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Impact of carotid hemodynamics on carotid plaque location: Age difference.

Xia Ren[1], Fan Su[1], Jian Hu[1], Lei Cao[1], Yumei Zhou[1], Yuhan Fu[1], Grace Tavengana[1], Mingfei Jiang[2], Huan Wu[3], Yufeng Wen[1]

1 School of Public Health, Wannan Medical College, Wuhu, Anhui Province, China.
2 School of Clinical Medicine, Wannan Medical College, Wuhu, Anhui Province, China.
3 School of Laboratory Medicine, Wannan Medical College, Wuhu, Anhui Province, China.

Correspondence to: Yufeng Wen
No.22, Wenchang Xi Road, Wuhu City, Anhui Province, 241002, China.
E-MAIL: wyf2015w@sina.com

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Abstract

PURPOSE: This study was aimed to investigate the influence of carotid hemodynamics in common carotid artery (CCA) and internal carotid artery (ICA) on carotid plaque location.
METHODS: A total of 4444 participants from Anhui Maanshan People's Hospital were selected from December 2013 to December 2018. Doppler ultrasound was used to measure the location of carotid plaque. Patients were divided into four groups according to plaque location: LEFT, RIGHT, BOTH, and NONE. Multiple logistic regression and smooth curve were applied to determine the relationship of carotid plaque location and hemodynamic indexes.
RESULTS: Compared with the NONE group, the ratio of artery systolic and diastolic blood flow velocity in right internal carotid (RICA S/D) was a risk factor for LEFT group (OR=1.548) after adjustment; artery systolic and diastolic blood flow velocity ratio of left common carotid artery (LCCA S/D) was a risk factor for RIGHT group (OR=1.250); resistance index of right internal carotid (RICA RI) was a protective factor for BOTH group (OR=0.097), while LCCA S/D and RICA S/D were risk factors for BOTH group (OR=1.201, OR=1.457). Compared with the RIGHT group, artery systolic and diastolic blood flow velocity ratio of right common carotid (RCCA S/D) was the risk factor for the LEFT group (OR=1.463), LCCA S/D and RICA S/D were the risk factors for BOTH group (OR=1.706, OR=2.111). After age stratification, resistance index of right common carotid artery (RCCA RI) and resistance index of left internal carotid artery (LICA RI) were protective factors for BOTH group (OR=0.046, OR=0.042) in group younger than 52. RCCA S/D and RICA S/D were risk factors for BOTH group (OR=1.557, OR=1.843). Resistance index of left common carotid artery (LCCA RI) was a protective factor in the LEFT group compared with the RIGHT group (OR=0.476). In group older than 52, RICA S/D was a risk factor for LEFT group (OR=1.388). LCCA S/D was a risk factor for RIGHT group (OR=1.575). LCCA S/D and RICA S/D were risk factors for BOTH group (OR=1.348, OR=1.311). RICA S/D and RCCA S/D were protective factors in the LEFT group compared with the RIGHT group (OR=0.567, OR=0.680).

ORIGINAL ARTICLE

CONCLUSIONS: In people younger than 52 years of age, left-sided plaque formation is associated with increased left-sided blood flow, and bilateral carotid plaque formation is strongly associated with increased right-sided carotid blood flow. In people older than 52, abnormal blood flow on one side is more likely to plaques on the opposite side.

Abbreviations:

RCCA PSV	- artery systolic blood flow velocity ratio of right common carotid
RCCA EDV	- diastolic blood flow velocity ratio of right common carotid
RICA PSV	- artery systolic blood flow velocity in right internal carotid
RICA EDV	- diastolic blood flow velocity in right internal carotid
LCCA PSV	- artery systolic blood flow velocity ratio of left common carotid artery
LCCA EDV	- diastolic blood flow velocity ratio of left common carotid artery
LICA PSV	- artery systolic blood flow velocity ratio of left internal carotid artery
LICA EDV	- diastolic blood flow velocity ratio of left internal carotid artery
RCCA S/D	- artery systolic and diastolic blood flow velocity ratio of right common carotid
RICA S/D	- the ratio of artery systolic and diastolic blood flow velocity in right internal carotid
LCCA S/D	- artery systolic and diastolic blood flow velocity ratio of left common carotid artery
LICA S/D	- artery systolic and diastolic blood flow velocity ratio of left internal carotid artery
RICA RI	- resistance index of lift common carotid artery
RCCA RI	- resistance index of right common carotid artery
LICA RI	- resistance index of left internal carotid artery
LCCA RI	- resistance index of left common carotid artery
VIF	- Variance Inflation Factor
MGCV	- Mixed Generalized additive models Computation Vehicle

INTRODUCTION

Atherosclerosis is an important concerned issue to public health worldwide (Jiang *et al.* 2020). There are no obvious symptoms in the early stages of atherosclerosis. However, when plaque ruptures, the incidence of serious acute cardiovascular and cerebrovascular events is higher (Barquera *et al.* 2015). Atherosclerotic plaque formation is a chronic insidious process with a number of potential contributors to the formation of such plaques. The definition of atherosclerosis is not only limited to abnormal deposition of lipid but also includes a chronic, complex, inflammatory process (Bir & Kelley 2022). The localization of atherosclerotic lesion formation to regions of disturbed blood flow associated with certain arterial geometries, in humans and experimental animals, suggests an important role for hemodynamic forces in the pathobiology of atherosclerosis (Lu *et al.* 2019). In addition, hemodynamic changes will also aggravate vascular lesions and accelerate the development of atherosclerosis (Au *et al.* 2020). At present, there are many studies focus on the relationship between hemodynamics and atherosclerosis, but in view of the complex relationship between them, it is still necessary to further explore the law of their interaction. We have known that carotid plaque formation is affected by hemodynamics, but it is worth investigating whether it affects plaque location change.

In recent years, carotid color Doppler ultrasound is widely used to detect hemodynamic stenosis and assess cardiovascular risk (Cheng *et al.* 2022). Carotid artery plaque is a direct and vital index of carotid artery disease (Pinho *et al.* 2019; Wang *et al.* 2017), and carotid ultrasound can estimate the degree of carotid atherosclerosis by measuring the stenosis degree of plaque with the peak systolic velocity (PSV), end diastolic velocity (EDV), resistance index (RI). RI is a reflection of vascular resistance, which is the resistance encountered in front of blood flow at the detection site. The higher the RI is, the greater the resistance is. Studies confirmed that the combined application of PSV and EDV has advantages in studying the pathological characteristics of carotid arteries (Lal *et al.* 2004).

Due to the plaque location being one of the important characteristics to carotid artery plaque, the aim of this study is to explore the relationship between carotid artery plaque location and hemodynamic indexes and improve the understanding of the internal relationship between carotid hemodynamics and plaque location.

PARTICIPANTS AND METHODS

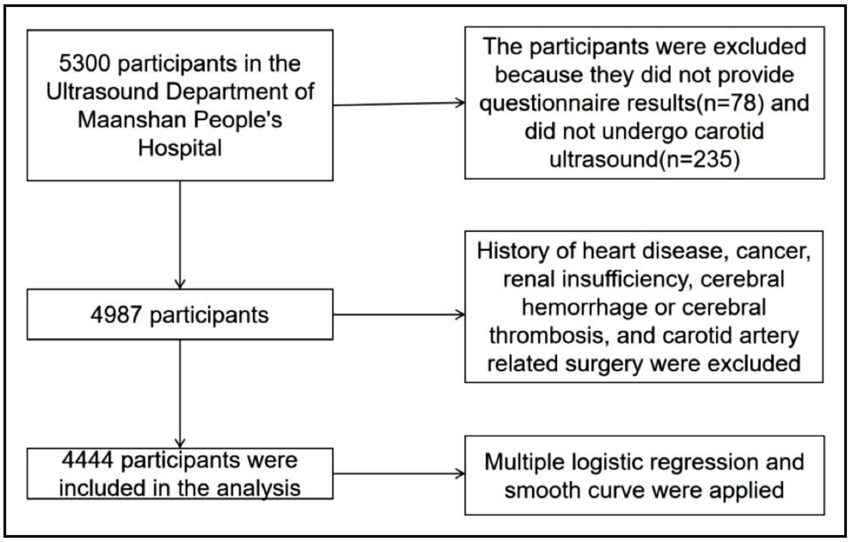
Study design and population

This cross-sectional study was conducted in Maanshan People's Hospital, and the study subjects were selected who underwent carotid artery examination in the ultrasound department between December 2013 and December 2018. Finally, the study involved a total of 4444 participants made up of 2236 females (50.32%) and 2208 males (49.68%). Inclusion criteria: (1) age between 18 and 80 years; (2) have a duplex examination from the carotids; (3) subjects with available data on age, sex, Body Mass Index (BMI), Coronary Heart Disease (CHD), hypertension, dyslipidemia, diabetes, smoking and alcohol. Exclusion criteria: (1) heart disease; (2) cancer; (3) renal insufficiency; (4) history of cerebral hemorrhage or cerebral thrombosis; (5) carotid artery related surgery history. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. This study was approved by review board of the hospital (NO.2014001), and all participants in the study signed informed consent (World Medical Association General Assembly 2004).

Research methods

Questionnaire survey

The questionnaire was developed by radiologists and epidemiologists and was reviewed and revised by clinicians and radiologists. All investigators were trained uniformly prior to the study. The contents of the questionnaire included general demographic characteristics



(such as age, sex, etc.), behavioral characteristics (such as smoking, alcohol, etc.), and previous disease history (such as hypertension, diabetes, etc.). All the investigations were conducted by face-to-face interviews with the subjects themselves or their accompanying family members.

Physical examination

Physical examination includes blood pressure measurement, body mass index calculation. Data are obtained by professionally trained surveyors who are skilled in operating instruments and equipment in accordance with standardized measurement methods.

Blood pressure measurement: After resting in a quiet environment for 15 minutes, ask the participants to take a sitting position with both legs vertical and both feet flat on the floor with the brachial artery in the right arm flush with the heart. A desktop Hg sphygmomanometer (Fish Jump, Jiangsu, China) was used for measurement. Systolic and diastolic blood pressure were represented by Korotkoff stage I and V readings, respectively. Blood pressure was taken three times and averaged, with rest intervals of 1-2min. It needs to measure again if the results of the three measurements differ greatly. The average of the last two records was used for analysis.

Body mass index calculation: All participants took off their shoes and socks and stood at attention with their eyes straight in front of them, their chest out, their arms hanging naturally, their heels together, and their heels, hips, and shoulder blades on the same plane. Height and weight were accurate to 0.1 cm and 0.1 kg, respectively. BMI = weight (kg)/ height^2 (m^2).

Carotid ultrasound

The participants were placed in a supine position with a pillow placed under their neck to fully expose the neck area for examination. The participants' head was deflected to one side to check the opposite side. The professional physicians used 5-13 MHz linear array probe (AlOKA-A7 and AlOKA-A10, Tokyo; Philips-IU22, Colombia) to start from the anterior edge of the sternocleidomastoid muscle, and the proximal, middle, and distal ends of the participants' left common carotid artery (LCCA) and right common carotid artery (RCCA). The left internal carotid artery (LICA) and right internal carotid artery (RICA) were scanned from multiple angles and sections to observe the plaque situation in the carotid artery. After completion, the other side was examined to ensure the integrity of the examination. The blood flow was measured by color Doppler flow imaging, and the average value was taken after 3 consecutive measurements. Intimal thickness and hemodynamic indexes (PSV, EDV, RI) of common carotid artery and internal and external carotid artery were recorded and printed by another physician. The blood flow velocity parameter values of normal people's total carotid artery and internal carotid artery are shown in Table 1 (Brott *et al.* 2013; AbuRahma *et al.* 2011).

Definition

(1) Hypertension: Taking antihypertensive drugs or systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg (Judd & Calhoun 2014).
(2) Diabetes: Plasma glucose concentration ≥11.1 mmol/L at any time; fasting plasma glucose (FPG) ≥7.0 mmol/L or oral glucose tolerance test (OGTT) ≥11.1 mmol/L for 2 hours (Alberti & Zimmet 1998).
(3) Smoking: Smokers who have smoked continuously or cumulatively for 6 months or more in their life (Qasim *et al.* 2019).

Tab. 1. Parameters of blood flow velocity in normal carotid artery and internal carotid artery

	PSV (cm/s)	EDV (cm/s)	RI
CCA	91.30±20.70	27.10±6.40	0.70±0.005
ICA	67.70±14.30	27.30±6.40	0.59±0.06

Tab. 2. Clinical features of patients with different carotid plaque location

Variable	Left (n=186)	Right (n=188)	Both (n=2468)	None (n=1602)	F/χ^2	*p*
Age (year)	63.97±8.86	64.54±9.49	64.40±11.34	57.42±11.50[abc]	3.773	<0.001
BMI (kg/m^2)	24.03±3.60	23.88±3.18	24.27±5.62	24.36±3.46	0.684	0.562
Gender, male (%)	90(48.39)	94(50.00)	1275(51.62)	749(46.67)[c]	9.674	0.022
CHD (%)	16(8.60)	21(11.17)	324(13.12)	102(6.36)[bc]	48.490	<0.001
Hypertension (%)	130(69.89)	143(76.06)	1597(64.66)[b]	894(55.70)[abc]	55.167	<0.001
Dyslipidemia (%)	64(34.41)	54(28.72)	630(25.51)[a]	570(35.51)[c]	48.913	<0.001
Diabetes (%)	86(46.24)	89(47.34)	1122(45.43)	702(43.74)	1.736	0.629
Smoking (%)	69(37.10)	74(39.36)	793(32.11)[b]	488(30.40)[b]	8.791	0.032
Alcohol (%)	65(34.95)	66(35.11)	620(25.14)[ab]	441(27.55)[ab]	16.793	0.001

Note: CHD coronary heart disease. The letter a indicates comparison with the left group, $p < 0.05$; the letter b indicates comparison with right group, $p < 0.05$; the letter c indicates comparison with both group; $p < 0.05$.

Tab. 3. Comparison of hemodynamic indexes among the four groups

Variable	Left (n=186)	Right (n=188)	Both (n=2468)	None (n=1602)	F	*p*
RCCA PSV	61.08±16.070	58.28±16.16	63.21±22.69[b]	64.12±18.38[b]	5.225	0.001
RCCA EDV	16.96±5.58	16.10±5.39	17.29±7.53[b]	18.45±6.18[abc]	13.267	<0.001
RICA PSV	52.86±35.43	50.79±20.61	53.00±25.43	50.41±15.86[c]	4.442	0.004
LCCA PSV	63.90±17.20	61.29±17.58	65.92±20.84[b]	67.08±19.35[ab]	5.704	0.001
LCCA EDV	18.47±5.92	17.52±6.42	18.51±7.53	20.37±7.13[abc]	25.094	<0.001
LICA PSV	51.22±17.54	48.13±15.95	53.27±20.73[b]	51.01±18.56[c]	7.200	<0.001
RCCA RI	0.72±0.06	0.72±0.06	0.72±0.06	0.71±0.06[abc]	16.389	<0.001
RICA RI	0.62±0.06	0.62±0.07	0.63±0.08	0.61±0.07[ac]	23.046	<0.001
LCCA RI	0.71±0.06	0.71±0.07	0.72±0.07	0.70±0.06[abc]	38.590	<0.001
RCCA S/D	3.75±0.80	3.80±1.00	3.85±1.04	3.63±0.88[bc]	18.455	<0.001
RICA S/D	2.89±2.07	2.714±0.61	2.84±1.06	2.64±0.52[ac]	16.030	<0.001
LCCA S/D	3.60±0.81	3.709±1.00	3.77±1.12[a]	3.44±0.86[abc]	34.101	<0.001
LICA S/D	2.68±0.48	2.690±0.62	2.78±1.08	2.61±0.69[c]	12.243	<0.001

Note: the letter a indicates comparison with the left group, $p < 0.05$; the letter b indicates comparison with right group, $p < 0.05$; the letter c indicates comparison with both group; $p < 0.05$.

(4) Alcohol: It was defined as having at least 50 ml of alcohol daily and at least five times a week (Lancaster & Stead 2017).
(5) Carotid artery disease: Plaques are focal structures encroaching into the arterial lumen of at least 0.5 mm or 50% of the surrounding intima-media thickness (IMT) value, or demonstrates a thickness >1.5 mm as measured from the intima-lumen interface to the media-adventitia interface (Homburg *et al.* 2010).
(6) Carotid plaque location: Subjects were divided into four groups according to cervical plaque location: LEFT group, RIGHT group, BOTH group and NONE group. LEFT was defined as plaque only in the left internal carotid artery, common carotid artery, and sinus detected by Doppler ultrasound. Plaque detected only in the right internal carotid artery, common carotid artery, and sinus was defined as RIGHT group. The plaque detected in both internal carotid artery, common carotid artery and sinus was defined as BOTH group. NONE group was defined as no plaque detected in both internal carotid artery, common carotid artery and sinus.

Method

Continuous variables are represented by mean and standard deviation and categorical variables by percentage. Differences in demographic characteristics, laboratory indicators and hemodynamic characteristics were analyzed by analysis of variance and Chi-square test. Multiple logistic regression was used to analyze

Tab. 4. Colinear diagnosis of hemodynamic

Variable	β	S.E.	t	p	Tolerance	VIF
intercept	3.449	0.116	29.761	<0.001		
LCCA S/D	-0.016	0.017	-0.945	0.345	0.367	2.723
RCCA S/D	-0.010	0.026	-0.382	0.703	0.185	5.395
RICA S/D	-0.030	0.014	-2.143	0.032	0.635	1.574
LICA S/D	-0.013	0.012	-1.013	0.311	0.882	1.134
RCCA RI	0.010	0.026	0.404	0.686	0.174	5.737
RICA RI	-0.018	0.015	-1.232	0.218	0.544	1.837
LCCA RI	-0.050	0.019	-2.62	0.009	0.325	3.081
LICA RI	0.014	0.011	1.288	0.198	0.999	1.001

the relationship between carotid plaque location and hemodynamics. Plaque location is selected as the independent variable, hemodynamic indexes as dependents variables, and age, gender, CHD, hypertension, diabetes, dyslipidemia, smoking and alcohol were included in the model as adjustment factors. The relationship between the ratio of PSV and EDV (S/D) of carotid artery and age was tested using generalized smoothing splines, and the knot locations was generated automatically in generalized additive models with R package Mixed Generalized additive models Computation Vehicle (MGCV), and the nodes are used as the basis for age stratification. All p values were two-tailed, with a significance level of 0.05.

RESULTS

Clinical characteristics of different carotid plaque position

The basic characteristics of participants are shown in Table 2. The average age of the subjects was 61.88±11.72 years, 49.6% were male, and 63.95% had carotid plaque. There were significant differences in age, sex, CHD, hypertension, dyslipidemia, alcohol and smoking among four carotid plaque location groups ($p < 0.05$).

Comparison of hemodynamic indexes

The characteristics of hemodynamic indexes are shown in Table 3. There were statistically significant differences in RCCA RI, LCCA RI and LCCA S/D between LEFT and NONE, RIGHT and NONE, and BOTH and NONE. There were statistically significant differences between LEFT and NONE and between BOTH and NONE for RICA RI and RICA S/D. There were statistically significant differences in RCCA S/D between RIGHT and NONE, and between BOTH and NONE. There was significant difference between LICA S/D and LICA S/D.

Relationship between hemodynamics and carotid plaque location

The analysis results of relationship between hemodynamics and carotid plaque location are shown in

Tab. 5. Relationship between carotid plaque and hemodynamics

	Location	Variable	Unadjusted				Adjusted[a]			
			β	S.E.	p	OR(95%CI)	β	S.E.	p	OR(95%CI)
None	Left	RICA S/D	0.366	0.124	0.003	1.442(1.131,1.840)	0.448	0.135	0.001	1.564(1.202,2.036)
	Right	LCCA S/D	0.219	0.112	0.05	1.245(1.001,1.550)	0.212	0.125	0.091	1.236(0.967,1.581)
	Both	LCCA S/D	0.197	0.081	0.016	1.217(1.038,1.428)	0.181	0.083	0.029	1.199(1.019,1.410)
		RICA S/D	0.308	0.116	0.008	1.361(1.085,1.708)	0.383	0.127	0.003	1.467(1.144,1.881)
		RICA RI	-0.031	0.072	0.667	0.970(0.842,1.116)	-0.182	0.080	0.022	0.833(0.713,0.974)
Right	Left	RCCA S/D	0.301	0.259	0.246	1.351(0.813,2.246)	0.38	0.102	0.019	1.463(1.065,2.008)
	Both	LCCA S/D	0.599	0.183	0.001	1.820(1.272,2.606)	0.534	0.204	0.009	1.706(1.144,2.543)
		RICA S/D	0.537	0.24	0.017	1.773(1.107,2.841)	0.747	0.186	0.001	2.111(1.465,3.042)

Note: compared with none group.95% CI 95% confidence interval. a Adjusted for age, gender, BMI. CHD, hypertension, diabetes, dyslipidemia, smoking and alcohol.

Tab. 6. Association between carotid plaque location and hemodynamics in different age groups

		Location	Variable	Unadjusted				Adjusted[a]			
				β	**S.E.**	**p**	**OR(95%CI)**	**β**	**S.E.**	**p**	**OR(95%CI)**
≤52year	None	Left	LCCA S/D	-0.939	0.465	0.043	0.391(0.157,0.972)	-0.901	0.492	0.067	0.406(0.155,1.066)
		Both	RCCA S/D	0.388	0.220	0.077	1.474(0.958,2.267	0.445	0.227	0.050	1.561(1.001,2.434)
			RICA S/D	0.600	0.269	0.026	1.822(1.076,3.086)	0.557	0.279	0.046	1.745(1.011,3.013)
			RCCA RI	-0.308	0.171	0.071	0.735(0.525,1.027	-0.348	0.178	0.050	0.706(0.498,1.000)
	Right	Left	LCCA RI	-0.094	0.164	0.564	0.910(0.660,1.54)	-0.743	0.347	0.032	0.476(0.241,0.938)
>52year	None	Left	RICA S/D	0.336	0.138	0.015	1.400(1.068,1.835)	0.354	0.147	0.016	1.425(1.069,1.899)
		Right	LCCA S/D	0.436	0.171	0.011	1.546(1.105,2.163)	0.446	0.188	0.018	1.562(1.080,2.258)
		Both	LCCA S/D	0.290	0.100	0.004	1.336(1.097,1.626)	0.322	0.105	0.002	1.379(1.123,1.695)
			RICA S/D	0.277	0.131	0.034	1.319(1.021,1.705)	0.294	0.140	0.035	1.342(1.020,1.764)
	Right	Left	RICA S/D	-0.224	0.114	0.049	0.800(0.640,0.999)	-0.567	0.223	0.011	0.567(0.367,0.878)
			RCCA S/D	-0.060	0.008	0.001	0.942(0.926,0.958)	-0.386	0.174	0.027	0.680(0.483,0.957)

Note: compared with none group. a Adjusted for age, gender, BMI. CHD, hypertension, diabetes, dyslipidemia, smoking and alcohol.

Table 5. The Variance Inflation Factor (VIF) of hemodynamic indexes were all less than 10, and there was no collinearity between them, thus hemodynamic indexes all be entered in the regression model (Table 4). Results showed that RICA S/D was significant higher in LEFT group than in NONE group (OR=1.564, 95%CI: 1.202-2.036). RICA RI, LCCA S/D, and RICA S/D in BOTH group were 0.833 times (95%CI: 0.713-0.974), 1.199 times (95%CI: 1.019-1.410), and 1.467 times (95%CI: 1.144-1.881) higher than NONE group, respectively. RCCA S/D on the LEFT group was 1.463 times (95%CI: 1.065~2.008) higher than RIGHT group, LCCA S/D and RICA S/D on BOTH group were 1.706 times (95%CI: 1.144~2.543) higher than RIGHT group and 2.111 times (95%CI: 1.465 ~ 3.042) higher than RIGHT group, respectively.

Association between carotid plaque location and hemodynamics in different age groups

Figure 1-8 shows the relationship between hemorheological indicators and age. After adjusting for gender, BMI, CHD, hypertension, diabetes, dyslipidemia, smoking and alcohol, the curve trend of the relationship between hemorheology indexes and age changed at 52 years old. This suggests that age (52 years) may be an important adjustment factor. Therefore, we stratified the relationship between hemorheological indicators and plaque location by age 52 years. Table 6 shows that after age stratification and adjustment for gender, BMI, CHD, hypertension, diabetes, dyslipidemia, smoking and alcohol, in group younger than 52, RCCA S/D (OR=1.561, 95%CI: 1.001-2.434), RICA S/D in BOTH group were significant higher than NONE group (OR=1.745, 95%CI: 1.011-3.013), RCCA RI (OR=0.706, 95%CI: 0.498-1.000) in BOTH group were significant lower than NONE group. LCCA RI on the LEFT group was 0.476 times (95%CI: 0.241~0.938) higher than RIGHT group. In group older than 52, RICA S/D (OR=1.425, 95%CI: 1.069-1.899) in LEFT group were significantly higher than NONE group. LCCA S/D (OR=1.562, 95%CI: 1.080-2.258) in the RIGHT group was significantly higher than NONE group. The LCCA S/D and RICA S/D levels in BOTH group were 1.379 (95%CI: 1.123-1.695) and 1.342 (95%CI: 1.020-1.764) times higher than those in the NONE group, respectively. RICA S/D and RCCA S/D on LEFT group were 0.567 times (95%CI: 0.367~0.878) higher than RIGHT group and 0.680 times (95%CI: 0.483 ~ 0.957) higher than RIGHT group, respectively.

DISCUSSION

In the process of carotid plaque formation, carotid plaque also has asymmetry, for instance, the formation of both carotid artery plaque is uncertain, it only presents as plaque on one side of the carotid artery (Touboul *et al.* 2012; Cai Y *et al.* 2021; Spacek *et al.* 2018). Previous studies have found significant correlation between blood flow and carotid plaque formation before and after carotid artery bifurcation (Hoi *et al.* 2010; Palaiodimou *et al.* 2021). In this study, we further explored the relationship between the location of carotid plaque and the hemodynamic indexes by detecting blood flow velocity and plaque location, and the results of this study would further understand

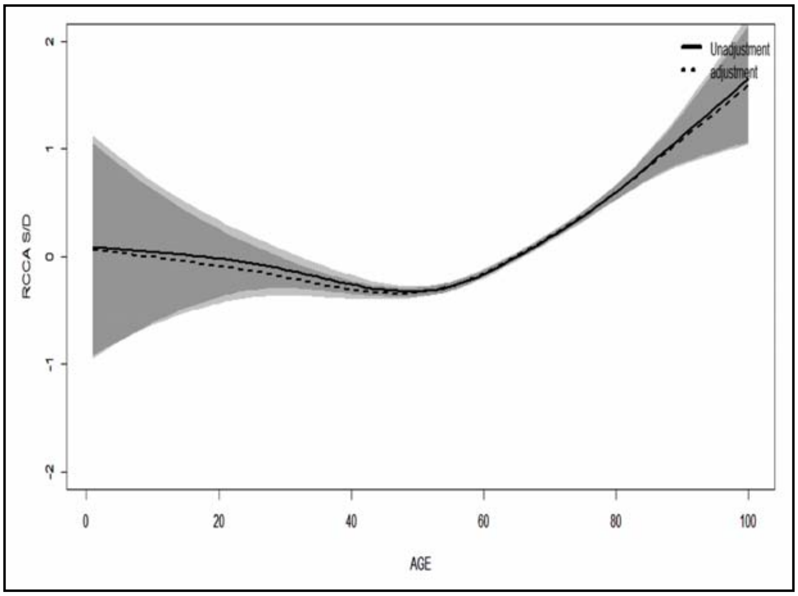


Fig. 1. Generalized smoothing splines for RCCA S/D and AGE. Horizontal coordinates represent diferent ages, while vertical coordinates represent residuals of RCCA S/D. Solid line: no adjustment; dashed line: adjusted for gander, BMI, CHD, HBP, diabetes mellitus, dyslipidemia, smoking and alcohol. Shaded area shows the 95% confdence interval.

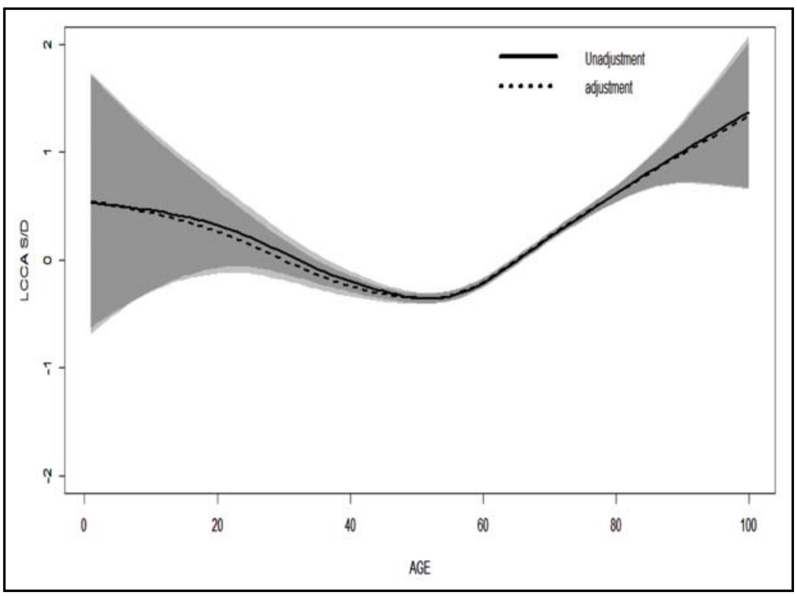


Fig. 2. Generalized smoothing splines for LCCA S/D and AGE. Horizontal coordinates represent diferent ages, while vertical coordinates represent residuals of LCCA S/D. Solid line: no adjustment; dashed line: adjusted for gander, BMI, CHD, HBP, diabetes mellitus, dyslipidemia, smoking and alcohol. Shaded area shows the 95% confdence interval.

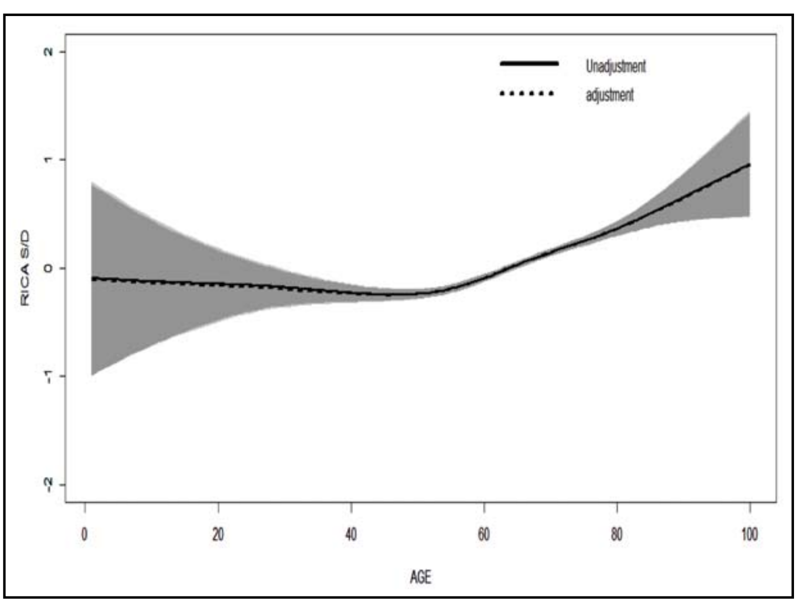


Fig. 3. Generalized smoothing splines for RICA S/D and AGE. Horizontal coordinates represent diferent ages, while vertical coordinates represent residuals of RICA S/D. Solid line: no adjustment; dashed line: adjusted for gander, BMI, CHD, HBP, diabetes mellitus, dyslipidemia, smoking and alcohol. Shaded area shows the 95% confdence interval.

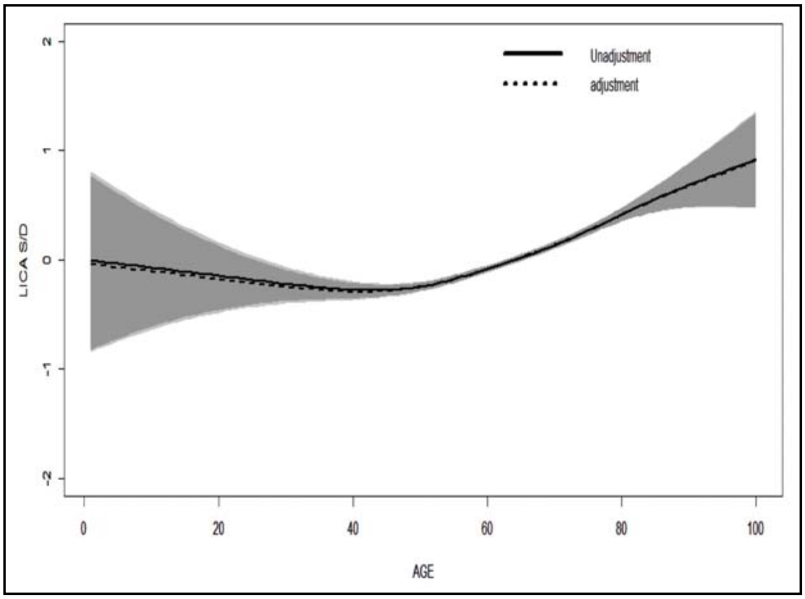


Fig. 4. Generalized smoothing splines for LICA S/D and AGE. Horizontal coordinates represent diferent ages, while vertical coordinates represent residuals of LICA S/D. Solid line: no adjustment; dashed line: adjusted for gander, BMI, CHD, HBP, diabetes mellitus, dyslipidemia, smoking and alcohol. Shaded area shows the 95% confdence interval.

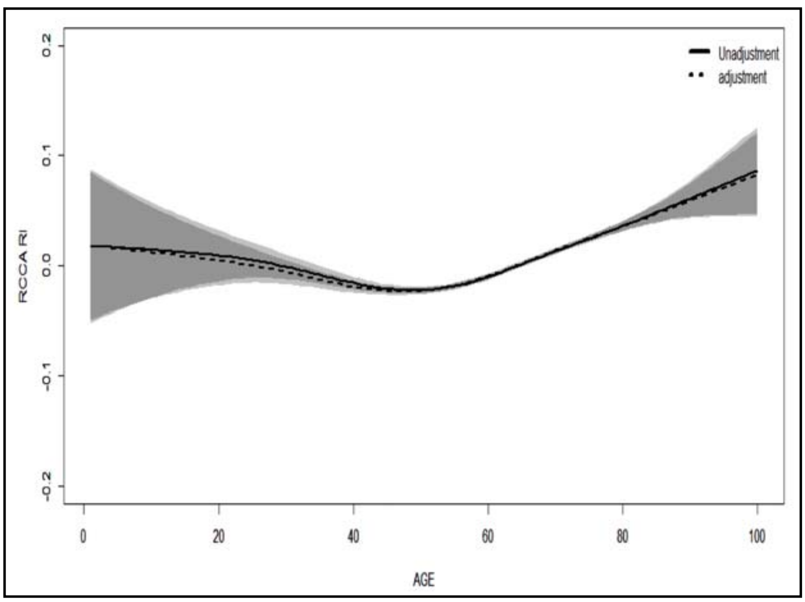


Fig. 5. Generalized smoothing splines for RCCA RI and AGE. Horizontal coordinates represent diferent ages, while vertical coordinates represent residuals of RCCA RI. Solid line: no adjustment; dashed line: adjusted for gander, BMI, CHD, HBP, diabetes mellitus, dyslipidemia, smoking and alcohol. Shaded area shows the 95% confdence interval.

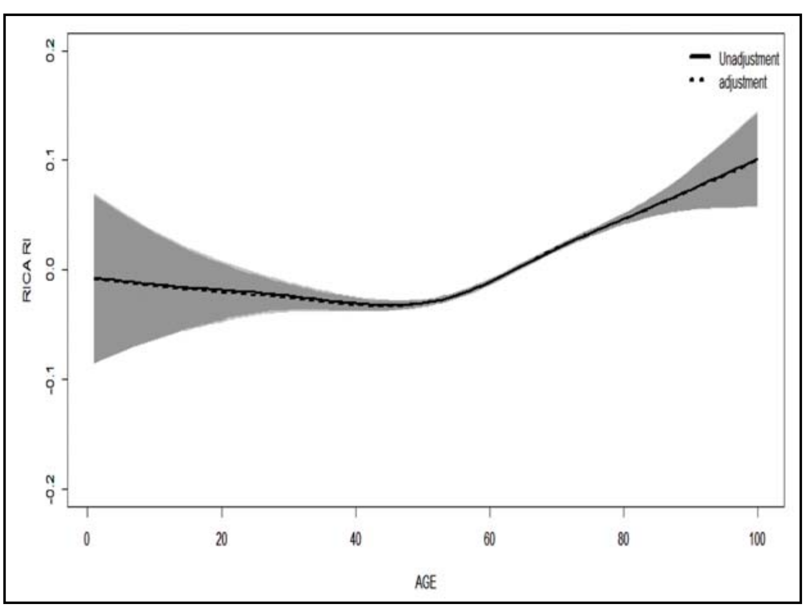


Fig. 6. Generalized smoothing splines for RICA RI and AGE. Horizontal coordinates represent diferent ages, while vertical coordinates represent residuals of RICA RI. Solid line: no adjustment; dashed line: adjusted for gander, BMI, CHD, HBP, diabetes mellitus, dyslipidemia, smoking and alcohol. Shaded area shows the 95% confdence interval.

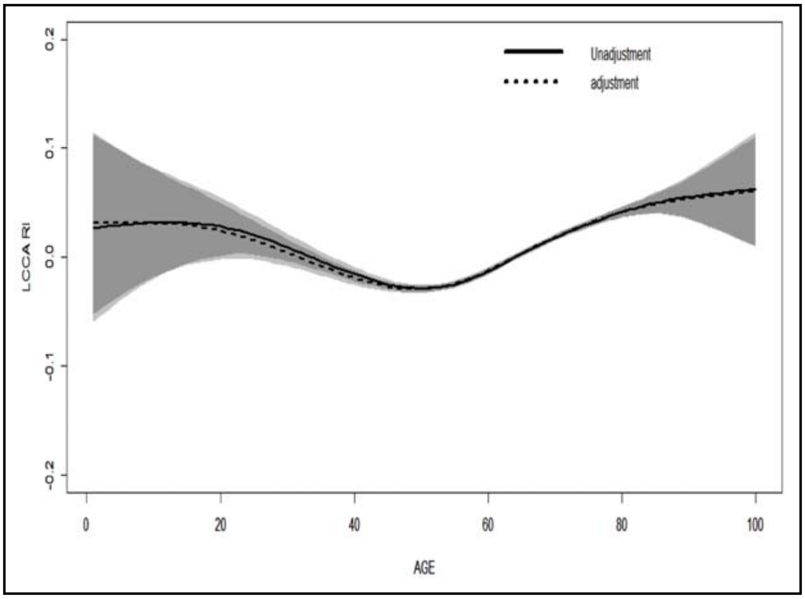


Fig. 7. Generalized smoothing splines for LCCA RI and AGE. Horizontal coordinates represent diferent ages, while vertical coordinates represent residuals of LCCA RI. Solid line: no adjustment; dashed line: adjusted for gander, BMI, CHD, HBP, diabetes mellitus, dyslipidemia, smoking and alcohol. Shaded area shows the 95% confdence interval.

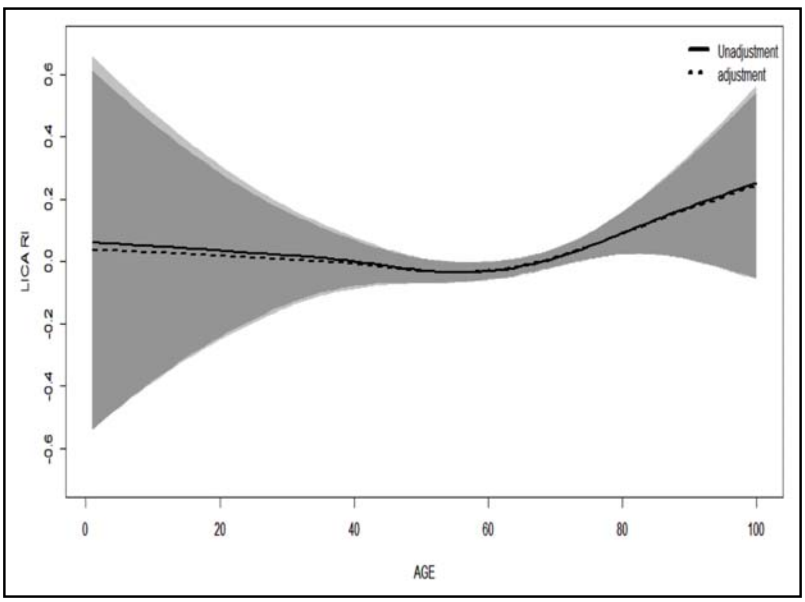


Fig. 8. Generalized smoothing splines for LICA RI and AGE. Horizontal coordinates represent diferent ages, while vertical coordinates represent residuals of LICA RI. Solid line: no adjustment; dashed line: adjusted for gander, BMI, CHD, HBP, diabetes mellitus, dyslipidemia, smoking and alcohol. Shaded area shows the 95% confdence interval.

the influence of carotid hemodynamics on carotid plaque which could be objectively judged deeply (Bir & Kelley 2022; Ahmadpour-B M, *et al.* 2021).

The results of this study revealed that S/D and RI of common carotid artery and internal carotid artery had an impact on plaque location. The ratio of PSV to EDV was used as an indicator of carotid blood flow velocity (Zarrinkoob *et al.* 2019; Filipovic *et al.* 2013). RICA S/D is a high risk factor for left side plaque. LCCA S/D, RICA S/D is a risk factor for both plaques, and RICA RI is a protective factor for both plaques. The carotid system is a entirety in which slowing down of blood flow on one side inevitably leads to increased blood flow on the other side (Ciccone *et al.* 2013). In the study of ZHAO *et al.* atherosclerotic lesions were found on the contralateral side after ligation of one side of the carotid artery in mice, indicating that the change of blood flow in one side of the carotid artery will affect the contralateral blood flow state, which is in line with the results of this study (Zhao *et al.* 2021). The increase of blood flow velocity will cause blood to damage blood vessels, resulting in increased friction of the blood vessels. Concurrently, cholesterol and lipid deposits in the blood promote the formation of plaque (Marrocco-Trischitta *et al.* 2020). The left carotid artery originates from the aortic arch, which acts to lower blood pressure (Costa *et al.* 2021; Rajput & Zeltser 2023). The aortic arch immediately adjusts its vascular pressure when blood flow is abnormal in the left carotid artery, which does not necessarily lead to plaque on the right side. But when the blood flow of both carotid arteries is abnormal, it has exceeded the adjustment range of the aortic arch, that is, plaque formation.

In this study we confirmed that age is an important factor in atherosclerosis. There are 76.58% participants in this study were over 52 years old, when age ≤52 years, the blood velocity of the right cervical and internal carotid arteries slowed down, resulting in a large number of both plaques. The possible reason is that 66.9% subjects under the age of 52 have hypertension, and hypertension is a high-risk factor for carotid plaque. The blood pressure of bilateral carotid arteries is already high because of hypertension. When the blood flow of one carotid artery is abnormal, the contralateral side can no longer compensate for the blood flow. At this point, blood flow in the left carotid artery increases and vascular pressure exceeds the regulatory domain of the aortic arch, preferentially causing intimal injury on this side and leading to plaque formation. There may also be damage to the intima on the right side but not yet plaque formation due to the chronic progression of atherosclerosis. In group older than 52, as age increase, the aortic arch's regulatory capacity is correspondingly reduced. Blood flow on one side increases as blood flow on the other side decreases, possibly accelerates plaque formation. When blood flow is abnormal on both sides, plaques are more likely to form on both sides.

CONCLUSION

In conclusion, we found that carotid artery plaque location was correlated with hemodynamics at different age groups. In people younger than 52 years of age, left-sided plaque formation is associated with increased left-sided blood flow, and both-sided carotid plaque formation is strongly associated with increased right-sided carotid blood flow. In people older than 52, abnormal blood flow on one side is more likely to plaques on the opposite side. Carotid hemodynamics is a significant factor in assessing the location of carotid plaque, which may help clinicians make a diagnosis of the location of carotid plaque. At the same time, it provides the basis for the prevention and treatment of plaque.

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AUTHOR CONTRIBUTIONS

YFW was involved in data management, formal analysis, supervision, and project management. XR participated in the conceptualization of professional terms, data management, formal analysis, software installation and drafted the manuscript. MFJ and HW participated in data management, formal analysis, and questionnaire design. YMZ and YHF was responsible for methodology selection and software use. FS, LC and JH was responsible for methodology selection and data collection. Grace Tavengana was involved in review. All authors read and approved the final manuscript.

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AVAILABILITY OF DATA AND MATERIALS

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

DECLARATIONS

Ethics approval and consent to participate

All protocols are carried out in accordance with relevant guidelines and regulations. Ethical approval was received from the Medical Ethics Committee of Maanshan People's Hospital. This study was based on data from Ultrasonic Department at Maanshan People's Hospital in Anhui, China. This study has obtained the participants' written informed consent.

Consent for publication

Not applicable.

Conflict of interest

The authors declare that they have no competing interests.

Data Availability statements

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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