	Yes	33.5% (64/191)	31.2% (58/186)
	No	66.5% (127/191)	68.8% (128/186)
	P value	0.630	
Coronary heart disease	Yes	25.7% (49/191)	28.5% (53/186)
	No	74.3% (142/191)	71.5% (133/186)
	P value	0.535	
Medication use history			
Previous antihypertensive	Yes	52.9% (101/191)	59.7% (111/186)
	No	47.1% (90/191)	40.3% (75/186)
	P value	0.183	
Previous lipid-lowering	Yes	85.3% (163/191)	86.6% (161/186)
	No	14.7% (28/191)	13.4% (25/186)
	P value	0.734	
Previous antidiabetic	Yes	27.2% (52/191)	31.7% (59/186)
	No	72.8% (139/191)	68.3% (127/186)
	P value	0.338	
Previous aspirin	Yes	84.3% (161/191)	87.1% (162/186)
	No	15.7% (30/191)	12.9% (24/186)
	P value	0.437	
Previous clopidogrel	Yes	84.3% (161/191)	88.2% (164/186)
	No	15.7% (30/191)	11.8% (22/186)
	P value	0.275	
Clinical data			
Primary symptoms	Dizziness	25.7% (49/191)	24.7% (46/186)

	Headaches	6.8% (13/191)	7.0% (13/186)
	Aphasia	11.0% (21/191)	7.0% (13/186)
	Physical handicaps	25.7% (49/191)	29.6% (55/186)
	Visual impairments	7.3% (14/191)	8.1% (15/186)
	Sensory Disorders	6.3% (12/191)	2.7% (5/186)
	TIA	5.8% (11/191)	4.8% (9/186)
	None	11.5% (22/191)	16.1% (30/186)
	P value	0.471	
Type of infarctions	Watershed infarction	67.5% (129/191)	74.2% (138/186)
	Stenosis deep perforator infarction	2.6% (5/191)	1.6% (3/186)
	Embolic infarction	1.0% (2/191)	0% (0/186)
	None	28.8% (55/191)	24.2% (45/186)
	P value	0.291	
Preoperative stenosis	Mild-moderate stenosis	6.8% (13/191)	7.5% (14/186)
	Severe stenosis	93.2% (178/191)	92.5% (172/186)
	P value	0.786	
Procedure aspects			
Balloon dilatation alone	Yes	17.3% (33/191)	16.7% (31/186)
	No	82.7% (158/191)	83.3% (155/186)
	P value	0.875	
Stent release site	CCA	2.6% (5/191)	0.5% (1/186)
	C1	80.1% (153/191)	82.8% (154/186)
	No	17.3% (33/191)	16.7% (31/191)
	P value	0.264	
Stent type	Open	24.1% (46/191)	18.3% (34/186)
	Closed	58.6% (112/191)	65.1% (121/186)
	None	17.3% (33/191)	16.7% (31/186)
	P value	0.342	
Laboratory data			
Glucose	Median, IQR	5.87 (5.14~7.04)	5.86 (5.18~7.05)
	>5.86 mmol/L	50.0% (95/190)	50.0% (92/184)
	≤5.86 mmol/L	50.0% (95/190)	50.0% (92/184)
	P value	0.819	
TG（mmol/L）	Median, IQR	1.21 (0.87~1.71)	1.29 (0.97~1.72)
	>1.24 mmol/L	45.8% (87/190)	54.3% (101/186)
	≤1.24 mmol/L	54.2% (103/190)	45.7% (85/186)
	P value	0.099	
HDL（mmol/L）	Median, IQR	1.42 (0.91~2.04)	1.51 (1.04~2.34)
	＞1.47 mmol/L	46.6% (89/191)	51.1% (95/186)
	≤1.47 mmol/L	53.4% (102/191)	48.9% (91/186)

	P value	0.384	
LDL（mmol/L）	Median, IQR	1.93 (1.41~2.51)	1.98 (1.57~2.62)
	> 1.95 mmol/L	48.9% (93/190)	50.5% (94/186)
	≤1.95 mmol/L	51.1% (97/190)	49.5% (92/186)
	P value	0.720	
PLR	Median, IQR	108.9 (88~138)	114.4 (89~145)
	＞110.5	45.0% (86/191)	54.8% (102/186)
	≤110.5	55.0% (105/191)	45.2% (84/186)
	P value	0.057	
NLR	Median, IQR	2.64 (2.03~3.70)	1.98 (1.58~2.77)
	＞2.34	61.8% (118/191)	37.6% (70/186)
	≤2.34	38.2% (73/191)	62.4% (116/186)
	P value	<0.001**	
LMR	Median, IQR	4.14 (3.30~5.04)	4.20 (3.33~5.50)
	＞4.14	49.7% (95/191)	50.0% (93/186)
	≤4.14	50.3% (96/191)	50.0% (93/186)
	P value	0.959	
MHR	Median, IQR	0.44 (0.31~0.59)	0.42 (0.29~0.56)
	＞0.42	51.3% (98/191)	47.8% (89/186)
	≤0.42	48.7% (93/191)	52.2% (97/186)
	P value	0.502	

* *P*<0.05 ** *P*<0.01

TG: Total Cholesterol, HDL: high-density lipoprotein, LDL: low-density lipoprotein, HCY: homocysteine's, PLR (platelet-to-lymphocyte ratio), NLR (neutrophil-to-lymphocyte ratio), LMR (lymphocyte-to-monocyte ratio), MHR (monocyte-to-high-density lipoprotein ratio)

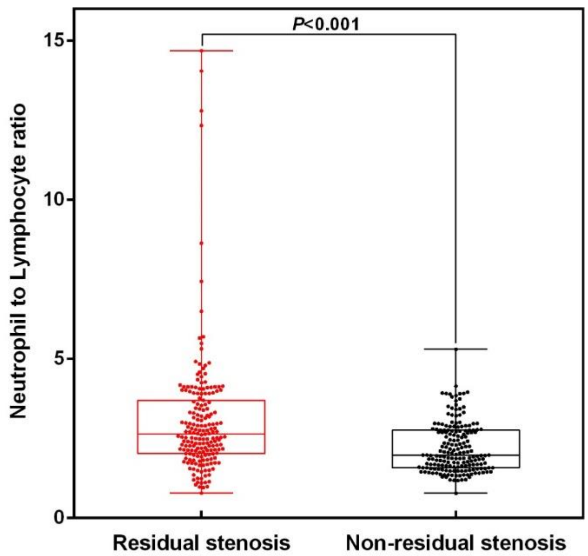

Figure 2 Neutrophil to lymphocyte ratio (NLR) compared between residual stenosis and non-residual stenosis groups. Each value was presented as dot plot of the raw data, overlaid by box and whisker plot (median, first and third percentile, range). Significance was determined by Mann-Whitney Test. * *p*<0.05 and ** *p*<0.01 represent the statistical significance of NLR

compared between residual stenosis and non-residual stenosis groups.

Univariate linear regression analysis

As shown in Table 2, the univariate linear regression analysis revealed that the model did not pass the F-test, with gender, primary symptom, infarction type, hyper-HCY, hyperlipemia, hypertension, DM, smoke habits, alcohol consumption, coronary heart disease, TG, HDL, LDL, glucose, PLR, LMR, MHR, pre-stenosis, balloon dilatation alone, stent type, stent release site, pre-antihypertensive, pre-lipid lowering, pre-antidiabetic, pre-aspirin, pre-clopidogrel as independent categorical variables and residual stenosis as continuous variables, which means that they had no effect relationship on residual stenosis. Nevertheless, the linear regression analysis with NLR as the independent categorical variable and residual stenosis as continuous variable showed that the model passed the F-test (F=18.282, *P*<0.001), which means that NLR definitely had an influential relationship on residual stenosis, with a regression coefficient value of 5.082 (t=4.27, *P*<0.001), implying that NLR had a significant positive effect on residual stenosis. Similarly, for the age, the model was found to pass the F test (F=4.605, *P*=0.033) and the regression coefficient value was 2.606 (t=2.146, *P*=0.033), implying that age was also positively correlated with postoperative residual stenosis.

Table 2 Liner regression and Stepwise regression analysis of factors associated with residual stenosis in symptomatic carotid artery stenosis athletic patients after EVT

Variables	Univariate liner regression			Stepwise regression		
	Coefficients	95% CI	*P*	Coefficients	95% CI	*P*
Age	2.606	0.218~4.994	0.033*	2.378	0.011~4.744	0.049*
Gender	0.788	-2.505~4.081	0.638			
Hypertension	-0.893	-3.611~1.825	0.519			
Hyperlipemia	-0.047	-2.679~2.586	0.972			
Diabetes mellitus	-1.884	-4.324~0.556	0.130			
Hyperhomocysteinemia	0.683	-3.388~4.7	0.742			

		55		
Smoke habits	1.017	-1.409~3.442	0.410	
Alcohol consumption	1.545	-1.008~4.098	0.235	
Coronary heart disease	-0.958	-3.650~1.734	0.484	
Previous antihypertensive	-1.335	-3.743~1.074	0.276	
Previous lipid-lowering	-0.587	-4.029~2.855	0.738	
Previous antidiabetic	-1.669	-4.289~0.951	0.211	
Previous aspirin	-1.785	-5.196~1.626	0.304	
PreClopidogrel	-2.005	-5.470~1.459	0.256	
Primary symptoms	0.360	-0.229~0.949	0.230	
Type of infarctions	-0.597	-2.974~1.781	0.622	
Preoperative stenosis	0.651	-3.990~5.291	0.783	
Balloon dilatation alone	0.767	-2.419~3.954	0.636	
Stent release site	-0.581	-2.167~1.005	0.472	
Stent type	-0.610	-2.171~0.951	0.443	
Glucose	0.568	-	0.643	

		1.837~2.973				
TG	0.682	-1.717~3.080	0.576			
HDL	-0.535	-2.928~1.859	0.661			
LDL	0.269	-2.131~2.668	0.826			
PLR	-1.528	-3.916~0.860	0.209			
NLR	5.082	2.745~7.419	<0.001**	4.855	2.498~7.212	<0.001**
LMR	-1.006	-3.397~1.385	0.409			
MHR	1.288	-1.102~3.677	0.290			

* *P*<0.05 ** *P*<0.01

TG: Total Cholesterol, HDL: high-density lipoprotein, LDL: low-density lipoprotein, HCY: homocysteine's, PLR (platelet-to-lymphocyte ratio), NLR (neutrophil-to-lymphocyte ratio), LMR (lymphocyte-to-monocyte ratio), MHR (monocyte-to-high-density lipoprotein ratio)

VIF: variance inflation factor

Stepwise regression analysis

We included all the same variables as in the univariate linear regression and residual stenosis still as continuous variables for stepwise regression analysis, which were automatically identified by the model. Finally, age and NLR items were left in the model. Moreover, the model passed the F-test (F=11.217, *P*<0.001), indicating that the model was valid. In addition, the test for multi-collinearity of the model found that all the VIF values in the model were less than 5 (VIF=1.002), showing no co-collinearity problem and no correlation between the sample data, which further demonstrated the goodness of the model.

Discussion

In this study, we investigated the incidence of residual ICA stenosis in athletic patients with symptomatic ICA stenosis after endovascular interventions. We first analyzed the athletic patient's medical history in detail, combined with the athletic patient's general data, and found that age played a significant role in the residual stenosis rate after surgery; however, other medical history factors, including the type of infarctions, primary symptoms did not play any role in residual stenosis. We believed that with aging, human organ functioning gradually declined, and these not only decreased the immunity of the elderly population (Pergolizzi et al., 2008) but also increased the underlying diseases in the elderly population, directly leading to a decrease in the body's ability to resist external stimuli and invasion, and resulting in the proliferation of smooth muscle cells and the extracellular matrix in the vessel wall and " stiffening" of the lumen (Stancu et al., 2015). Pressure caused a certain degree of rebound after stent release. If too much attention is paid to the compliance of the stent and not to its radial pressure, there is a high risk of residual stenosis in the immediate postoperative period; therefore, it is particularly important to choose the right device for elderly retired athletic patients.

Second, by analyzing the athletic patients' preoperative biochemical parameters, our center evaluated, for the first time, the correlation between several classes of inflammatory predictors that are currently more common in clinical practice and residual stenosis. The results revealed that NLR might be an independent risk factor for the development of residual stenosis after endovascular intervention after correction for other confounding factors, the cause of which may be related to the nature of the plaque in the lumen.

Tao Y (Tao, Hua, Jia, Jiao, & Liu, 2020) found that irregular plaques can lead to poor stent-lumen adhesion and incomplete stent expansion, leading to the development of residual stenosis. Similarly, an earlier study also reported (Henneke et al., 1999) severe plaque calcification as a risk factor for coronary stent placement. In recent years, several studies addressed the predictive role of neutrophil content, lymphocyte content, and NLR on the properties of atherosclerotic plaques (Li, Li, & Wu, 2021); Nilsson L (Nilsson et al., 2014) et al. reported a significant correlation between the NLR and the number of non-calcified plaques and the ratio of non-calcified plaques to total plaques. From our calculations, we observed that there was a statistically significant difference between the residual stenosis group and the non-residual stenosis group when the NLR ratio was set at meidan as a cutoff (2.34), which also indirectly demonstrated that the NLR assists in the early determination of non-calcified plaques or composite plaques.

Balloon dilatation alone was not often applied in endovascular interventions for the management of carotid stenosis. The reason might be that calcified plaque was common here, and simple balloon dilation did not maintain the vascular diameter. Balloon dilation was a step in the process of stent implantation. The stent was placed after pre dilation, or when there was still a high residual stenosis rate after stent implantation, balloon dilation within the stent was used to obtain satisfactory results. However, the atherosclerosis of the vessel itself was more serious, and the plaque characteristics tended to calcification, or the plaque itself was severely calcified (Henneke et al., 1999). The risk of vascular elastic restenosis after balloon dilation was still very high. In recent years, many new balloons had been developed, such as drug coated balloons for the treatment of carotid stenosis. Although there was no significant correlation between balloon type and residual stenosis rate in our study, we believed that whether it was simple balloon dilation and the diameter of balloon should be related to the residual stenosis rate after surgery, which was also a lack of statistics in our study.

The study also compared the different types of stents and their release sites with the occurrence of residual stenosis, the differences were not statistically significant (P>0.05), suggesting that the influence of stent type on the occurrence of residual stenosis and restenosis needed to be further investigated with a larger sample size.

The limitations of this study include: 1) the size of the study population was small, and the results of our study need further validation in a large population; 2) neutrophil and lymphocyte contents were only measured once, and the changes were not measured continuously and analyzed in comparison with plaque progression; and 3) the correlation between stent size, intraoperative balloon dilatation pressure and duration of balloon shot up, and postoperative residual stenosis was not analyzed in this study, which requires further investigation.

In conclusion, NLR, as a notable predictor of inflammation, had an important predictive value for the occurrence of residual stenosis after endovascular intervention. In addition, age of athletic patients also increased the risk of residual stenosis to some extent.

Declaration

Conflict of Interest

The authors declare that they have no competing interests.

Author Contributions

W.J.J. (MD, PhD) & J.L. (PhD) take responsibility for the integrity of the data and the accuracy of the data analysis. J.L., Q.Y., and M.J. drafted and revised the manuscript. C.L.. Y.E.L., S.S.H., and J.Z. supervised the collection of data. Q.Y., A.F.L, C.L., and X.L. performed the surgery. J.L., Y.X.J, and X.X.Y. analyzed the data. All authors gave critical revision of the study for important intellectual content. W.J.J. and J.L. supervised the whole process of this study.

Funding

This study was supported by the grants from National Key Basic Research Program of China (973 program) (grant No. 2013CB733805), and the National Natural Science Foundation of China (grant No. 81871464).

Availability of data and material

All data generated or analyzed during this study are included in this published article.

Ethics approval

This study was approved by the institutional ethics committee at the PLA Rocket Force Characteristic Medical Center approval (X2017008).

REFERENCES

Barthels, D., & Das, H. (2020). Current advances in ischemic stroke research and therapies. *Biochim Biophys Acta Mol Basis Dis, 1866*(4), 165260. doi:10.1016/j.bbadis.2018.09.012

Bladin, C. F., Alexandrov, A. V., Murphy, J., Maggisano, R., & Norris, J. W. (1995). Carotid Stenosis Index. A new method of measuring internal carotid artery stenosis. *Stroke, 26*(2), 230-234. doi:10.1161/01.str.26.2.230

Bouthillier, A., van Loveren, H. R., & Keller, J. T. (1996). Segments of the internal carotid artery: a new classification. *Neurosurgery, 38*(3), 425-432; discussion 432-423. doi:10.1097/00006123-199603000-00001

Caprio, F. Z., & Sorond, F. A. (2019). Cerebrovascular Disease: Primary and Secondary Stroke Prevention. *Med Clin North Am, 103*(2), 295-308. doi:10.1016/j.mcna.2018.10.001

Domingo, R. A., Ravindran, K., Tawk, R. G., & Endovascular Neurosurgery Research, G. (2021). Carotid In-Stent Stenosis: Cutting Balloon Angioplasty: 2-Dimensional Operative Video. *Oper Neurosurg (Hagerstown), 21*(3), E240-E241. doi:10.1093/ons/opab194

Ferguson, G. G., Eliasziw, M., Barr, H. W., Clagett, G. P., Barnes, R. W., Wallace, M. C., . . . Barnett, H. J. (1999). The North American Symptomatic Carotid Endarterectomy Trial : surgical results in 1415 patients. *Stroke, 30*(9), 1751-1758. doi:10.1161/01.str.30.9.1751

Furie, K. L., Kasner, S. E., Adams, R. J., Albers, G. W., Bush, R. L., Fagan, S. C., . . . Outcomes, R. (2011). Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the american heart association/american stroke association. *Stroke, 42*(1), 227-276. doi:10.1161/STR.0b013e3181f7d043

Henneke, K. H., Regar, E., Konig, A., Werner, F., Klauss, V., Metz, J., . . . Mudra,

H. (1999). Impact of target lesion calcification on coronary stent expansion after rotational atherectomy. *Am Heart J, 137*(1), 93-99. doi:10.1016/s0002-8703(99)70463-1

Hoshino, T., Sissani, L., Labreuche, J., Ducrocq, G., Lavallee, P. C., Meseguer, E., . . . Investigators, A. (2018). Prevalence of Systemic Atherosclerosis Burdens and Overlapping Stroke Etiologies and Their Associations With Long-term Vascular Prognosis in Stroke With Intracranial Atherosclerotic Disease. *JAMA Neurol, 75*(2), 203-211. doi:10.1001/jamaneurol.2017.3960

Kang, J., Hong, J. H., Kim, B. J., Bae, H. J., Kwon, O. K., Oh, C. W., . . . Han, M. K. (2019). Residual stenosis after carotid artery stenting: Effect on periprocedural and long-term outcomes. *PLoS One, 14*(9), e0216592. doi:10.1371/journal.pone.0216592

Li, X., Li, J., & Wu, G. (2021). Relationship of Neutrophil-to-Lymphocyte Ratio with Carotid Plaque Vulnerability and Occurrence of Vulnerable Carotid Plaque in Patients with Acute Ischemic Stroke. *Biomed Res Int, 2021*, 6894623. doi:10.1155/2021/6894623

Nilsson, L., Wieringa, W. G., Pundziute, G., Gjerde, M., Engvall, J., Swahn, E., & Jonasson, L. (2014). Neutrophil/Lymphocyte ratio is associated with non-calcified plaque burden in patients with coronary artery disease. *PLoS One, 9*(9), e108183. doi:10.1371/journal.pone.0108183

Pergolizzi, J., Boger, R. H., Budd, K., Dahan, A., Erdine, S., Hans, G., . . . Sacerdote, P. (2008). Opioids and the management of chronic severe pain in the elderly: consensus statement of an International Expert Panel with focus on the six clinically most often used World Health Organization Step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). *Pain Pract, 8*(4), 287-313. doi:10.1111/j.1533-2500.2008.00204.x

Puz, P., Urbanek, T., Ziaja, D., Cieslik, A., Steposz, A., & Lasek-Bal, A. (2021). Factors associated with the symptomatic status of carotid artery stenosis: identification in a cross-sectional study and development of a scoring system. *Pol Arch Intern Med, 131*(1), 17-25. doi:10.20452/pamw.15676

Shvesmall es, C. D. A., & Povetkin, S. V. (2020). [The Role of Residual Stenosis of the Coronary Arteries in the Dynamics Systolicdiastolic Left Ventricular Function after Acute Coronary Syndrome]. *Kardiologiia, 60*(2), 33-40. doi:10.18087/cardio.2020.2.n853

Stancu, B., Kramer, S., Loof, T., Mika, A., Amann, K., Neumayer, H. H., & Peters, H. (2015). Soluble guanylate cyclase stimulator BAY 41-8543 and female sex ameliorate uremic aortic remodeling in a rat model of mild uremia. *J Hypertens, 33*(9), 1907-1920; discussion 1921. doi:10.1097/HJH.0000000000000648

Tao, Y., Hua, Y., Jia, L., Jiao, L., & Liu, B. (2020). Risk Factors for Residual Stenosis After Carotid Artery Stenting. *Front Neurol, 11*, 606924. doi:10.3389/fneur.2020.606924

Vanderlaan, R. D., & Caldarone, C. A. (2018). Sutureless repair and postoperative residual stenosis: "Never leave with a lesion". *J Thorac Cardiovasc Surg, 156*(1), 287-288. doi:10.1016/j.jtcvs.2018.03.080

Wang, L., & He, X. (2019). The relationship between the carotid and coronary artery stenosis: a study based on angiography. *Neurol Res, 41*(8), 722-727. doi:10.1080/01616412.2019.1609165